Where No Genome Has Gone Before: Star Trek and Genetic Medicine at the Advent of Gene Therapy

Where No Genome Has Gone Before:

Star Trek and Genetic Medicine at the Advent of Gene Therapy.

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Abstract

The development and adoption of gene therapy as a new therapeutic modality represents a fundamentally new approach to treating diseases by directly modifying human genetic material. No longer the speculations of visionary scientists and science fiction authors, gene therapy makes the genetic engineering of humans a reality in the early 21st century. This MLA thesis identifies and describe the ways that the science fiction franchise *Star Trek* has portrayed the speculative potential of genetic medicine within the context of emerging real-world applications of gene therapies. This analysis illustrates how *Star Trek* episodes from 1966 through 2005 have anticipated and predicted the potential consequences of gene therapy and provides a framework for understanding and navigating the social and cultural challenges of genetic engineering technologies.

Author's Biographical Sketch

Jarrod Trainque is a biotechnology marketing professional with over a decade of experience working in rare genetic diseases. He has worked full-time for Genzyme Corporation, Sanofi, and most recently, Sarepta Therapeutics. In these roles, he developed marketing strategies and campaigns that increase awareness and treatment of rare genetic diseases. He also is an avid collector of science fiction. He graduated from Boston University with a B.S. in Communication.

Dedication

This work is dedicated to the many men, women, and children who have suffered from the irrational cruelty of genetic diseases, and to the doctors and scientists who work on their behalf. I hope that one day gene therapies may be used to deliver a sort of genetic justice to the genetically disadvantaged, and that human genetic engineering is used for the good of humankind.

Acknowledgments

The completion of this project would not have happened if not for the inspiration and support of my wife, Annie. You accompanied me on long stretches of this voyage into uncharted space, joined me in watching hundreds of *Star Trek* episodes, and accidentally became somewhat of a Trekkie in the process. Your encouragement and support are much appreciated.

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Chapter I.

Introduction

Within the last half-century, the pace of scientific advancement has steadily accelerated, resulting in new tools and techniques offering potentially transformative applications to the practice of medicine. Among the many medical and scientific breakthroughs of the late 20th and early 21st century, it has been suggested that genetic engineering may be the among the most powerful and far-reaching new medical development, with potential significance on par with the invention of antibiotics or immunization.[1]

Not all speculations on the benefits of this emerging technology, however, are completely optimistic. The new abilities that genetic engineering technologies make possible introduce new moral, ethical, legal, and public-policy-related challenges for which limited relevant frameworks for understanding and evaluation exist.[2] A recent announcement on the genetic engineering of humans has been met with outcry and controversy within the international scientific community.[3] Public anxieties about human cloning, designer babies, human-animal hybrids, and other perceived risks of genetic engineering may help to popularize an understanding of this technology based more on

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[1] B Pomidor and A Pomidor,"Essay 'With Great Power…' The relevance of science fiction to the practice and progress of medicine." Accessed August 12, 2019. https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(06)69908-X.pdf

[2] B Pomidor and A Pomidor, "Essay 'With Great Power…'

[3] Jing-Ru Li, Simon Walker, Jing-Bao Nie, and Xin-Qing Zhang, "Experiments That Led to the First Gene-Edited Babies: the Ethical Failings and the Urgent Need for Better Governance." *Journal of Zhejiang University*-SCIENCE B 20, no. 1 (2019): 32–38. https://doi.org/10.1631/jzus.b1800624.

imagination and fear than on scientific fact. And while society copes with the Brave New World thrust upon it, controversial scientific and medical research continues to proceed,[4] seemingly independent of public understanding or approval

Research Problem

In 2018, A publication in the journal Science announced that "Gene Therapy Comes of Age."[5] Within this context, I propose that now, at the advent of commercially successful gene therapy, we should seek to consider where this technology could and should take humanity, how it might shape culture, what potential pitfalls and challenges it may raise, and what considerations are needed to guide the use of this technology. Questions like these live comfortably within the realm of science fiction. For this thesis I investigated depictions of genetic medicine and its cultural implications in works of science fiction, specifically within the *Star Trek* universe.

This thesis project describes the speculative potential of genetic medicine portrayed in *Star Trek* (1966 through 2005) within the context of emerging real-world applications of gene therapies, answering the following questions:

1. How has *Star Trek* portrayed gene therapy and genetic medicine? Science fiction has long been used as a mechanism for predicting and commenting on the impact of potential future technology on modern society and culture through a distanced and

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[4] Karen Weintraub, "Despite Controversy, Human Studies of CRISPR Move Forward in the U.S." *Scientific American*, August 13, 2019. https://www.scientificamerican.com/article/despite-controversy-human-studies-of-crispr-move-forward-in-the-u-s/.

[5] Cynthia E. Dunbar, Katherine A. High, J. Keith Joung, Donald B. Kohn, Keiya Ozawa, and Michel Sadelain, "Gene Therapy Comes of Age." *Science* 359, no. 6372 (2018): 175.

detached extrapolation.[6] Is *Star Trek*'s portrayal of genetic technology a dystopian warning of technology misuse, an optimistic view of unrealized positive potential, or a mix of warnings and support? Are there themes or topics within genetic medicine (e.g., genetic enhancement, genetic determinism, medical eugenics, etc.) that are often explored within the *Star Trek* universe, and if so, what do those recurrent themes tell us about the context in which they are expressed?

2. Has *Star Trek*'s portrayal of potential applications of genetic medicine been realized by the scientific and medical research community? Science fiction often makes broad assumptions or speculations to explore early-stage technologies, often when these technologies are at their earliest stages of development. Likewise, seemingly unrelated technologies can inform one another in ways unimaginable, directing the advancement towards previously unforeseen directions.[7] Using the current state of development of genetic medicine as a baseline for evaluation, this research will seek to understand ways the past five decades of *Star Trek* has predicted the development of genetic medicine and identified its relevant concerns.

Hypothesis

It is hypothesized that depictions of genetic medicine within the *Star Trek* franchise are substantially different from the emerging practice and application of this technology. My analysis reveals that the representation of genetic medicine generally

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[6] Darko Suvin, *Metamorphoses of Science Fiction : On the Poetics and History of a Literary Genre.* New Haven: Yale University Press, 1979.
[7] Thomas S. Kuhn, *The Structure of Scientific Revolutions.* 3rd ed. Chicago, IL: University of Chicago Press, 1996.

exaggerates possibilities and potentialities, while conflating loosely connected concepts such as genetics, evolution, and gene-altering diseases. Additionally, I propose that *Star Trek*'s depiction of genetic medicine is overwhelmingly critical of this technology, emphasizing a potential for misuse and the risk of danger. Rarely does *Star Trek*'s portrayal of genetic medicine and genetic engineering cast a favorable light on the potential benefits of this technology, instead often choosing to make it the tool of the bad guy, or the source of conflict or problems. Whereas *Star Trek* has demonstrated reasonable success in predicting future technological advances in the information and communications fields, I hypothesize that predictions of genetic medicine will be shown to have been inaccurate, populated with unrealistic, impractical, and non-medically necessary applications. *Star Trek*'s portrayal of genetic medicine and gene transfer technology contrasts with the emerging reality of gene therapy as a medically valuable tool used to treat serious, life-threatening, and debilitating diseases.

Science Fiction and *Star Trek* as Source Material for Analysis

Star Trek is considered one of the most influential and culturally important science fiction media franchises in history,[8] and therefore it provides a suitable source material for analysis. Speculative ideas related to gene therapy & genetic manipulation have often been explored and addressed within the fictional *Star Trek* universe. This research seeks to leverage *Star Trek* as a shared cultural point of reference for this emerging technology and highlight the ways science fiction and reality are informed by one another.

[8] M. Keith Booker, *Star Trek: a Cultural History*. Lanham, MD: Rowman & Littlefield, 2018.

An enormous amount of *Star Trek*-related media has been created in the past five decades since *Star Trek: The Original Series* first aired on CBS television in 1966. Hundreds of novels have been set in the *Star Trek* universe,[9] as well as numerous comics, games, and other works, most of which are generally considered non-canonical.[10] My research focuses on the major canonical works of live-action film and television set in the original *Star Trek* timeline. This body of work is composed of the following:

- Television series:
    - *Star Trek: The Original Series* (1966–1969), 3 seasons (79 episodes)
    - *Star Trek: The Next Generation* (1987-1994), 7 seasons (178 episodes)
    - *Star Trek: Deep Space Nine* (1993-1999), 7 seasons (176 episodes)
    - *Star Trek: Voyager* (1995-2001), 7 seasons (172 episodes)
    - *Star Trek: Enterprise* (2001-2005), 4 seasons (98 episodes)
- Feature-length films:
    - *Star Trek: The Motion Picture* (1979), Directed by Robert Wise
    - *Star Trek II: The Wrath of Khan* (1982), Directed by Nicholas Meyer
    - *Star Trek III: The Search for Spock* (1984), Directed by Leonard Nimoy
    - *Star Trek IV: The Voyage Home* (1986), Directed by Leonard Nimoy
    - *Star Trek V: The Final Frontier* (1989), Directed by William Shatner

[9] Jeff Ayers, *Voyages of the Imagination: The Star Trek Fiction Companion.* New York: Pocket Books, 2006. ISBN 978-1-4165-0349-1.

[10] An enormous amount of unofficial *Star Trek*-related material has been created with varying degrees of internal narrative coherence and consistency. To address this, distinction is made between "canonical" and "non-canonical" material. The official *Star Trek* website defines canon as comprising the television series: *The Original Series*, *The Next Generation*, *Deep Space Nine*, *Voyager*, *Enterprise*, *Discovery*, *Picard*, and *Short Treks*, as well as the feature-length films in the franchise.

- *Star Trek VI: The Undiscovered Country* (1991), Directed by Nicholas Meyer
- *Star Trek Generations* (1994), Directed by David Carson
- *Star Trek: First Contact* (1996), Directed by Jonathan Frakes
- *Star Trek: Insurrection* (1998), Directed by Jonathan Frakes
- *Star Trek: Nemesis* (2002), Directed by Stuart Baird

For the purposes of this research I have excluded *Star Trek: The Animated Series* (1973-1974) because it is considered by many (including *Star Trek* creator Gene Roddenberry) to be non-canon.[11] I am excluding *Star Trek: Discovery*, as only two seasons are complete as of this writing, and at least one additional season is in development. Likewise, the *Star Trek: Discovery* spin-off *Star Trek: Short Treks* has only aired six episodes to date and have been excluded. The television series *Star Trek: Picard* has been announced but has not yet aired and will be excluded from my research. Lastly, the three most recent feature-length film "reboots," *Star Trek* (2009), *Star Trek Into Darkness* (2013), and *Star Trek Beyond* (2016), set in the so-called "Kelvin timeline" are excluded from my scope of research because they differ significantly from the previous films and television series in their overall treatment of scientific possibilities.

The product of this research provides a detailed description of the ways genetic medicine has been portrayed within the fictional *Star Trek* universe contextualized against the non-fictional reality of emerging genetic medicine. By highlighting, evaluating, and analyzing both the concerns and aspirational possibilities of genetic medicine as imagined by science fiction, this work may serve medical researchers,

[11] Jeff Ayers, *Voyages of the Imagination*

ethicists, and historians seeking to better understand our present though the imagining of a future, and provide a possible framework for understanding and navigating the social and cultural challenges of genetic engineering technologies.

Science Fiction and History of Medicine

Science fiction has long been used to reflect the fears and aspirations of medical science technologies. In "The Science Fiction of Medicine," H. Bruce Franklin argues that science fiction emerged simultaneously with modern Western medicine as part of the same historical process, reflecting a contradictory attitude towards medicine and disease, rooted in existential ideas of life and death.[12] Mary Shelly's novel Frankenstein tells the tale of a doctor reanimating the dead only to be killed by his creation, perhaps as a warning against the hubris of medical science.[13] Aldous Huxley's Brave New World imagines biotechnology-based reproductive technology replacing natural procreation which leads to a sort of genetically engineered class-based society.[14] The film Blade Runner (1982) explores the limits of cloning and bioengineered synthetic humans, ultimately posing the question about what it means to be human.[15] The 1997 film GATTACA imagines a near future society where genetic enhancements of strength and intelligence are available to privileged, and genetic registries are used to discriminate against individuals with a genetic predisposition to disease.[16] *Star Trek*'s ubiquitous

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[12] H. Bruce Franklin, "The Science Fiction of Medicine." Annual Bibliography of English Language and Literature (ABELL) - Unstructured, 2002, (pp. 9-22).
[13] Mary Wollstonecraft Shelley, *Frankenstein or, the Modern Prometheus.* London: Penguin, 2007.
[14] Aldous Huxley, *Brave New World: with the Essay "Brave New World Revisited"*. New York: Harper Perennial Modern Classics, 2010.
[15] *Blade Runner.* Warner Brothers, 1982.
[16] *GATTACA*. Columbia Pictures. 1997.

medical tricorder device imagines a portable handheld medical diagnostic tool able to remotely scan a body, record health measurements, and diagnosis disease almost instantaneously.

Prior scholarly work has investigated the benefit healthcare practitioners may get from reading science fiction. Pasco et al draw parallels between the work of medical practitioners and the writers of science fiction by suggesting that both are invested in imagining the possible:

> Medicine is invested in speculation; its practice is inextricable from the practice of future imagining. Using information available in real time, physicians in the clinical encounter begin the work of time travel: backward to old labs and family histories, and forward to diagnoses, prognoses and treatment plans. By imagining new cures, new discoveries and new futures for human beings in the face of illness, medicine is akin to science and speculative fiction in that it is necessarily always dissecting the art of the possible through acts of radical imagination.[17]

The authors describe the application of fictional speculation to the practice of medicine as a kind of 'visionary medicine' in which healthcare professionals can imagine a more just or freer world instead of reinforcing current power structures. Similarly, the reading of science fiction provides a way to understand our present by imagining the future.

[17] John Carlo Pasco, Camille Anderson, and Sayantani DasGupta. "Visionary Medicine: Speculative Fiction, Racial Justice and Octavia Butler's 'Bloodchild'." *Medical Humanities*. Institute of Medical Ethics, December 1, 2016. https://mh.bmj.com/content/42/4/246.

Scholars have previously used *Star Trek* as a cultural point of reference to explore topics such as medical technology,[18] medical ethics,[19] and even orthodontics,[20] but this research is the first comprehensive scholarly investigation of *Star Trek*'s depiction of medical gene therapy. This is surprising, considering Spark Therapeutics's CEO Jeff Marrazzo recently referred to Luxturna as "*Star Trek* medicine."[21] Similarly, in the context of medicine or the history of medicine, *Star Trek* is often used to frame a discussion of an emerging technology (as in "…perhaps it won't be too long before there is a real smartphone equivalent of the *Star Trek* tricorder"),[22] but little or no serious analysis is given *Star Trek*'s depiction of medical technology. This suggests an opportunity for this research to contribute meaningfully by focusing exclusively on the intersection of *Star Trek* and gene therapy as viewed through the lens of the history of science and medicine.

While there appears to be significant gaps in the literature focusing on connections between gene therapy and *Star Trek*, some scholars have used *Star Trek* as a basis for exploring other topics related to medicine and medical technologies. I will

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[18] Mark E. Lasbury, *The Realization of Star Trek Technologies: The Science, Not Fiction, behind Brain Implants, Plasma Shields, Quantum Computing, and More.* Cham: Springer, 2017.
[19] J.J. Hughes and J Lantos, "Medical ethics through the Star Trek lens." *Lit Med* 2001; 20.1: 26–38.
[20] "Star Trek Orthodontics." JCO Online. Accessed November 24, 2019. https://www.jco-online.com/archive/2014/08/461/.
[21] Jeff Marrazzo, "Modern Medicine in an Outdated World." Spark Therapeutics. Accessed November 24, 2019. https://sparktx.com/voices/modern-medicine-in-an-outdated-world/.
[22] Sancy A. Leachman and Glenn Merlino. "The Final Frontier in Cancer Diagnosis." *Nature* 542, no. 7639 (2017): 36–38. https://doi.org/10.1038/nature21492.

briefly provide some examples, in order to demonstrate the utility of using *Star Trek* as a basis for analysis.

A 2007 article in Law, Culture and Humanities entitled "Echo and Mirror: Clone Hysteria, Genetic Determinism and *Star Trek Nemesis*" uses a parallel reading of Australia's Prohibition of Human Cloning Act 2002 and the film *Star Trek: Nemesis* to investigate controversies related to human cloning.[23] *Star Trek: Nemesis* is used because it is a reflection on cloning and clone hysteria. The film explicitly addresses two types of anxieties related to human cloning which the authors identify as clone as double, and clone as artefact. Clone as double explores the cultural anxiety around an indistinguishable twin, a common fictional narrative that pits good versus evil, with the original twin threatened to be replaced by the evil twin. Clone as artefact investigates the essence of identity and consciousness, the premise being that the existence of a clone threatens the self-identity of the original. Through an analysis of these concepts as depicted in the film, the authors offer a critique that argues that prevailing attitudes of genetic determinism (the idea that genes are the source of human behavior) lies at the source of clone hysteria, and that clone hysteria, not cloning itself, is to be feared. The authors also argue that through *Star Trek: Nemesis'* commitment to genetic determinism the film directly participates in clone hysteria.

The essay "Medical Ethics through the *Star Trek* Lens" published in Literature and Medicine argues that *Star Trek* can provide a useful source material for teaching

[23] Kieran Tranter and Bronwyn Statham. "Echo and Mirror: Clone Hysteria, Genetic Determinism and Star Trek Nemesis" *SAGE Journals*. 2017. Accessed August 12, 2019. https://journals.sagepub.com/doi/abs/10.1177/1743872107081425.

medical ethics to first-year medical school students.[24] Using the 1992 *Star Trek: The Next Generation* episode "Ethics" as an example, the authors argue that moral and ethical dilemmas addressed in the context of science fiction facilitate stimulating conversation and deeper understanding of issues, better preparing the students for real-world medical practice. The example provided focuses on the ethics of medically assisted suicide and the use of an unapproved experimental treatment on humanoids. In the episode, a character is paralyzed and states a desire to die rather than live a lifetime with severe disability. One doctor refuses to comply with the patient's wishes, while another doctor advocates a high-risk, unproven and unapproved treatment, "genotronic replication." Before the episode's conclusion, students are asked to complete a writing assignment exploring the ethical dilemmas presented by the episode.

The authors cite three advantages in using *Star Trek* as a teaching tool. First, it uses an allegorical framework to present aspects of a topic from multiple perspectives. Second, the moral dilemmas are presented within a fantasy context involving familiar characters that allow students to analyze challenging moral issues without having to think of them in the abstract. Lastly, the dramatization of an ethical or moral issue allows students to simultaneously observe each of the opposing viewpoints, which encourages more emotional engagement than separately presenting each viewpoint and supporting evidence. Though it is not my intent to evaluate *Star Trek* as a teaching tool, I believe these cited advantages are applicable to my research. As the authors are already using *Star Trek* to inform the practice of medicine, this example illustrates the potential value of this research, particularly when gene therapies become available in the clinic. That is,

[24] Hughes and Lantos, "Medical ethics through the Star Trek lens".

my research could extend on this work to provide a basis for using *Star Trek* to help practitioners better understand the moral and ethical challenges of gene therapy.

A product of this research is to evaluate fictional depictions of gene therapy in *Star Trek* over the past five decades against real-world gene therapy technology and practice into the present day. Scholars and fans of *Star Trek* have done similar work, albeit with a different focus. Mark Lasbury's *The Realization of Star Trek Technologies* seeks to draw parallels between the fictional technologies portrayed in *Star Trek* and their closest real-world analogs.[25] His focus is on *Star Trek* hardware explained through the physical sciences (mechanics, chemistry, optics, quantum physics) and applied sciences (engineering and materials science), but genetic medicine remains largely unexplored. One example of gene therapy is discussed, that of optogenetics, or the controlling of a downstream cellular process through the insertion of a gene encoded a light-sensitive protein. However, this example is provided in the context of explaining a potential way of restoring vision, inspired by the sight-restoring hardware visor worn by *Star Trek*: *The Next Generation*'s blind engineer, Geordi LaForge. In this example, actual gene therapy is used to explain an imaged *Star Trek* technology, whereas my research instead focuses on depictions of gene therapy within *Star Trek*. Despite this, Lasbury's approach – that of cataloguing fictional *Star Trek* technologies and comparing against real-world equivalent technologies – provides a suitable model for my proposed research. Finally, Lasbury's work investigates many *Star Trek* technologies, including phasers, cloaking devices, replicators, deflector shields, tractor beams, universal translators, Geordi's visor,

[25] Lasbury, "The Realization of Star Trek Technologies"

transporters, and tricorders, but it highlights a knowledge gap with respect to the life sciences and gene therapy which this work addresses.

Chapter II:

The Real-World of Gene Therapies

Current State of Gene Therapy Development

In May of 2019, the United States Food and Drug Administration approved Novartis' Zolgensma (onasemnogene abeparvovex-xioi) for the treatment of spinal muscular atrophy.[26] The approval of Zolgensma made national news for being the most expensive therapy ever, with a single dose costing approximately $2 million dollars.[27] Importantly, Zolgensma is the second *in vivo* gene therapy to be FDA-approved, following Spark Therapeutics' approval of Luxturna (voretigene neparvovec-rzyl) in December of 2017 to treat a rare genetic mutation that causes blindness.[28] Like Zolgensma, Luxturna also carries an extremely high price of approximately $850,000 per dose.[29] And yet pharmaceutical pricing watchdog groups have stated that these therapies

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[26] Office of the Commissioner, U.S. Food and Drug Administration. "FDA Approves Innovative Gene Therapy to Treat Pediatric Patients with Spinal Muscular Atrophy, a Rare Disease and Leading Genetic Cause of Infant Mortality." U.S. Food and Drug Administration. FDA. Accessed November 24, 2019. https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-gene-therapy-treat-pediatric-patients-spinal-muscular-atrophy-rare-disease.

[27] "Second US Gene Therapy, Approved for Rare Muscle Disease, to Cost $2M - Page 2 of 2." Xconomy, May 24, 2019. https://xconomy.com/national/2019/05/24/second-us-gene-therapy-approved-for-rare-muscle-disease-to-cost-2m/2/

[28] Office of the Commissioner, U.S. Food and Drug Administration. "FDA Approves Novel Gene Therapy to Treat Patients with a Rare Form of Inherited Vision Loss." U.S. Food and Drug Administration. FDA. Accessed November 24, 2019. https://www.fda.gov/news-events/press-announcements/fda-approves-novel-gene-therapy-treat-patients-rare-form-inherited-vision-loss.

[29] "First U.S. Gene Therapy, Approved for Vision Loss, to Cost $850,000." *Xconomy*, January 3, 2018. https://xconomy.com/national/2018/01/03/first-u-s-gene-therapy-approved-for-vision-loss-to-cost-850000/.

fall within value-based price benchmarking ranges, highlighting the potentially transformative nature of the gene therapy modality.[30] This has driven large pharmaceutical companies to invest in gene therapy through acquisitions of smaller companies (Spark Therapeutics agreed to be acquired by Roche; Novartis' Zolgensma is the product of the acquisition of AveXis).[31] A recent article in Cell & Gene indicates continued expansion of investigational gene therapies from less than 250 assets in development in 2014 to over 600 assets by the end of 2019, with most in a pre-clinical phase.[32] This data suggests that gene therapy (and other related medical genetic technologies such as gene editing) may have the potential to one day become a relatively common approach to treating diseases.

Gene therapy differs from previous therapeutic approaches in that it uses foreign DNA to change a cells' protein-coding abilities.[33] In *in vivo* gene therapy, exogenous genetic instructions in the form of protein-coding nucleic acids are transferred into cells to restore or add to existing gene function in order to treat disease. Using a viral capsid as a vector for transduction, trillions of genome copies of DNA are injected or intravenously infused into a patient's body in a single dose. Once transduced by the cells, the newly introduced genetic material becomes available for protein translation as part of gene expression. Current technology limits the number of times a patient can be treated with

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[30] "ICER Comments on the FDA Approval of Zolgensma for the Treatment of Spinal Muscular Atrophy." ICER. Accessed August 12, 2019. https://icer-review.org/announcements/icer_comment_on_zolgensma_approval/.

[31] R Brau and P Jacquet, "Gene Therapy: Commercial Challenges and Strategic Choices." *Cell & Gene. 2019*

[32] Brau and Jacquet, "Gene Therapy…"

[33] Katherine A. High and Maria G. Roncarolo. "Gene Therapy." *New England Journal of Medicine* 381, no. 5, January 2019: 455–64. https://doi.org/10.1056/nejmra1706910.

gene therapy to just once, since antibodies formed in response to the viral vector prevent transduction using the same vector. Gene therapies may or may not be incorporated in the patient's genome, and the long-term durability of gene therapy is generally unknown.

Major Milestones in the Development of Gene Therapies

To appreciate the rate at which medical gene therapies technologies have advanced, I will briefly describe the major milestones in the history of the development of this technology.

The fundamentals of genetics were first established in 1866 when scientist Gregor Mendel described how genetic information was passed to offspring, discovered through the careful observation and breeding of thousands of pea plants.[34] Mendel's work described patterns of inheritance that distinguished between dominant and recessive traits, and provided the basis for the idea of a hereditable unit for certain characteristics.[35] In 1889 Hugo de Vries introduced the term "pangen" to describe "the smallest particle of one hereditary characteristic" in his book Intracellular Pangenesis, although this work was completed without knowledge of Mendel.[36] By 1909 the Danish botanist Wilhelm Johannsen had coined the term "gene" to describe the fundamental physical unit of heredity.[37] The following year, the location of genes on chromosomes was identified by

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[34] D Noble, "Genes and causation." *Philosophical Transactions of the Royal Society of London.* Series A, Mathematical and Physical Sciences. 366 (1878): 3001–3015. Bibcode:2008RSPTA.366.3001N. doi:10.1098/rsta.2008.0086. PMID 18559318.
[35] Noble, "Genes and causation."
[36] H. de Vries, "Intracellulare Pangenese," Verlag von Gustav Fischer, Jena, 1889. Translated in 1908 from German to English by C. Stuart Gager as Intracellular Pangenesis, Open Court Publishing Co., Chicago, 1910
[37] W Johannsen, Arvelighedslærens elementer ("The Elements of Heredity". Copenhagen, 1905). Rewritten, enlarged and translated into German as Elemente der exakten Erblichkeitslehre (Jena: Gustav Fischer, 1909;

Thomas Hunt Morgan through his work on fruit flies.[38] In 1928, British bacteriologist Frederick Griffith showed that genetic information could be transferred between bacteria.[39] By 1944, the "transforming factor" from Griffith's experiment was discovered to be something other than the protein content of chromosomes (as it was previously thought), but it would be another decade before deoxyribonucleic acid (DNA) would be identified as the molecule responsible for genetic transference. This major discovery, the double-helical description of the structure of DNA, was first described in 1953 by James Watson, Francis Crick, and Maurice Wilkins, for which they were awarded the Nobel Prize in Physiology or Medicine in 1962.[40]

In 1962, Polish oncologist Wacław Szybalski documented the first successful DNA transfer in mammalian cells.[41] In this experiment, Szybalski was able to rescue cells containing genetic defects by introducing foreign DNA.[42] He also demonstrated that the newly acquired traits of the rescued cells were inherited by daughter cells.[43] This pioneering work demonstrated a basic principle of gene therapy, i.e., that foreign DNA could be introduced to correct defective genes, and that the correction could be passed on to daughter cells.

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[38] Thomas H. Morgan, "Sex Limited Inheritance in Drosophila." *Science* (1910): 120–2. http://www.jstor.org/stable/pdf/1635471.pdf

[39] F Griffith, "The Significance of Pneumococcal Types." *J. Hyg*. 1928. (Lond) 27, 113–159.

[40] The Nobel Prize in Physiology or Medicine 1962. Nobel Prize Site for Nobel Prize in Physiology or Medicine 1962. https://www.nobelprize.org/prizes/medicine/1962/summary/

[41] E.H Szybalska and W. Szybalski, "Genetics of human cell line. IV. DNA-mediated heritable transformation of a biochemical trait." *Proc. Natl. Acad. Sci.* 1962. U. S. A. 48, 2026–2034.

[42] Szybalska and Szybalski, "Genetics of human cell line."

[43] Szybalska and Szybalski, "Genetics of human cell line."

In 1961 Howard Temin discovered that chicken cells that had been infected with the Rous sarcoma virus would inherit stable gene mutations.[44] Since this virus is an RNA virus, it meant that genetic information contained in RNA could be transferred to DNA through stable chromosomal insertion. With this knowledge, Edward Tatum suggested in 1966 that viruses might be used to transfer genes into target cells, and that this might be used to treat genetic defects, although the technology needed to remove the pathogenic properties of viruses and insert therapeutic genes inside the viral capsid did not yet exist.[45]

This meant that the earliest attempts to transfer genes needed to rely on wild-type viruses encoding genes of interest. In 1973, Rogers et al. performed the first human gene therapy trial using the Shope papilloma virus in an attempt to treat two girls suffering from a urea cycle disorder.[46] It was thought that the wild-type Shope papilloma virus contained a gene for encoding arginine, and that the gene could be transferred to the patients through contact with the virus. The trial failed to show positive results, and it was later shown through gene sequencing that the Shope papilloma virus does not in fact contain the encoding instructions for arginine.

Advances in recombinant DNA technology in the mid-1970's and throughout the 1980's made it possible to modify cells to contain genetic material from multiple sources. In 1980, Martin Cline attempted to transfect two β-thalassemia patients with recombinant

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[44] H. M. Temin, "Mixed infection with two types of Rous sarcoma virus." *Virology* 13, 158–163. 1961.
[45] E. L. Tatum, "Molecular biology, nucleic acids, and the future of medicine." *Perspect. Biol. Med*. 10, 19–32. 1966.
[46] S Rogers, A Lowenthal, H.G. Terheggen, and J.P. Columbo, "Induction of arginase activity with the Shope papilloma virus in tissue culture cells from an argininemic patient." *J. Exp. Med.* 137, 1091–1096. 1973.

bone marrow containing the β-globin gene, with the hope that the hematopoietic stem cells carrying the gene would successfully encode β-globin and alleviate disease. This attempt at recombinant gene transfer was unsuccessful, but much of the details remain unpublished due to a controversy around Clines' attempt, as he was denied permission from his institutional review board for the proposed treatment, but proceeded nonetheless.[47]

The first FDA-approved therapeutic gene transfer in humans occurred in 1990. Michael R. Blaese treated two children suffering from a severe immunodeficiency using genetically modified copies of the patients' white blood cells. The patients' donor cells had been genetically modified ex vivo to include the gene that encoded the deficient protein.[48] The effect of the therapy showed mixed results, as only one patient showed a significant response, it was temporary, and the patient had been receiving concomitant therapy at the time she received the gene therapy. Throughout the 1990's other gene therapy trials were initiated for several diseases, and although therapeutic results were lower than expected, gene therapy remained promising because these trials demonstrated that efficient *in vivo* gene transfer was possible.[49,50]

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[47] Ernest Beutler, "The Cline Affair." *Molecular Therapy*. Cell Press, December 14, 2016. https://www.sciencedirect.com/science/article/pii/S1525001601904861?via=ihub.
[48] R.M. Blaese, K.W. Culver, A.D. Miller, C.S. Carter, T. Fleisher, M. Clerici, G. Shearer, L. Chang, Y. Chiang, P. Tolstoshev, J.J. Greenblatt, S.A. Rosenberg, H. Klein, M. Berger, C.A. Mullen, W.J. Ramsey, L. Muul, R.A. Morgan, and W.F. Anderson, "T lymphocyte-directed gene therapy for ADA-SCID: initial trial results after 4 years." *Science* 270, 475–480. 1995.
[49] C. Bordignon, L.D. Notarangelo, N. Nobili, G. Ferrari, G. Casorati, P. Panina, E. Mazzolari, D. Maggioni, C. Rossi, P. Servida, A.G. Ugazio, F. Mavilio, "Gene therapy in peripheral blood lymphocytes and bone marrow for ADA-immunodeficient patients." *Science* 270, 470–475. 1995.
[50] A.M. Puumalainen, M. Vapalahti, R.S. Agrawal, M. Kossila, J. Laukkanen, P. Lehtolainen, H. Viita, L. Paljarvi, R. Vanninen, S. Yla-Herttuala, "Beta-galactosidase

Developments in gene therapy hit a major setback in 1999 when 18-year old Jesse Gelsinger died after participating in a gene therapy trial.[51] Gelsinger received a high dose of *in vivo* gene therapy that used adenovirus as the gene delivery vector, which caused a serious immune response and led to multi-organ failure and death within days of receiving treatment. In response, the United States regulatory authorities stopped several gene therapy trials, effectively slowing down gene therapy development out of fear of safety-related issues. Further setbacks occurred in 2002 and 2003 when four patients in France who received gene therapy to treat severe immunodeficiency developed leukemia.[52,53]

In 2003, the China State Food and Drug Administration approved the world's first gene therapy, Gendicine, an adenovirus vector-based therapy for the treatment of head and neck cancer.[54,55] Cells transduced with Gendicine express protein p53, a tumor suppressor activated by cellular stress. Gendicine is delivered by minimally invasive injection. Although its approval was met with controversy,[56] over a decade of use has

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gene transfer to human malignant glioma in vivo using replication-deficient retroviruses and adenoviruses." *Hum. Gene Ther*. 9, 1769–1774. 1998.

[51] S.G. Stolberg, "The biotech death of Jesse Gelsinger." *N.Y.Times Mag*. 136-140, 149-150. 1999

[52] S. Hacein-Bey-Abina et al, "Insertional oncogenesis in 4 patients after retrovirus-mediated gene therapy of SCID-X1." *Journal of Clinical Investigation*, 2008; DOI: 10.1172/JCI35700

[53] Journal of Clinical Investigation. "Why Gene Therapy Caused Leukemia In Some 'Boy In The Bubble Syndrome' Patients." *ScienceDaily*. www.sciencedaily.com/releases/2008/08/080807175438.htm (accessed November 6, 2019).

[54] *Hum Gene Ther*. 2018 Feb;29(2):160-179. doi: 10.1089/hum.2017.218.

[55] S. Pearson, H. Jia H, K. Kandachi, "China approves first gene therapy". *Nature Biotechnology*. (2004) 22: 3–4. doi:10.1038/nbt0104-3. PMID 14704685.

[56] H. Jia, "Controversial Chinese gene-therapy drug entering unfamiliar territory." *Nat Rev Drug Discov* **5,** 269–270 (2006) doi:10.1038/nrd2017

shown it to be both safe and effective, with no serious adverse events reported except for vector-associated transient fever which occurs in approximately half of all patents and lasts a few hours.[57] In 2008, the U.S. Food and Drug Administration refused to approve a similar p53 tumor suppression therapy, Advexin, based on an incomplete Biologics License Application.[58] The Chinese regulatory agency approved a second gene therapy in 2005. Called Oncorine, this therapy is indicated for the treatment of nasopharyngeal cancer when used in combination with chemotherapy.[59]

In 2012, The European Medicines Agency (EMA) approved Glybera (alipogene tiparvovec) for treatment of reverse lipoprotein lipase deficiency, marking the first gene therapy approved outside of China.[60] Once the most expensive drug in the world,[61] the drug was removed after only two years on the European market following bankruptcy of its manufacturer and later acquisition. Its current rights-owner, uniQure, has no plans to sell the drug,[62] and to date only 31 people have ever been treated with Glybera.[63]

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[57] *Hum Gene Ther*. 2018 Feb;29(2):160-179. doi: 10.1089/hum.2017.218.
[58] "Introgen Receives Notice Advexin U.S. BLA Not Sufficiently Complete to File." Drugs.com. Accessed November 24, 2019. https://www.drugs.com/nda/advexin_080902.html.
[59] Jerry Guo and Hao Xin. "Chinese Gene Therapy. Splicing out the West?" *Science* (New York, N.Y.). U.S. National Library of Medicine, November 24, 2006. https://www.ncbi.nlm.nih.gov/pubmed/17124300.
[60] "Glybera." European Medicines Agency, September 25, 2018. https://www.ema.europa.eu/en/medicines/human/EPAR/glybera.
[61] Kelly Crowe, "The Million-Dollar Drug." CBCnews. CBC/Radio Canada, November 17, 2018. https://newsinteractives.cbc.ca/longform/glybera.
[62] Evelyn Warner, "Goodbye Glybera! The World's First Gene Therapy Will Be Withdrawn." Labiotech.eu, September 2, 2019. https://www.labiotech.eu/medical/uniqure-glybera-marketing-withdrawn/.
[63] Crowe, "The Million-Dollar Drug."

In 2015, both the FDA and the EMA approved Imlygic (talimogene laherparepvec) for the treatment of melanoma.[64] Imlygic consists of a genetically modified herpes virus, with two genes removed and an additional gene added that modifies cancer cells to make them susceptible to viral infection and triggers an immune response.[65] Although the treatment approach uses a genetically modified virus to attack cancer cells, it should be noted that the approach does not transfer genes in order to induce endogenous protein expression.

The first *ex vivo* gene therapy, Strimvelis, was approved by the EMA in 2016 for the treatment of an extremely rare condition called Severe Combined Immunodeficiency due to Adenosine Deaminase deficiency (ADA-SCID).[66] ADA-SCID is the same disease Michael R. Blaese sought to treat in the first FDA-approved gene therapy trial in 1990, although Strimvelis uses genetically modified hematopoietic stem cells (HSCs) instead of white blood cells.[67] Strimvelis therapy is intended for use by patients for whom a compatible HSC donor is unavailable. As such, it is customized to each individual patient; Stem cells are extracted from the donor, purified, genetically modified to encode for adenosine deaminase, and reintroduced into the donor.

In 2017, the FDA approved two chimeric antigen receptor (CAR) T cell therapies, Kymriah and Yescarta, which use genetically modified autologous T cells to target and

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[64] "FDA Approves IMLYGIC™ (Talimogene Laherparepvec) As First Oncolytic Viral Therapy In The US." Amgen.com. Accessed November 24, 2019. https://www.amgen.com/media/news-releases/2015/10/fda-approves-imlygic-talimogene-laherparepvec-as-first-oncolytic-viral-therapy-in-the-us/.
[65] Imlygic (talimogene laherparvepvec) [package insert] Thousand Oaks, CA: Amgen Inc.; 2015
[66] "Strimvelis." European Medicines Agency, July 31, 2019. https://www.ema.europa.eu/en/medicines/human/EPAR/strimvelis.
[67] Blaese et al., "T lymphocyte-directed gene therapy…".

attack cancer cells expressing a specific cell surface antigen. Kymriah is indicated for use in certain pediatric and young adult patients with a form of acute lymphoblastic leukemia (ALL), whereas Yescarta is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy. Yescarta and Kymriah can be considered both a type of cell therapy and a type of gene therapy, as they use a patient's own autologous cultured T lymphocytes to attack cancerous cells, and those cells are genetically modified with a new gene to increase their potency.

The first *in vivo* virally-delivered FDA-approved gene therapy in the United States was Luxturna (voretigene neparvovec-rzyl), approved in 2017 for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy, a condition that can result in complete blindness. Luxturna is notable as it is the first gene therapy approved for an inherited genetic disease. Patients with retinal dystrophy experience a progressive loss of vision due to retinal cells being unable to encode a protein involved in the conversion of light into electrical signals capable of being processed and understood by the brain. By injecting AAV2-based viral vectors containing the RPE65 gene directly into the eye, retina cells are transduced with genetic instructions for encoding the protein RPE65 which halts disease progression and potentially restores sight. Treatment with Luxturna results in the creation of episomal DNA in the cell's nucleus that does not integrate into the patient's DNA. This means that despite its use in treating an inherited genetic condition, the defective gene may still be passed onto offspring.

The latest gene therapy to be FDA-approved, Zolgensma, approved in in 2019 for the treatment of spinal muscular atrophy (SMA), is perhaps the most promising example

of gene therapy's curative potential. SMA is a serious inherited condition characterized by muscle weakness, difficulty breathing, inability to move limbs, and difficulty feeding. The signs and symptoms of SMA usually appear before the age of 6 months, and without treatment it is often fatal within a year. Zolgensma therapy consists of a vector-delivered copy of the SMN1 gene that codes for a protein needed by motor neurons to function, delivered by a one-time intravenous infusion. In the first clinical studies, Zolgensma was shown to improve motor function overall and prevent the need for mechanical ventilation. Twenty-four months following treatment, all 15 clinical trial participants were still alive, none required ventilatory assistance, and most had shown a measurable improvement in motor function.[68] These promising results have motivated researchers and manufacturer Novartis to pursue expanded use of Zolgensma. One experimental approach involves direct injection of Zolgensma into the spine, rather than infused intravenously. As of October 2019, the FDA has since put a halt on further testing of Zolgensma delivery by spinal injection, citing safety concerns in animal models related to the development of cellular inflammation and potential nerve damage.[69]

"Gene Therapy": A Working Definition

Research on the history of scientific developments that led to gene therapies suggests that for purposes of this project I will need to be selective about what constitutes

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[68] "Gene Transfer Clinical Trial for Spinal Muscular Atrophy Type 1 - Study Results." Study Results - ClinicalTrials.gov. Accessed November 24, 2019. https://clinicaltrials.gov/ct2/show/results/NCT02122952?term=AVXS-101.

[69] John Miller, "Novartis' Zolgensma Study Halted by FDA amid Safety Questions." *Reuters*. Thomson Reuters, October 30, 2019. https://www.reuters.com/article/us-novartis-gene-therapy/novartis-zolgensma-study-halted-by-fda-amid-safety-questions-idUSKBN1X90XS.

gene therapy, particularly when analyzing hypothetical technologies in the context of science fiction. It is worth noting that many of the previously described milestones in gene therapy use different therapeutic approaches, and that the term "gene therapy" groups together several different technologies and techniques with important differences. This makes more specific definitions and delineations of differences within the category of gene therapy necessary.

For the purposes of this research, I have considered "gene therapy" as generally referring to any change in a person's genetic coding abilities through directed gene transfer, especially to treat or cure disease. The change need not be permanent, nor must it modify one's genome. The source of the new genetic material may be wild-type (as in the Shope papilloma gene transfer experiments by Rogers et al.) or recombinant-based (as in Cline's experiment on β-thalassemia). I have considered therapies that rely on genetically modified cells to be gene therapies, whereas cell therapies that use unmodified donor cells (e.g. transplantation of non-genetically engineered hematopoietic stem cells) would not be considered gene therapy for the purposes of my research (despite the presence of donor cells with different genes). Likewise, fictional depictions of interspecies hybrids, organ/tissue donors, or symbiotic species have been considered out of scope *unless* there was a particular emphasis or reliance on genetic engineering or directed gene transfer.

Current investigational applications of gene therapy focus on serious and debilitating diseases such as cancer and rare inherited diseases. But the therapeutic approach – modifying protein expression through genetic modification – is theoretically applicable well beyond the treatment of serious diseases. It is these speculative potential

uses of gene therapy and gene transfer technologies that have been explored within science fiction, and it is helpful to understand how an expanded use of gene therapy may serve as a compelling subject to the sci-fi writer.

Possible expanded uses of gene therapy include treating less serious disease or addressing genetic risk factors. Gene therapy could theoretically be used to correct conditions like nearsightedness or obesity, which may negatively affect one's quality of life but are currently manageable. Similarly, gene therapy could be used as a preventative approach by correcting for a genetic predisposition to disease. For example, gene therapy might one day be used to correct mutations in the BRCA1 gene that would otherwise increase a woman's risk of developing breast cancer. And while breast cancer is a serious and potentially life-threatening diagnosis, the mere presence of BRCA1 at birth does not condemn one to a future cancer diagnosis. If the technology existed, it is not difficult to imagine a public desire to use gene therapies for these kinds of purposes, and to see the ethical slippery slope presented.

Just as cosmetic surgery and other elective medical procedures have found their place within society, one might imagine readily available gene therapy applications that exceed medical necessity. For example, it is theoretically possible to use gene therapy to make cosmetic modifications to physical features. Societal attitudes or personal tastes may one day give individuals new choices to make about their height, eye color, skin color, predisposition to baldness, breast size, degree of athleticism, or other physical features that might be modified by gene transfer technology. Parents may consider performance-improving modifications as opportunities to provide their offspring with perceived physical advantages, offering their children lives devoid of the challenges or

insecurities they themselves faced. Such a practice threatens to usher in a new social and cultural divide based on modified genetics. And with general societal acceptance of elective medical procedures (such as LASIK, facelifts, liposuction, total knee replacement, etc.), it is reasonable to suspect that attitudes towards "elective" genetic therapy may one day be normalized as well.

Gene therapy promises the ability to modify one's physical makeup, but there also exists the possibility that gene therapy may be used to unlock previously unseen potentials of human intelligence. Scientists have noted that approximately 99% of chimpanzee DNA is identical to that of human beings,[70] and yet humans are uniquely possessing a capacity for reason and self-awareness. If these differences in cognition among related species can be attributed to differences in genetic makeup, one might imagine using directed gene additions to change aspects of intelligence and behavior, such as eliminating mental illness, curing psychological addictions, reducing anti-social behavior, and enhancing human intelligence. This last prospect, of using gene therapy to rapidly enhance human intelligence, introduces various profound bioethical considerations related to class, access to technologies, human potential, social equality, and the ultimate destiny of humanity. Indeed, this idea of a genetically enhanced super-human is extensively explored throughout the *Star Trek* universe, as my research reveals.

Feature enhancement through gene transfer may be used to overcome physiological or cognitive limitations of the human body. Bioethicist Lee Silver has suggested that through gene transfer, the human body could be augmented with new

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[70] "Initial Sequence of the Chimpanzee Genome and Comparison with the Human Genome." Nature News. *Nature Publishing Group*. Accessed November 24, 2019. https://www.nature.com/articles/nature04072.

features and abilities "borrowed" from other species.[71] From this perspective, anything observed in nature (and encoded in DNA) becomes a possibility. For example, humans could be modified with genes taken from nocturnal animals that allow them to see into the infrared or ultraviolet ranges, improving their vision at night. Or perhaps humans could be given the ability to use echolocation, as bats do, to visualize space using sound. Using nature as inspiration and gene transfer as the tool, humans might one day be granted fantastic abilities to emit light much in the way fireflies do, photosynthesize their own energy, or generate electricity like eels. Extrapolating further, Silver imagines a new organ not inspired by nature but designed for purpose, such as a radio wave-sensing organ capable of detecting and processing electromagnetic wavelengths beyond the visible light spectrum.[72]

These speculative ideas of "enhanced humans" may sound wildly imaginative and best left to science fiction, but they exist as real possibilities in the era of gene therapy. One can draw clear parallels between the previously suggested genetic enhancements and Luxturna, for example. Luxturna's mechanism of action consists of gene delivery to retinal cells responsible for the biological conversion of a photon of light into an electrical signal (phototransduction). One could rewrite this only slightly and imagine a therapy where a gene responsible for phototransduction of infrared light is delivered to retinal cells, enabling enhanced vision. In this case, the distinction between possible and plausible appears to be a mere technicality, limited only by time, effort, and will. In discussing these technologies, Silver uses the terms "genetic engineering," "genetic

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[71] Lee M. Silver, *Remaking Eden: How Genetic Engineering and Cloning Will Transform the American Family.* New York: Harper Perennial, 2007. 278-279
[72] Silver, *Remaking Eden*

enhancement," and "gene therapy," interchangeably, citing that "… in every case, genetic engineering will be genetic enhancement – whether it's to give children something that other children receive naturally, or to give them something entirely new."[73]

Not surprisingly, Silver's Remaking Eden closes with a fictional epilogue set in the years 2350-2997 A.D. The epilogue serves to speculate on the long-term effects of cloning, genetic engineering, and reproductive technologies on the destiny of the human race, using common tropes of science fiction: a technology-based class struggle, inter-species hybrids, interplanetary colonization, corporate technology run amok, science vs. religion, and the next-level evolution of mankind to a state of super-consciousness. It's a familiar extrapolation, reminiscent of countless science fiction tales attempting to illustrate where humanity might be headed.

[73] Silver, *Remaking Eden*

Chapter III

Genetic Medicine in the *Star Trek* Universe

To identify instances of genetic medicine in the *Star Trek* universe, programmatic keyword-based searches for terms relevant to genetics in general were performed against a corpus of 605 scripts spanning from 1966 to 2005 from *Star Trek: The Original Series* (1966-1969), *Star Trek: The Next Generation* (1987-1994), *Star Trek: Deep Space Nine* (1992-1999), *Star Trek: Voyager* (1994-2001), *Star Trek: Enterprise* (2001-2005), and the first 10 feature length Star Trek films. Target keywords consisted of the following:

- "DNA"
- "genetic"
- "gene"
- "gene therapy"
- "genetic medicine"
- "coding"
- "base pair"
- "nucleotide"

Care was taken to address irrelevant keyword matches and false positives. Negative keywords were applied to screen out results were not relevant to gene therapy. For example, "Roddenberry" was excluded from searches for "gene") to avoid returning results simply based on inclusion of the name of *Star Trek*'s creator, Gene Roddenberry. Similarly, the keyword "coding" could refer to computing or communication, and so

results not referring specifically to coding of genetic material were manually excluded. Matches containing the keyword "DNA" but unrelated to genetic medicine (e.g., "kidnap," "ordnance," etc.) were similarly removed from the search results. Lastly, the keyword "genetic" used a broad matching approach which allowed for positive matching of words that contain "genetic," such as "geneticist," "genetics," "genetically," etc., all of which were worthy of review.

A total of one hundred and ninety works were identified via keyword analysis as containing at least one of the target terms. Each was then individually reviewed and categorized by general theme and whether it referenced genetic medicine as previously defined, i.e., a change in genetic coding abilities via the directed transfer of genetic material for the purpose of treating or curing disease. Of the one hundred and ninety works that matched one or more of the genetics-related keyword matches, thirty-two works (17%) were identified as having a specific reference to genetic medicine. One hundred and fifty-eight works (83% of the search results) were screened out for not specifically referencing genetic medicine (That is, they contained a positive hit for one of the target keywords, but upon closer investigation were determined to be related to something other than genetic medicine. See *Appendix 1. Themes Identified Following Keyword Analysis* for a complete list of other topics identified following keyword analysis.)

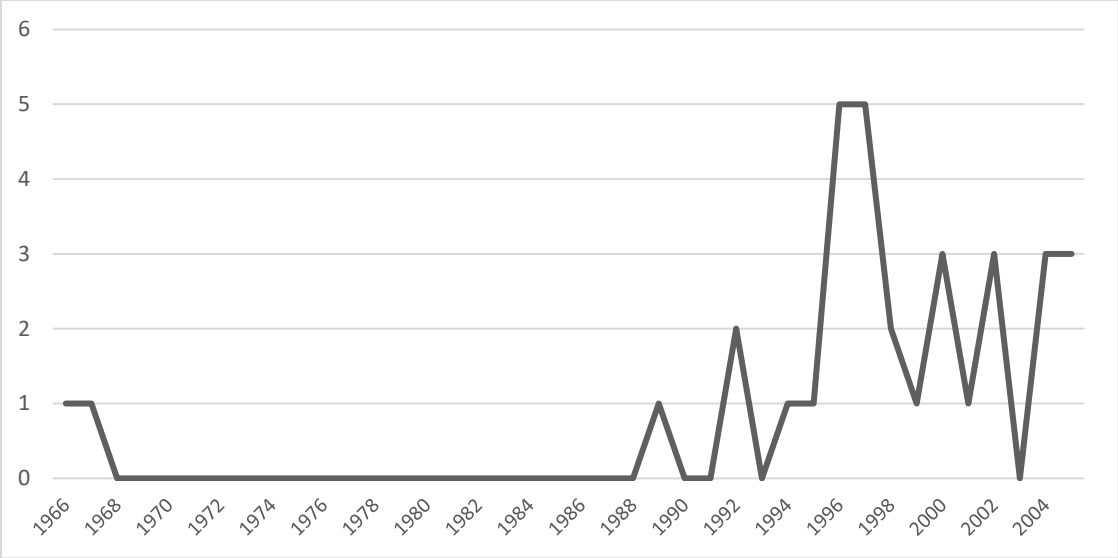
The low hit rate is likely due to frequent usage of keywords that in and of themselves are not specific enough to be indicative of genetic medicine. Keyword searches included rather broad terms such as "dna," "gene," and "genetic," and because of the low barrier constituting a positive hit, many works needed to be manually reviewed,

and a large number screened out. This keyword-sensitive approach was designed to cast a wide net to ensure that keyword searching was sufficiently aggressive to catch most (if not all) genetic medicine references. Note any references that may exist that do not use any of the target keywords or variants thereof would not have been caught.

Frequency and Distribution of Genetic Medicine References

References to genetic medicine in *Star Trek* begin as early as the first season in 1966 with the episode "Miri" from *Star Trek: The Original Series*. Genetic medicine next appears the following year in the season two episode "Space Seed" (1967). A nearly two decade hiatus separates *Star Trek: The Original Series* from *Star Trek: The Next Generation*, but genetic medicine is again reintroduced in season two's episode, "Unnatural Selection" (1989). Three additional references are made through the remainder of *Star Trek: The Next Generation*'s seven season run ("The Masterpiece Society" and "Rascals" in 1992, "Genesis" in 1994). Beginning in 1996, the number of references to genetic medicine increases to five in that year alone, all contributions from *Star Trek: Voyager*. The following year also sees five references to genetic medicine, with each following year averaging just over two references per year through 2005. See Figure1. below.

Fig 1. Genetic Medicine References in *Star Trek,* by Year



Gene Therapy Themes and Issues

My research reveals recurrent themes and issues in the way genetic medicine is depicted and described within the *Star Trek* universe. The five primary themes are as follows:

- Genetic enhancement, life-prolongation, and eugenics (via selective breeding)
- Genetic medicine as treatment for inherited conditions
- Genetic medicine as treatment for infectious or pathogenic gene-altering diseases
- Genetic medicine as treatment for non-inherited genetic disorders and accidents
- Genetic medicine as advanced technology
- Ethics of genetic medicine and evolution

In the following I will discuss these themes and the context of their appearance in more detail.

Genetic Enhancement, Life-Prolongation, and Eugenics

The most common application of genetic medicine in the *Star Trek* universe involves genetic enhancement, or the altering of one's genetic material to make the recipient stronger, smarter, more resistant to disease, etc. The scientific mechanism for genetic enhancement is rarely described in sufficient detail, but it is reasonable to assume that genetic enhancement implies directed genetic modification. However, genetic enhancement doesn't cure disease per se, unless one embraces the broadest definition of disease to include natural inabilities or disadvantages. Regardless, genetic enhancement plays such a large role in *Star Trek*'s treatment of genetic engineering of humans that it's worth reviewing in detail, even if it's not strictly genetic medicine by modern medical standards. That is to say, so much of science fiction's treatment of the subject tends towards the enhancement end of the spectrum that it deserves recognition as a broader (and often more extreme) variation of genetic medicine.

The foundation for *Star Trek*'s attitudes towards genetic medicine and genetic engineering are first laid out in the 1967 *Star Trek: The Original Series* episode "Space Seed." This episode describes the discovery of a vessel containing genetically enhanced superhumans in suspended animation from the Earth's distant past. Upon discovery of the vessel, we learn that the last World War on earth was called the Eugenics War:

> SPOCK: No such vessel listed. Records of that period are fragmentary, however. The mid-1990s was the era of your last so-called World War.
>
> MCCOY: The Eugenics Wars.

> SPOCK: Of course. Your attempt to improve the race through selective breeding.
>
> MCCOY: Now, wait a minute. Not our attempt, Mister Spock. A group of ambitious scientists. I'm sure you know the type. Devoted to logic, completely unemotional.

Although it refers to selective breeding and not gene transfer, the ideas and concerns of 1960's science fiction are applicable, i.e., that science might one day make it possible to improve upon mankind's natural state through controlled genetics, and that it would result in undesirable consequences.

Later in the episode, we are introduced to Khan Noonien Singh, a former dictator and genetically enhanced superhuman who sought to use his mental and physical advantages to seize power during 20th century earth:

> KIRK: Forgive my curiosity, Mister Khan, but my officers are anxious to know more about your extraordinary journey.
>
> SPOCK: And how you managed to keep it out of the history books.
>
> KHAN: Adventure, Captain. Adventure. There was little else left on Earth.
>
> SPOCK: There was the war to end tyranny. Many considered that a noble effort.
>
> KHAN: Tyranny, sir? Or an attempt to unify humanity?
>
> SPOCK: Unify, sir? Like a team of animals under one whip?
>
> KHAN: I know something of those years. Remember, it was a time of great dreams, of great aspiration.
>
> SPOCK: Under dozens of petty dictatorships.
>
> KHAN: One man would have ruled eventually. As Rome under Caesar. Think of its accomplishments.
>
> SPOCK: Then your sympathies were with…
>
> KHAN: You are an excellent tactician, Captain. You let your second in command attack while you sit and watch for weakness.

> KIRK: You have a tendency to express ideas in military terms, Mister Khan. This is a social occasion.
>
> KHAN: It has been said that social occasions are only warfare concealed. Many prefer it more honest, more open.
>
> KIRK: You fled. Why? Were you afraid?
>
> KHAN: I've never been afraid.
>
> KIRK: But you left at the very time mankind needed courage.
>
> KHAN: We offered the world order!
>
> KIRK: We?

It is subsequently established that Khan and his genetically enhanced companions left Earth in order to establish a new world comprised of superior humans, and that the Eugenics Wars led to a Federation ban on human genetic engineering, included genetic engineering to treat illness.

The ban on genetic engineering did not stop all from practicing it. In *Star Trek: Enterprise*, a prequel series to *Star Trek: The Original Series*, we are introduced to Dr. Arik Soong, a brilliant scientist who objects to the Federation ban on genetic engineering on moral grounds. In the *Star Trek: Enterprise* episode "Borderland" (2004), an imprisoned Dr. Soong makes the case for genetic medicine to an interrogating Captain Archer:

> ARCHER: (looks at a paper)
>
> SOONG: Go ahead. They're DNA sequences. That one is for a modification of the human T-cell. It would render Sharat Syndrome a thing of the past. That one increases the visual spectrum by five percent. Of course, none of this will ever be tested. They clear out my room every few months. I'm told it all gets vaporised.
>
> ARCHER: Why invest so much time and energy on things no one will ever use?

> SOONG: How can a supposedly intelligent species reject technology that would enhance ability, relieve suffering?
>
> ARCHER: Genetic engineering has caused a lot of suffering.
>
> SOONG: So did splitting the atom, yet the first ships to colonise the solar system were nuclear-powered. But you're not here to discuss that.

Later in the same episode, it is revealed that Dr. Soong is not only an advocate of genetic engineering but is personally responsible for a group of genetically enhanced rogue individuals called Augments, created from embryo remnants from the Eugenics Wars.

It should be noted that by 2004, when *Star Trek: Enterprise* "Borderland" first aired, the Eugenics Wars back-story explicitly described genetically enhanced individuals as the product of genetic engineering of embryos and not selective breeding as in *Star Trek: The Original Series* "Space Seed" (1968), reflecting a shifting understanding of the potentialities of genetic science. Directed gene transfer, however, is not directly described by this point, despite some high-profile real-world gene transfer attempts (e.g., Jesse Gelsinger's death in 1999).

The Federation ban on genetic medicine and the fallout of the Eugenics War is addressed once more within the *Star Trek: Enterprise* series. In the episode "Cold Station 12" (2004), Captain Archer and the Denobulan doctor Phlox debate the risks and benefits of genetic engineering technology:

> PHLOX: You might be interested to know Smike's become quite the student of Earth history. He's been reading up on the Eugenics Wars.
>
> ARCHER: I doubt Soong gave him the whole story.
>
> PHLOX: I'm quite familiar with the subject myself. Human intellect and human instinct were out of sync. So many people were killed.

ARCHER: The official number was thirty million. Some historians say it was closer to thirty five.

PHLOX: I can understand why Earth banned genetic engineering.

ARCHER: (sitting) What do you know about Clarke's syndrome?

PHLOX: It's a degenerative brain disorder that afflicts humans.

ARCHER: My father died of it when I was twelve.

PHLOX: I'm sorry.

ARCHER: He had frequent pain, hallucinations, he talked to people who weren't there. Often couldn't recognize me or my mother. The last two years of his life

PHLOX: And you were thinking if genetic engineering had been permitted

ARCHER: Maybe Soong has a point.

PHLOX: I've had time to examine his work more closely. I'm forced to admit some of it is extremely inventive. He's really quite brilliant. It's a shame such a man has to remain incarcerated.

ARCHER: He broke the law. That's why he was in prison. And that's why I'm going to make sure he goes back. Denobula perfected genetic engineering a long time ago, but you never came close to destroying yourselves.

PHLOX: Perhaps we were simply fortunate.

ARCHER: Or maybe your instincts had caught up with your intellect. Food's getting cold.

This exchange illustrates the tension created by new technologies that have both the power to heal and to destroy. Captain Archer's lament of his father's suffering portrays the 22nd century society as struggling with the desire to responsibly cure disease while also living with the historical reminder of the consequences of misuse of genetic engineering technology. These are apparently resolved at some point in the *Star Trek* timeline, although it's unclear what prompted the change. By the 24th century genetic research was permitted to correct genetic disease, but genetic enhancement would

remained banned and any individual who had been genetically enhanced would be limited in their activities (and in some cases institutionalized) to prevent a repeat of events that led to the Eugenics Wars.

Perhaps the best example of a genetically enhanced human character is that of *Star Trek: Deep Space Nine*'s Doctor Julian Bashir, a brilliant but exceedingly arrogant Starfleet physician who is revealed to be genetically enhanced in the episode "Doctor Bashir, I Presume" (1997). Interestingly, Dr. Bashir was genetically enhanced as a child using a procedure called "DNA resequencing," which implies that DNA can be modified in a living, complete organism. While not equivalent to gene transfer, this is notably different from the embryo-based genetic engineering of *Star Trek: Enterprise "Borderland"* which was released seven years later, and the selective breeding of *Star Trek: The Original Series* "Space Seed" from twenty-nine years earlier.

The revelation that Dr. Bashir was genetically enhanced as a child in violation of law provides opportunity for Star Trek to explore the ethics of corrective genetic medicine vs. genetic enhancement. As a child, a young Julian Bashir was struggling to keep up with peers physically and mentally, and it is suggested that he may have suffered from a developmental disorder. His parents, seeking to help their son, provided him with illegal DNA resequencing treatments, which cured him of his deficiencies, but also provided certain selective advantages. As Starfleet officer, though, Dr. Bashir's career requires that his enhancement be kept secret by his parents:

> RICHARD: And just so there's no misunderstanding: I give you my word that at no time in our interview with Doctor Zimmerman, will we ever mention or even hint at the fact that you were genetically enhanced as a child.

> AMSHA: Jules, you can trust us. Your father and I have kept the secret of your DNA resequencing for almost twenty-five years and we're not going to let it out now.
>
> RICHARD: But I would just add that, despite what the authorities would like us to believe, genetic engineering is nothing to be ashamed of. You're not any less human than anyone else. In fact, you're a little more.

Ultimately, Dr. Bashir's status as genetically enhanced is revealed, but it is his father who admits to wrongdoing and is sentenced to 2 years in a penal colony for seeking out genetic enhancement for his son. At a meeting to determine his fate, a Judge Advocate General Bennet of Starfleet remarks on the need for punishment, recapitulating the threat of genetic enhancement:

> BASHIR: (to Bennett) Two years? Isn't that a little harsh?
>
> BENNETT: I don't think so. Two hundred years ago, we tried to "improve" the species through DNA resequencing and what did we get for our trouble? The Eugenics Wars. For every Julian Bashir that can be created, there's a Khan Singh waiting in the wings -- a "superhuman" whose ambition and thirst for power have been enhanced along with his intellect. The law against genetic engineering provides a firewall against such men and it's my job to keep that firewall intact.
> (to Richard) I've made my offer. Do you accept?
>
> RICHARD: Yes

Society's unwillingness to accept genetic enhancement is explored in two additional *Star Trek: Deep Space Nine* episodes featuring Dr. Bashir: "Statistical Probabilities" (1997) and "Chrysalis" (1998). Both episodes feature the same cast of genetically enhanced outcasts who assist the Federation with their extraordinary abilities, guided and restrained by Dr. Bashir. These episodes explore the challenges of incorporating enhanced individuals in a society that refuses to accept them. In both episodes, genetic medicine plays little role other than providing the backstory for the genetically enhanced individuals.

An exception to the prohibition on genetic engineering is mentioned in *Star Trek: The Next Generation* "Unnatural Selection" (1989). This episode references the Darwin Genetic Research Station where genetic research is performed on children, giving them enhanced abilities. It is not stated why this is permitted and not a violation of Federation law. The enhancements given to the children include accelerated growth, telepathy, telekinesis, and an enhanced immune system.

The conflict between genetic enhancement and medically necessary genetic modification is explored in *Star Trek: Voyager* "Lineage" (2001). B'Elanna Torres, a half-human-half-Klingon member of the Voyager crew is pregnant, and the Emergency Medical Hologram (EMH) has determined through holographic extrapolation that her child will have a deviated spine due to a common Klingon genetic defect, although it is easily corrected through genetic modification. After learning this information, B'Elanna asks the EMH to delete all Klingon DNA sequences from her unborn daughter via a fetal resequencing procedure. This procedure would prevent the child from possessing the defect, as well as any Klingon features (including appearance and behavior). B'Elanna's request is met with resistance from the EMH:

> EMH: There's no valid medical reason to do what you're proposing.
>
> TORRES: I disagree.
>
> EMH: You want to delete entire DNA sequences. The genes that create redundant organs, for example.
>
> TORRES: They're superfluous.
>
> EMH: Those redundancies are there for a reason.
>
> TORRES: Does my daughter need a third lung to survive?

EMH: Strictly speaking, no. But having it may be beneficial. Some geneticists believe the extra lung evolved to give Klingons greater stamina on the battlefield.

TORRES: My daughter is not going to be a Klingon warrior.

EMH: With all due respect, you have no idea what your daughter's going to be. What if she develops an interest in athletics? Greater lung capacity would be an advantage. The point is, there's no reason to arbitrarily remove genetic traits.

TORRES: It's not arbitrary. It's preventive.

EMH: How so?

TORRES: That third lung could become diseased, couldn't it?

EMH: I suppose.

TORRES: Then what I'm suggesting is no different than removing an appendix before it becomes inflamed.

EMH: Why tamper with biological systems that evolved over eons?

TORRES: Like curvature of the spine?

EMH: If I make these changes, it'll affect her appearance.

TORRES: I'm aware of that.

EMH: Are you also aware that some of these genes influence behavior, personality?

TORRES: None of that's as important as her health.

EMH: What does Tom think about all this?

TORRES: I wanted to see what you thought first.

EMH: As you can see, I'm very dubious.

B'Elanna's motivation for removing the Klingon DNA from her child mostly personal. It is well-established that her character is uncomfortable with the Klingon aspects of her personality, and likely wishes for her daughter to avoid some of the social

difficulties she experienced. Motivations aside, her rationale for wanting to genetically modify her unborn child are worth exploring.

First, she characterizes some of the DNA sequences as redundant, and characterizes them as posing potential medical risk (e.g., curved spine, a diseased 3rd lung, and an inflamed appendix). By reframing the natural state as unnecessary and risky, she is arguing that her requested genetic modifications be interpreted as a medically necessary preventative measure. Similarly, she is arguing against preserving features that "evolved over eons" as being worth preserving. In a society that outlaws medically unnecessary genetic enhancement, but permits corrective measures, she highlights the inherent subjectivity of what is considered "medically necessary."

Later in the episode, she confronts Captain Janeway and Tom Paris (the father of the child) to ask that the EMH be ordered to perform the fetal resequencing procedure. In her exchange, she makes an equivalency argument referencing Seven of Nine, the former Borg-assimilated member of the crew, who had her cybernetic implants removed on order of the Captain:

> JANEWAY: I'm not exactly sure what you want me to do.
>
> TORRES: I want you to order the Doctor to genetically alter my child.
>
> PARIS: Do you see what I'm dealing with here?
>
> JANEWAY: What you're asking for is ethically questionable. The Doctor has reservations. Your husband is against it.
>
> TORRES: I only want to do what you did, for Seven of Nine.
>
> JANEWAY: I beg your pardon?
>
> TORRES: You had her implants removed.
>
> JANEWAY: I don't see the connection.
>
> TORRES: You altered her physiology. You changed who she was.

JANEWAY: I was acting in her best interests.

TORRES: That's all I'm doing.

PARIS: Seven was born human. The captain just helped to restore her original physiology.

TORRES: And gave her a much better life in the process.

PARIS: Our child isn't even born yet. How do you know what's going to make her life better?

TORRES: I just don't want her to start at a disadvantage.

Note that B'Elanna continues to describe the requested genetic modification as removing a disadvantage and not as selective genetic enhancement or personal preference, further blurring the lines between what is medically necessary and arbitrary. She is arguing that if the genetic modifications to correct the curved spine are allowable, and the choices made by Captain Janeway to Seven of Nine on the basis of "best interest" are permitted, then by logical extension her request to genetically resequence her unborn should also be permitted.

Unable to convince anyone of the medical necessity of the resequencing procedure, B'Elanna turns to modifying the Doctor's program so that he agrees with her:

EMH: Actually, I've changed my opinion.

PARIS: What?

EMH: The genetic alterations you've suggested are necessary.

PARIS: On what grounds?

EMH: The clash I mentioned between Klingon and human metabolism? It's more extensive than I realized.

TORRES: How extensive?

EMH: Theoretically, it could lead to complete metabolic failure.

TORRES: But you can fix it.

EMH: By eliminating most of her Klingon genetic material.

Ultimately B'Elanna's ruse is discovered and it is revealed that her desire to remove Klingon DNA from her child has little to do with medical necessity, and everything to do with a resentful relationship she held towards her human father for divorcing her Klingon mother, an event for which B'Elanna felt responsible. The conclusion --accepting the baby's DNA and genetic defect instead of performing the medically unnecessary fetal resequencing procedure-- aligns with the post-Eugenics War attitudes dominant in the *Star Trek* universe against pre-emptive or preventative genetic medicine.

Just as *Star Trek* has explored the use of genetic intervention to address limitations or enhance capabilities (physical strength, mental abilities, etc.), genetic medicine has also been used as a fictional mechanism allowing life extension beyond its current natural limits. This was first explored in the 1966 *Star Trek: The Original Series* episode "Miri," in which the Enterprise crew investigates a laboratory on what seems to be an abandoned planet:

> KIRK: (reading) Intermediate experimentation report project on life prolongation.
>
> SPOCK: Progress report, genetics section, Life Prolongation Project.
>
> RAND: So that's what it was.
>
> MCCOY: Life prolongation. Didn't have much luck, did they?

The crew later discovers that the planet is inhabited by children who experience extremely slow aging and extended lifespans.

> SPOCK: According to their life prolongation plan, what they thought they were accomplishing, a person would age only one month for every one hundred years of real time.

> RAND: One hundred years and only one month?
>
> SPOCK: Exactly, Yeoman. Evidently through some miscalculation, this virus annihilated the entire adult population in a very short period, leaving only the children.
>
> RAND: But that means these children
>
> SPOCK: Could very well be immensely old.
>
> KIRK: That would certainly answer the question of what happened to their parents.

The scientific mechanism behind the project is specifically described as a "chain reaction of viruses" meant to extend the life of human cells. When members of the crew begin to develop sores, they suspect they have been infected by the same virus used in the failed experiment. According to the children, the virus only affects adults, and once the children reach puberty, they too become subject to infection.

Much of the episode's conclusion focuses on the crew's efforts to develop a vaccine for the virus to prevent their own premature aging and death. Ultimately, a vaccine is found and provided to the children, but it is not stated whether the vaccine is itself genetic medicine, or a more traditional antibody-producing inert version of the virus. It is also not clear if vaccination eliminates the slow-aging effect experienced by the children, or if their genomes were affected or changed by the virus. Were it not for the script specifically referring to the Life Prolongation Project as part of genetics section, it would hard to classify this as genetic intervention. But it's worth noting the connection between genetic modification and viral infection, as this theme appears frequently in the Star Trek universe as I later show.

The association of old age and illness is explored in *the Star Trek: The Next Generation* episode "Too Short a Season" (1988), which tells the story of an aging,

wheelchair-bound Admiral Jameson who suffers from an incurable progressive muscle-wasting disorder called Iverson's Disease. Admiral Jameson self-medicates using an alien drug which rewrites his genetic code, making him younger, much to the surprise of his tending physician, Dr. Beverly Crusher:

> BEVERLY: His red cell count is running riot. Then there's the cellular structure of his body tissue. It's -- changing. I can't even begin on that until I see what it's changing to. His DNA is all skewed. I don't know how it's possible, but he even looks younger. And Captain... there is absolutely no sign of Iverson's Disease.
>
> PICARD: You said there is no cure for Iverson's.
>
> BEVERLY (shakes head) None we know of. Whatever else these substances are doing to his body, at least they've done that for him. But how or why, I can't say on the information I have now.

After curing himself of Iverson's Disease and regaining ambulation, Admiral Jameson continues to self-medicate into order to get younger and stronger, pushing the limits of medically necessary disease treatment into the realm of enhancement or improvement. Eventually, he falls severely ill and dies from the stress put on his body brought on by the over-consumption of the drug. His demise echoes the sentiment that DNA-modifying therapies as may have the ability to cure the previously uncurable but may also present temptations for use beyond addressing disease.

The film *Star Trek: Insurrection* (1998) also explores the potential of genetic medicine to slow the process of aging. After leaving their homeworld, the Son'a people discovered that the absence of "metaphasic radiation" leads to genetic damage which causes premature aging and undesirable changes to their appearance. It also prevents their procreation. As a result, they become obsessed with having as youthful of an appearance as possible. Their long-term goal is to return to their home planet with the

help of the Federation, but in the short-term they rely on using genetic medicine-based procedures:

> SON'A DOCTOR: Your body is producing far too many toxins... we've reached the limit of genetic manipulation...
>
> RU'AFO (member of the Son'a people): I won't need any more genetic manipulation if our Federation friends will allow us to complete this mission.

As before, this example demonstrates the dichotomy of genetic medicine as both a potential cure for a serious medical condition (widespread infertility that threatens the species' survival) and as tool to improve their aesthetic appearance. Again, the distinction between necessary and frivolous uses of genetic medicine are brought into focus, echoing ideas that there are more and less appropriate uses of genetic medicine, but also some ambiguity as to where appropriate use ends and inappropriate use begins.

Star Trek's exploration of the potentialities of genetic medicine extend beyond the prolongation of life to also include immortality itself. In the *Star Trek: Deep Space Nine* episode "In the Cards" (1997), we are briefly introduced to Dr. Elias Giger, a misunderstood (and possibly insane) physician working on ways to avoid death. He has a brief exchange with the character Weyoun, (himself the product of alien genetic engineering and cloning). Weyoun confronts Dr. Giger:

> WEYOUN: (to Giger) Which still leaves the question of what you were doing beneath my quarters.
>
> NOG: He's harmless. He's been working on a way to become...
>
> (rolls his eyes)
>
> ... immortal.
>
> But instead of sneering, Weyoun perks up at this and seems genuinely interested.

> WEYOUN: Really? I have a background in... shall we say, creative genetics. I'd be most interested in hearing your theories.
>
> GIGER: Well... it will take some time to explain, but let me ask you a simple question -- do you want to die?

Dr. Giger's approach to immortality involve the use of a "Cellular Regeneration and Entertainment Chamber" that seeks to prevent what he believes to be the ultimate cause of death, "cellular ennui":

> GIGER: So now, after fifteen years of tireless effort... after being laughed at and hounded out of the halls of the scientific establishment... after scrounging and begging for materials across half the galaxy... I have nearly completed work on this -- the Cellular Regeneration and Entertainment Chamber.
>
> JAKE : What does it do?
>
> GIGER : I'm glad you asked. It is specially designed to transmit biogenic energy on a chromoelectric wavelength and send uplifting and entertaining messages to the nuclei of every cell in your body. Spend eight hours a day in this machine... and your cells will never get bored, you'll never grow old, and most important... you will never die. That is the goal of my work: nothing less than immortality itself!

Without knowing more about what kinds of messages cells find "uplifting" and "entertaining" it's a stretch to consider this genetic medicine. Aside from his brief appearance in this episode, Dr. Giger makes no additional appearances in the *Star Trek* universe, and no additional clues are given to his methods. However, if you allow for some poetic license, it's possible to see how this might be interpreted as gene transfer. First, it's plausible that cellular transcription of novel proteins might be euphemistically referred to as cellular "entertainment." Similarly, the "messages" he refers to could consist of nucleotide-based encoding instructions, much in the same way we think of messenger RNA (mRNA) as containing "messages." Even with these generous allowances, Dr. Giger's pursuit of immortality also requires that death be redefined as a

disease state (even when caused by "natural" conditions such as old age) in order to narrowly meet our definition of genetic medicine.

Just as mortality might be viewed as a treatable condition, *Star Trek* has also explored the possibility of using genetic engineering to create a "perfect" society free of all diseases. The *Star Trek: The Next Generation* episode "The Masterpiece Society" (1992) describes the planet Moab IV, occupied by colonists who for generations have genetically engineered their society to be free of all diseases. Counselor Troi learns about the practice through an exchange with Conor, an inhabitant of Moab IV:

> TROI: There must be other unexpected events you have to deal with --an untimely death, an accident...
>
> CONOR: Our geneticists are able to screen out any congenital health risks before conception... and the population is diverse enough to maintain a genetic balance in the event of accidental death. But very little that is unexpected occurs here...

The mechanism that the geneticists "screen out" health risks is not stated specifically, but might include embryonic screening, genetic engineering of fertilized embryos (either *in vivo* or *in vitro*), genetic engineering of fetal cells *in vivo*, or the genetic modification of parental germ-line cells. It is this last possibility--that the society genetically modifies (or treats) adults to remove disease risks from their offspring by modifying the germ-line--that could be considered genetic medicine, albeit preventative genetic medicine targeting future generations.

Consistent with much of the *Star Trek* universe, "The Masterpiece Society" is highly critical of genetic engineering of humans, arguing that genetic engineering robs individuals of a certain important quality, and that diversity of experience, including handicap and disease, is more favorable to a sterile notion of "perfection." Captain Picard states his opposition to genetic engineering clearly to Counselor Troi:

> PICARD: (frowns) They've managed to turn a dubious scientific endeavor into dogma...
>
> TROI: You don't approve of genetic engineering.
>
> PICARD: It was a bad idea whose time passed long ago.
>
> TROI: They seem to have made it succeed.
>
> PICARD: They have given their humanity away to this genetic manipulation... many of the qualities they breed out – the uncertainty, the self-discovery, the unknown - those are the very qualities that make Human life worth living... at least to me. I would not like to live with the knowledge that much of my future has been written, that my boundaries have been set. Would you?

Notably, Picard's opposition doesn't address disease, disability, or entertain the medical necessity of certain genetic interventions. Instead, Picard opposes the "dogma" of genetic engineering for reasons related to predeterminism, reflecting the equally scientifically dubious idea that DNA is largely responsible for determining one's overall destiny.

Within the realm of disease and disability, the episode uses an exchange between two characters to present an argument against genetic engineering. Hannah, an inhabitant of Moab IV is forced to consider the detriments of the practice during an exchange with Geordi, a blind member of the Enterprise crew who wears assistive technology (a "VISOR") to artificially restore his eyesight.

> HANNAH: Were you always blind?
>
> Geordi reacts, realizing that she's seeing him without the VISOR on for the first time.
>
> GEORDI: Ah, I'm sorry... I probably shocked the hell outta you, didn't I...
>
> HANNAH: No...
>
> GEORDI: Let me put it on...
>
> HANNAH: Don't.

(beat)

I'm sorry. I didn't mean to embarrass you.

GEORDI: I've never been embarrassed by this, Hannah. Never. I was blind at birth. It's the way I've always been.

HANNAH: May I see it... your VISOR?

He holds it out to her and she takes it.

GEORDI: I guess if I had been conceived on your world, I wouldn't be here right now, would I?

HANNAH: No.

GEORDI: I'd've been terminated as a fertilized cell.

HANNAH: It was the wish of our founders that no one have to suffer a life with disabilities...

GEORDI: Who gave them the right to choose whether or not I should be here? Whether or not I might have something to contribute...

HANNAH: (long beat) I don't know what to say.

Note that Hannah seems to confirm that their genetic engineering practice involves terminating fertilized cells, in apparent contradiction to the statement made by Conor about genetic screening taking place prior to conception.

Regardless, the mechanism is less relevant than the ideas presented: that the practice of society-wide genetic engineering carries with it the potential to cause a certain kind of unseen harm to subsequent generations of a society. The intention to eliminate disease and suffering may appear noble and justifiable at first, but genetic engineering of offspring necessarily imposes one individual's choices on another, and introduces complex questions related to the rights and freedoms of others. This parallels Lee Silver' fears of genetic engineering technologies being *first* accepted for use in treating disease but having its use *expanded* into more ethically or morally questionable purposes.

Genetic Medicine as Treatment for Inherited Conditions

A relatively small number of examples describing the use of genetic medicine to treat inherited (hereditary) conditions exist in the *Star Trek* universe. Often, genetic engineering is used to treat infectious diseases, chronic conditions, or accidents instead of inherited genetic defects or mutations. This is perhaps surprising considering that "genetic disease" is synonymous with inherited disease and rarely associated with infectious disease or mutagenic accidents.

The *Star Trek* back-story of the Eugenics Wars states that in the late 20th century attempts to improve the human species through genetic enhancement led to bans on the use of genetic engineering. Widespread opposition and skepticism towards genetic enhancement meant that potentially useful medical uses were banned as well. That is, little distinction was made between human-improving genetic enhancement and genetic therapies for medically useful purposes – they were both treated as illegal uses of genetic engineering. Nonetheless, 22nd century scientists apparently understood how to use genetic technology, and some such as Dr. Soong advocated for its use. In the previously discussed *Star Trek: Enterprise* episode "Borderland" (2004) Dr. Soong speaks of a cure for Sharat's Syndrome, and in doing so conflates genetic medicine for treatment of disease with genetic enhancement twice, without drawing a meaningful distinction between the uses.

> ARCHER: (looks at a paper)
>
> SOONG: Go ahead. They're DNA sequences. That one is for a modification of the human T-cell. It would render Sharat Syndrome a thing of the past. That one increases the visual spectrum by five percent. Of course, none of this will ever be tested. They clear out my room every few months. I'm told it all gets vaporized.

> ARCHER: Why invest so much time and energy on things no one will ever use?
>
> SOONG: How can a supposedly intelligent species reject technology that would enhance ability, relieve suffering?
>
> ARCHER: Genetic engineering has caused a lot of suffering.
>
> SOONG: So did splitting the atom, yet the first ships to colonize the solar system were nuclear-powered. But you're not here to discuss that.

Archer's response, "genetic engineering has caused a lot of suffering" doesn't consider genetic medicine's ability to cure Sharat Syndrome as an acceptable use of the technology, again highlighting the overwhelming opposition to genetic engineering in most forms, including treatment of disease.

In the *Star Trek: Enterprise episode* "The Augments" (2004), we learn that Dr. Soong has indeed been practicing clandestine genetic engineering and has successfully created genetically enhanced individuals. In another example of genetic medicine to treat genetically inherited conditions, Dr. Soong attempts to use genetic engineering to repair a genetic defect he himself introduced into one of his own genetically enhanced "children." He is confronted by Malik, one of his genetically enhanced children, who challenges Dr. Soong's right to genetic modify an embryo:

> MALIK: How are the embryos?
>
> SOONG: I'll be ready to incubate the first of them in a few hours.
>
> MALIK: You're manipulating its DNA.
>
> SOONG: These base-pairs sequences regulate the neurotransmitter levels in their brain. If I can modify them, aggression and violent behavior will be removed.
>
> MALIK: You're changing its personality.
>
> SOONG: I'm correcting a defect in its genome. Genetic engineering was in its infancy when you were created. They weren't able to repair all the mistakes.

> MALIK: Did you fix these mistakes in the rest of us?
>
> SOONG: I didn't know how until recently.
>
> MALIK: What right do you have to tamper with their genome?
>
> SOONG: Trust me. I know what I'm doing.
>
> MALIK: You don't know that this is a defect. Maybe this is the way our creators wanted us to be.

Malik, of course, is the genetically engineered product of his creator, Dr. Soong, and so his closing comment is both contradictory and puzzling. But it suggests that within the *Star Trek* universe, the opposition to and discomfort with genetic tampering extends to include those who themselves are the product of genetic tampering. In this case, the "error" introduced by Dr. Soong that leads to excess aggression and violent behavior is considered a "natural state" by Malik and not as a disease or condition worth correcting. Remarkably, this example shows opposition to genetic engineering in the 22nd century *Star Trek* universe includes opposition *by a genetically enhanced person* to using genetic medicine to correct medical problems resulting from genetic engineering.

Outside the Federation, there is evidence that genetic medicine was being practiced and shared with members of the Federation. In the episode *Star Trek: Enterprise* "Terra Prime" (2005) there is a mention of a Rigelian gene therapy, the only reference of "gene therapy" in the entirety of the *Star Trek* universe. John Paxton, the leader of a Terra Prime, a xenophobic extremist group, is revealed to be receiving an alien-derived treatment for a condition known as Taggart's Syndrome. The reveal comes courtesy T'Pol, a Klingon member of the Enterprise whom he has been holding hostage:

> T'POL: You will provide immediate transport for my child, Commander Tucker, and myself. The hospital at Utopia Colony will be suitable until Enterprise arrives.

PAXTON: What, have you been inhaling the atmosphere? What makes you think you can dictate terms to me?

T'POL: This.

(She grasps his twitching hand.)

T'POL: Taggart's Syndrome. Since you obviously didn't die by age twenty, you're receiving treatment. Rigelian gene therapy?

PAXTON: You're not a doctor.

T'POL: The very thing you're warning humans to avoid is what's keeping you alive. Alien knowledge, freely shared. You're not only a terrorist, you're a hypocrite.

PAXTON: This is not the time for timidity and second guessing. We cannot afford to doubt ourselves.

T'POL: Colonel Green also said, to be human is to be pure. Under his rule, you would have been euthanized for having a genetic disorder.

The hypocrisy of an anti-alien extremist leader benefiting from alien medical technology is played up for effect, rewriting familiar mid-20th century WWII-era xenophobia, genocide, and nationalism into the context of interplanetary relations among 22nd century humanoids. But no further explanation is given as to the legality or explanation for the availability of Rigelian gene therapy within the Federation, despite it being established that all genetic engineering, including medical applications, would have been banned during this period. Perhaps the narrative "twist" of a xenophobic character relying on life-saving alien-derived medicine was simply more compelling to the writers than the need to preserve narrative continuity.

By the 24th century, the use of genetic medicine to correct medical defects appears to be routine. *The Star Trek: Voyager* episode "Lineage" (2001), B'Elanna Torres is informed by the Emergency Medical Hologram that her unborn child suffers from a

deviated spine, and that genetic modification of an unborn child has superseded surgical intervention:

> EMH: Yes. It's a girl. And aside from the deviated spine, she's healthy.
>
> PARIS: Will she need surgery?
>
> EMH: Fortunately, we've advanced beyond that. Genetic modification is the treatment of choice.

A second example of 24th century genetic modification of a fetus is referenced in the *Star Trek: Voyager* episode "The Fight" (1999). Commander Chakotay describes a gene for an inherited neurological condition that was "suppressed" before he was born:

> EMH: Chakotay has the genetic marker for a cognitive disorder. Sensory tremens. The primary symptoms are visual and auditory hallucinations.
>
> CHAKOTAY: My family doctor suppressed the gene before I was even born, so I never had to go through what the others did, like my grandfather.
>
> EMH: For some reason, the gene's been switched on. I'm not saying for certain that's why Chakotay thought he was getting ready for a prize-fight, but it's a good bet. The holodeck boxing simulation was fresh in his memory. A few misfiring neurons did the rest.
>
> JANEWAY: This Chaotic space we've entered, could it be stimulating the gene?
>
> EMH: Possibly. The only way to make certain would be to get the ship out of here. In the meantime, the Commander will have to stay in Sickbay.

It is worth noting that whatever treatment Chakotay received *in utero* to suppress the gene, the protein-coding abilities must have been preserved in some capacity for the disease to re-emerge in the presence of stimulation by "chaotic space." This suggests that the practice of genetic medicine might have targeted gene expression rather than changing the genome. Such changes in gene expression or phenotype without changing the underlying genome are referred to as epigenetics, and so the hypothetical therapy Chakotay received might be more accurately called "epigenetic medicine."

In summary, *Star Trek* contains few references to genetic medicine being used to treat inherited conditions, limited to the following:

- A brief mention of a proposed treatment for Sharat Syndrome (*Star Trek: Enterprise* "Borderland," 2004)
- An example of genetic modification of an embryo to reduce violence/aggression, itself a condition resulting from genetic engineering (*Star Trek: Enterprise* "The Augments," 2004)
- A brief reference to Rigelian gene therapy for the treatment of Taggart's Syndrome (*Star Trek: Enterprise* "Terra Prime," 2005)
- Two different references of *in utero* genetic modification to treat genetic defects (*Star Trek: Voyager* "Lineage," 2001, and "The Fight," 1999)

Surprisingly, genetic medicine is frequently used to address non-inherited conditions, as discussed in the following sections.

Genetic Medicine for Pathogenic Gene-altering Diseases

Science has well-established that an organism's genotype (the genetic coding potential) remains generally unchanged throughout its life, although spontaneous mutations are possible.[74] This is very different from the *Star Trek* universe, where one's genetics are at risk of being changed by alien pathogens and advanced medical treatments gone wrong. Examples of the treatment of these diseases often involve the use of gene-modifying medicine which, despite their use treating non-inherited genetic conditions,

[74] Baye, Tesfaye M et al. "Genotype-environment interactions and their translational implications." Personalized medicine vol. 8,1 (2011): 59-70. doi:10.2217/pme.10.75 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3108095/

still meet the definition of gene therapy. What follows are examples of gene therapy in this context.

Star Trek: The Next Generation episode "Genesis" (1994) contains an example of what is arguably the most extreme change caused by a gene-altering pathogen. The story begins with a human patient, Barclay, presenting with symptoms of the fictional Urodelan flu. This presents as a medical curiosity since humans are assumed to have a natural immunity to the disease. Doctor Beverly Crusher treats the patient using a synthetic T-cell that allows his immune system to fight off the infection naturally. This inadvertently creates a pathogen that infects everyone aboard the Enterprise, resulting in dramatic transformations. It is later stated that the treatment given to the first patient created an infectious virus that makes dormant genes become active, reverting individuals to primitive creatures from their evolutionary past. The explanation is provided in the episode's closing scene:

> BARCLAY: So... this was my fault...
>
> BEVERLY: No... in a way, it was mine. I didn't realize it at the time, but there's an anomaly in your genetic chemistry that caused the synthetic T-cell to mutate...
>
> (beat)
>
> Instead of just activating one dormant gene, it started to activate all of them – including your introns.
>
> BARCLAY: And that... that caused me to devolve...
>
> BEVERLY: (nods) Along with every other member of the crew. The T-cell became airborne and started to spread like a virus...

The treatment approach is to create a retrovirus from amniotic fluid from a pregnant member of the crew:

> DATA: I have analyzed Nurse Ogawa's embryo. It has been unaffected by the virus. I believe I can use her amniotic fluid as a template for a retro-virus. It would neutralize the synthetic T-cell, and re-establish the original genetic patterns of each host.

Later, the derived retrovirus is injected into the patient, resulting a dramatic reversal to original form due to “genetic resequencing”:

> Data at the operating table. He INJECTS Ogawa with a hypospray, then looks at the wall monitor.
>
> DATA: (to computer) Computer, display progress of genetic re-sequencing.
>
> The wall monitor displays a GRAPHIC of a MUTATED DNA STRAND that is rapidly RE-ORDERING itself. Data watches the graphic closely as the strand shifts and twists and breaks apart in a frenzy of re-sequencing...
>
> The wall monitor shows that the DNA strand has now FROZEN and looks more normal than before.
>
> COMPUTER VOICE: Genetic re-sequencing in progress -- DNA to seventy percent normal.
>
> Data looks down at Ogawa. We can see a subtle change in Ogawa's appearance now -- her pronounced brow is gone, and she is pale, perspiring from the rigor of the transformation. Data injects her again with the hypospray, looks at the monitor.
>
> DATA: Computer, increase nucleotide substitution by thirty-two percent.
>
> The graphic shows the DNA re-ordering itself even further...

In its defense, “Genesis” acknowledges DNA as the product of an evolutionary process and emphasizes a connection between genotype and phenotype. At worst, many assumptions and creative liberties are used to tell this episode’s chain of events. These range from humanoids having complete dormant genetic instructions for every evolutionary ancestor written in their DNA, to ideas about T-cells potentially becoming airborne and infectious, like a virus. The episode casually conflates ideas about gene

activation (the dormant introns) with the fundamental changing of the structure of DNA (the computer monitor shows DNA rearranging itself, but this doesn't comport with the dormant intron explanation). The cure for the epidemic, genetic resequencing, is facilitated through a mediator (the creation of a virus targeting the virus-like t-cell) rather than directed gene editing. Perhaps revealing popular cutting-edge medicine of the mid-1990's, the episode also notably features treatments based on embryos and T-cells, likely reflecting contemporary attitudes towards what would have been promising medical advancements.

The idea of a DNA-altering virus also appears in *Star Trek: The Next Generation* episode "Unnatural Selection" (1989). In an example of technology gone awry, contact with the Darwin Research Station, where genetic engineering research is permitted to be performed on children, leads to a viral epidemic aboard the ship. The source of the infection is blamed on the genetically engineered children's advanced immune systems, which inadvertently changed the genetic pattern of the Thelusian flu virus. Non-genetically modified individuals become susceptible to the novel viral infection, which causes victim's DNA to be modified, leading to accelerated aging:

> PICARD: And Doctor Pulaski's DNA is altered -- and that's what brings on the aging?
>
> DATA: Precisely. An almost undetectable transposition in the human genome.

Restoring the infected victims' DNA is performed by "filtering" out the modified DNA using the transporter system – common *deus ex machina* used in Star Trek to restore genetic structure, as I'll show later on.

It's worth pausing to reflect on how seemingly disconnected ideas related to genetics come together in "Unnatural Selection." The story centers on genetically

enhanced children, whose genetics cause a change in the genetics of an unrelated virus, which infects humans and alters their individual genetics, done at a research station named for the scientist known for developing the revolutionary theory of evolution by natural selection.

One way to read this is as a continued warning about the dangers of genetic engineering. The Darwin Research Station is one of few Federation institutions permitted to perform genetic enhancement experiments, and yet even in this limited, isolated environment the consequences of genetic modification are disastrous, i.e., a new infectious disease targets not just the subjects of the genetic experimentation, but the genetic integrity of the greater population. By avoiding the distinction between intentional genetic modification and accidental exposure to gene modifying pathogen, the writers depict genetic experimentation as a Pandora's box that puts all members of a species at risk, not simply those closest to the experiment.

A simpler and more benign interpretation of the handling of tangentially related ideas about genetics could be that the writers relied on popular awareness and contemporaneously low levels of understanding of genetics concepts. For example, the basic understanding that viruses contain genetic material may convincingly explain to a lay audience how a virus might alter one's genetic structure. Likewise, the basic understanding that changes in genetics are the product of evolution connects both the episode title ("Unnatural Selection," a play on the concept of natural selection popularized by Charles Darwin) and the setting of the episode on the Darwin's namesake research station. In this interpretation, ideas related to virology, evolution, and directed genetic enhancement are mixed simply because they share a common connection to

genetic coding, rather than attempting to critique a technology. Given the overwhelming criticism of genetic engineering in the *Star Trek* universe, though, I suspect both explanations are accurate, i.e., “Unnatural Selection” is both an episode dealing with various loosely related aspects of genetics *and* a warning against the misuse of new technology.

Multiple episodes in the *Star Trek: Voyager* series involve an infectious genetic disease called the Phage that afflicts the race of humanoids called the Vidiians (*Star Trek: Voyager* “Phage” (1995), “Lifesigns” (1996), “Resolutions” (1996), “Coda” (1997), “Faces” (1995)). The Phage is described as a highly adaptive infectious disease that modifies Vidiian genetic code. Phage is likely short for “bacteriophage,” a type of virus that inserts its genetic code into host bacterial cells to create copies of itself.[75] The Phage is widespread, affecting all members of the Vidiian species, and so to survive the Vidiians must harvest and transplant organs from compatible humanoids. Although the Phage is an infectious viral disease, it also partially treated as if it were a hereditary genetic disease, since all Vidiians are infected and it is limited to one genetically unique species. As in “Unnatural Selection,” the distinction between infectious gene-altering disease and heritable genetic disease is blurred.

The potential to treat the Phage with genetic medicine is mentioned in *Star Trek: Voyager* "Resolutions" (1996), "Coda" (1997), and "Faces” (1995). Klingon DNA, which originates in a different quadrant of the galaxy than Vidiian DNA, is proposed as a cure, purportedly because Klingons are immune to the Phage. In keeping with their organ-

[75] Kasman LM, Porter LD. Bacteriophages. [Updated 2020 Oct 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493185/

pirating ways, Vidiians kidnap B'Elanna, a half-Klingon-half-human and the only person with Klingon DNA in the Vidiians' quadrant of the galaxy:

> SULAN (a Vidiian surgeon): Are you in pain?
>
> B'ELANNA: It's nothing.
>
> SULAN: Remarkable. One of the symptoms of the early stages of the phage is excruciating joint pain. I find it extraordinary that you can endure it. Some who have been infected have been known to die from the agony itself.
>
> B'ELANNA: It's going to take more than an infection to kill me.
>
> SULAN: It appears you are correct. Your body's successfully fighting off the phage. I am overjoyed.
>
> B'ELANNA: How delightful for you.
>
> SULAN: Soon we will begin a series of procedures replicating your genetic code and attempting various methods of integrating your DNA with our own. In time we'll be successful and eliminate the phage forever. When that time comes you will be honored as a hero by my people.
>
> B'ELANNA: I know I'm the first Klingon you've ever seen, so I'll tell you that Klingons find honor as warriors on the battlefield, not as guinea pigs in a laboratory.
>
> SULAN: Earlier you accused me of mutilating you. Now you sound positively proud to be Klingon. You have me to thank for that, B'Elanna.
>
> B'ELANNA: You'll get no gratitude from me.
>
> SULAN: Perhaps you'll feel different in time, but I don't blame you for your obstinacy. I would be proud too, with a form as handsome as yours. I believe Klingons are the most impressive species I have ever seen.

The research into integrating Klingon DNA with the Vidiian's DNA is ultimately thwarted by B'Elanna, and the proposed DNA integration mechanism is never specified in detail. The later episode "Think Tank" (1999) explicitly states that the Phage was cured, but it too doesn't specify how or if the cure involved DNA transfer or a form of genetic medicine.

Although Klingon genetics may have been resistant to the Phage, their susceptibility to a different virus required the use of genetic medicine to correct. In the *Star Trek: Enterprise* episodes "Affliction" (2005) and "Divergence" (2005), the Klingon race is threatened with extinction by a mutated form of the Levodian flu virus inadvertently created by the Klingon military during an attempt to genetically enhance soldiers using Augment DNA. Much as in the episode "Unnatural Selection," the mutated form of the virus resulted from attempted to enhance natural abilities, again with disastrous consequences.

The treatment for the Klingon Augment virus comes via the Federation doctor Phlox. It is described as a an anti-virus cure, but it is also suggested that the disfiguring side effects of the cure (a "smooth forehead" uncharacteristic of Klingons) will be passed on to Klingon offspring as a hereditary trait, suggesting gene transfer:

> PHLOX: There's no trace of the virus in your bloodstream.
>
> (Antaak touches his smooth forehead.)
>
> ANTAAK: My targ won't even recognize me.
>
> PHLOX: In the future, it may be possible to reverse the cosmetic effects.
>
> ANTAAK: I suppose this is what I deserve. Millions of my people will have to live with this disfigurement. It'll be passed on to our children. Life won't be easy for us.
>
> PHLOX: You did your best to correct your mistakes. That's all we can ask of ourselves.
>
> ANTAAK: I doubt my superiors will allow me to remain in my position. I'll need to find a new specialty. Perhaps cranial reconstruction.
>
> PHLOX: I have a feeling that's about to become very popular.

The cure for the Klingon Augment virus and the successive generations of Klingons with smooth foreheads is a rare example of using genetic engineering as a plot

device for retroactive continuity. The first appearance of the Klingon species in *Star Trek: The Original Series* portrayed them as dark-skinned humanoids with smooth foreheads. With *Star Trek: The Next Generation*, the Klingon species were reintroduced but with a very different appearance, notably their signature ridged foreheads. This discontinuity between Klingon appearances remained unexplained until *Star Trek: Enterprise* "Divergence." Because Enterprise is a prequel series taking place earlier chronologically than *Star Trek: The Original Series*, the change from Klingons with ridged forehead (*Enterprise*) to smooth foreheads (*The Original Series*) and back to ridged foreheads (*The Next Generation*) is thus explained as the result of genetic medicine necessary to combat a species-threatening viral outbreak.

Genetic medicine appears twice with the *Star Trek* universe as a treatment for pathogenic alien infections. Both examples involve alien reproduction via DNA modification.

The *Star Trek: The Next Generation* episode "Identity Crisis" (1991) tells of an "genetic parasite" that reproduces by infecting other species and transforming their DNA, which changes their appearance to that of the alien species:

> BEVERLY: (studying the figures, puzzled) Some kind of parasite. It's using Susanna's immune system to spread genetic instructions...
>
> OGAWA: How did it get there?
>
> BEVERLY: She could have been infected during the original mission. It's small enough to have entered through any of the mucous membranes...
>
> She taps the wall monitor again and a graphic display of cells undergoing rapid transformation comes up.
>
> BEVERLY: (continuing) But it certainly isn't acting like a typical parasite... it's not feeding off her -- it's actually transforming her DNA to match its own...
>
> Ogawa crosses to Susanna, scans her with an instrument.

> OGAWA: There's not much of her original DNA left.
>
> BEVERLY (acknowledges, urgent) And we're going to need unaltered genes... or we'll never get her back. We've got to get that thing out of her. Now.

Infected members of the crew are cured by surgically removing the parasite and applying some sort of genetic treatment to restore original DNA, which causes their physical appearance to return normal. How this is accomplished is unclear, but based on contextual information (i.e, patients lacking original DNA) it seems fair to assume some degree of gene transfer would be involved.

The *Star Trek: Voyager* episode "Ashes to Ashes" (2000) describes another gene-altering pathogen used by an alien species to procreate. But unlike the genetic parasite in "Identity Crisis," the Kobali species modify the DNA of corpses in order to "reproduce." That is to say, the entire alien species consists of genetically modified and reanimated corpses of various other species they encounter. This process changes their appearance to look "Kobali." Former Voyager crew member Lyndsay Ballard describes her reanimation experience to Captain Janeway:

> BALLARD: I woke up on a ship, in a stasis chamber surrounded by aliens. They told me they'd used their technology to reanimate me. I didn't believe them when they said I'd died, but they showed me visual scans of my own corpse lying in the torpedo casing I'd been buried in. The Kobali said I'd been drifting for weeks.
>
> JANEWAY: Kobali?
>
> BALLARD: If you ever met them, you'd remember. They look just like this. After the reanimation process, they spent months altering my DNA. They were constantly scanning me, injecting me.
>
> KIM: Just to make you look like one of them?
>
> BALLARD: That's how they procreate. They salvage the dead of other races. I was given a Kobali name and placed with a family to help me acclimate.

This is clearly an example of genetic engineering, but it is this genetic medicine? From a human-centric perspective, it's hard to call the Kobali practice "medicine". Even if one considers death as a disease, and reanimation as the corresponding cure, in this case the "cure" doesn't restore individuals to their former self or even species, but rather starts them down a new path, separate from their lives prior to death. Q'Ret, Ballard's Kobali "father" makes this point clear:

> Q'RET: Why did you leave us?
>
> BALLARD: I wanted to be with my people again.
>
> Q'RET: These people? The same ones who set you adrift in space?
>
> JANEWAY: We jettisoned her body in accordance with our customs.
>
> Q'RET: You abandoned her.
>
> KIM: You had no right to tamper with her remains.
>
> Q'RET: We were acting in accordance with our customs.
>
> KIM: You mutilated her.
>
> TUVOK: Ensign.
>
> Q'RET: The reanimation process usually results in extensive memory loss, which makes the transition less painful. Unfortunately, some remember their former lives more than others. Jhet'leya, for example.
>
> BALLARD: I told you to call me...
>
> Q'RET: Lyndsay Ballard. She's dead. She has been for three years. Forgive me for being so blunt, but when we found her she was a lifeless corpse. We salvaged that raw material to create a new person, my daughter, whom I love.
>
> BALLARD: I'm not your daughter.
>
> Q'RET: You may have altered your appearance, but do you still think like these people? Even now, the first words that come into your head, are they in their language or mine? I realize this place is familiar to you, but it's not where you belong. Your sister misses you.

BALLARD: Tynsia.

Q'RET: She keeps asking when you're coming home. What should I tell her?

BALLARD: Tell her that her sister's dead.

The passage highlights the extreme cultural relativism required to understand the Kobali perspective. The Kobali reanimation process can either be viewed as a disrespectful violation of an individual human's rights through mutilation of sacred remains, or as a customary and natural part of a species' reproductive cycle. Adopting the Kobali perspective gets us closer to accepting this example as genetic medicine, as it involves genetic modification for the purposes of reproduction (an accepted "medical" procedure.) But the actual disease at question is still uncertain unless we consider genetic modification and reanimation of corpses as a "cure" for sterility (and not, for example, the Kobali natural state). Part of the difficulty in determining whether the Kobali's practice is genetic medicine is that it blurs the line between natural reproduction and unnatural creation of life, asking the viewer to consider both sides, a continuation of themes reminiscent of Shelley's Frankenstein. In Frankenstein, the discovery of a new scientific principle makes it possible to bring non-living matter to life, and this capability is exploited to warn of the dangers of uncontrolled scientific and medical progress. In "Ashes to Ashes," the mechanism is genetic engineering and the setting is alien-inhabited space, but similar warnings about technological progress can be found in the suggestion that modifying DNA has the possibility to usher in the "unnatural."

The examples of infectious and pathogenic gene-altering diseases and genetic medicine-based treatments in *Star Trek* include four example of gene altering virus, and two examples of pathogens being used by alien species to procreate:

- Intron virus outbreak and treatment in *Star Trek: The Next Generation* "Genesis" (1994)
- Gene-altering viral outbreak and treatment in *Star Trek: The Next Generation* "Unnatural Selection" (1989)
- Speculative use of Klingon DNA to cure the Phage, a DNA-altering disease affecting the Vidiians, mentioned in *Star Trek: Voyager* "Lifesigns" (1996), "Resolutions" (1996), "Coda" (1997), and "Faces" (1995)
- Curing Klingon Augment virus through genetic medicine in *Star Trek: Enterprise* "Affliction" (2005) and "Divergence" (2005)
- Alien genetic parasite and treatment in *Star Trek: The Next Generation* "Identity Crisis" (1991)
- Reproductive practice of Kobali in *Star Trek: Voyager* "Ashes to Ashes" (2000) (Involves gene transfer, but is difficult to classify as "genetic medicine")

Three out of the six examples cited involve a contagious viral outbreak directly caused by doctors or scientists, and two of these examples of gene-altering viruses result from directed genetic enhancement attempts. This is remarkable considering the generally unchangeable nature of DNA. It seems the writers of *Star Trek* may have overly relied on fears of an out-of-control man-made contagion as a plot device to indirectly address fears and uncertainty of genetic engineering, perhaps because contagious conditions are more familiar and relatable than the mostly unseen world of

DNA. The association of genetic medicine to infectious gene-altering disease continues the constant critique and skepticism of genetic medicine within the Star Trek universe, blurring the lines between genetic disease causation and treatment of disease using genetic medicine.

Genetic Medicine for Non-inherited Genetic Disorders, Non-infectious diseases, and Accidents

The use of genetic medicine in the *Star Trek* universe includes applications to address non-inherited disorders and conditions, exemplifying the impermanent nature of DNA as it is represented within the series. In contrast to 21st century understanding of DNA as remaining mostly unchanged throughout an individual's life,[76] several influences within the *Star Trek* universe can cause DNA modifications that require genetic modification or genetic restoration. These include accidents (often involving advanced technology), alien influence, and genetic identity concealment. In the following I'll explore ways genetic medicine is used within these contexts.

One of the most recognized technological marvels of the *Star Trek* universe is the transporter, which allows individuals and objects to be moved (or "beamed") from one location to another instantaneously. Transporter technology purportedly works by converting matter into an energy signal, sending that energy through "subspace" to a different physical location in normal space, and reconverting the signal back into material form. An individual's transporter signal (or "trace") consists of their unique molecular

[76] Baye, Tesfaye M et al. "Genotype-environment interactions and their translational implications." Personalized medicine vol. 8,1 (2011): 59-70. doi:10.2217/pme.10.75 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3108095/

pattern, which includes DNA sequences. Transporters are widely accepted within the Federation as a safe way to travel, but accidents have occurred. Two transporter-related incidents have required the use of genetic medicine to restore DNA sequences to their prior state.

In the *Star Trek: The Next Generation* episode “Rascals” (1992) a transporter mishap causes four members of an away team to transform into physiologically younger versions of themselves upon returning to the Enterprise:

> BEVERLY, medical tricorder in hand, finishes her examination of Young Picard. Troi is with her. In the background Young Ro, Young Guinan and Young Keiko sit on biobeds while an N.D. conducts tests with a tricorder. NOTE: "child" versions now wear smaller, replicated clothes, with normal sized insignias. They are still examining the fit of their new clothes.
>
> As the "grown ups" talk, we can see Young Picard grow impatient as they talk above and about him, as if he weren't even there. Beverly is reporting to Riker.
>
> BEVERLY (to Riker): According to the bio-scans, their DNA structures are now consistent with those of pre-adolescents. But as far as I can tell, only their bodies have changed.
>
> TROI: Their individual intelligence and behavioral responses are all exactly the same as they were before the accident.

Dr. Beverly Crusher’s claim that their DNA structure is “consistent with those of pre-adolescents” suggests that DNA structure itself changes after adolescence, rather than explaining differences as the result in changes in gene expressions. This apparent contradiction with modern medical understanding of the nature of DNA is subsequently explanation by the Doctor:

> Beverly is showing Riker an Okudagram display of some medical information.
>
> BEVERLY: This is Captain Picard's rybo-viroxic-nucleic structure from a tissue sample I took this morning. It's the same as a sample I took before the accident -- except it's missing several key viroxic sequences.

> RIKER: I'm afraid it's been a long time since I took genetics, Doctor.
>
> BEVERLY: RVN is one of the key factors in our development during puberty. Unlike DNA, which never changes, RVN takes on additional viroxic sequences during adolescence. Those sequences determine how we develop physically. Without them...
>
> RIKER: We would never mature into adults.
>
> BEVERLY: Exactly. Somehow, those key sequences were eliminated in the Captain and the others during transport.

Note that Beverly's explanation of RVN contradicts her initial assessment which showed changes in DNA. Ribo-viroxic-nucleic sequences are fictional but could be understood as a stand-in for epigenetic information—heritable changes in phenotype than do not result in changes in the underlying DNA. The nucleotide-based structure of RVN suggests it may be a downstream product of genetic transcription, perhaps akin to messenger ribonucleic acid (mRNA).

Considering the RVN explanation, the requisite treatment involves reintroducing adult RVN to the affected subjects. This is performed by restoring their genetic material with the transporter device, using data contained in the transporter pattern buffers.

> BEVERLY: I do have adult RVN patterns on all four of them. I might be able to send them back through the Transporter pattern buffer and replace the missing sequences... but we can't even attempt that until we know why this happened in the first place.

The administration of treatment is immediate and overly simplified: children enter the transporter and moments later adults emerge, their genetics and appearances magically restored to the prior state:

> BEVERLY: I'm loading the adult patterns into the buffer...
>
> O'BRIEN: Transposition matrix locked in...
>
> Young Picard nods and then steps up onto the platform. A moment, then Young Picard gives the order...

YOUNG PICARD: Energize...

O'Brien works the console and Young Picard DEMATERIALIZES.

A moment of tension for Beverly and O'Brien as he REMATERIALIZES... it's the ADULT Picard. Beverly pulls out her tricorder and gives him a quick scan.

BEVERLY: How do you feel, Captain?

He looks around the room for a few seconds. He reaches up and runs a hand over his head where hair was only a moment ago.

PICARD: I feel fine. Everything just seems... smaller.

A different type of transporter accident is explored in the *Star Trek: Voyager* episode "Tuvix" (1996) in which the characters Tuvok and Neelix are genetically merged with an orchid into a single hybridized individual (named "Tuvix") containing traits from its component parts:

EMH: My scans indicate that all biological matter was merged on a molecular level. Proteins, enzymes, DNA sequences. The man you see before you is literally a fusion of two men. But he's surprisingly healthy considering the circumstances. All vital signs are stable.

JANEWAY: What's the last thing you remember?

TUVIX: I, we, that is to say, Tuvok and Neelix, we had just finished gathering the samples. We were beaming back to the ship. The next thing I knew, I was standing on the transporter pad, as you see me now.

EMH: I'm also picking up traces of a third genetic pattern. It appears to be plant-based.

TUVIX: The orchids. We had collected several dozen samples of orchids. They were in our sample containers when we beamed up.

EMH: Well, they're part of your genetic structure now. But they don't appear to be affecting your biochemistry.

The focus of the episode is on Tuvix's individuality and whether, as a sentient being, he has any right to exist, especially if restoring Tuvok and Neelix necessarily means the death of Tuvix.

JANEWAY: It's funny. If we'd had the ability to separate Tuvok and Neelix the moment Tuvix came aboard, I wouldn't have hesitated.

CHAKOTAY: Of course not.

JANEWAY: But now, in the past few weeks, he's begun to make a life for himself on this ship. He's taken on responsibilities, made friends.

CHAKOTAY: I count myself as one of them.

JANEWAY: So at what point, did he become an individual and not a transporter accident?

As in "Rascals," the treatment for Tuvix's "condition" requires the use of the transporter to separate the merged individuals. Again, the results are immediate and complete: Tuvix dematerializes into the transporter, and moments later Tuvok and Neelix materialize. But the ethical challenges surrounding the procedure makes it less routine. Indeed, the procedure is done against the will of Tuvix, and without the Doctor's support:

EMH: I'm sorry, Captain, but I cannot perform the surgical separation. I am a physician, and a physician must do no harm. I will not take Mister Tuvix's life against his will.

JANEWAY: Very well, Doctor. Please step aside.

(Janeway goes to Kim, who is holding a hypospray.)

JANEWAY: I assume this is the radioisotope.

(Kim gives it to her.)

JANEWAY: Please sit down on this biobed.

(Tuvix sits. Janeway looks straight into his eyes and administers the hypo. Then she goes to the medical transporter console.)

JANEWAY: Locking surgical targeting scanners onto the isotope probe. Initiating separation sequence. Energizing.

(As Tuvix is beamed away, two figures are beamed in, both wearing command gold uniforms.)

KES: Neelix!

NEELIX: Hello, sweetie.

(Neelix and Kes kiss.)

TUVOK: Greetings, Captain.

JANEWAY: Mister Tuvok. Mister Neelix. It's good to have you back.

A different kind of gene-altering accident appears in the *Star Trek: Voyager* episode "Threshold" (1996). Following a test flight attempting to travel faster than the fictional theoretical physical limit of "transwarp" velocity, Lieutenant Tom Paris experiences unexplainable changes to his DNA:

> EMH: He's body is going through some sort of mutation. His DNA is rewriting itself. To what end, I don't know.
>
> JANEWAY: Does this have anything to do with the enzymatic imbalance you found?
>
> EMH: No.
>
> JANEWAY: Can you stop it?
>
> EMH: So far, nothing has worked. The mutations are unlike anything in Starfleet medical records. His internal organs are being rearranged. Some have atrophied and been absorbed into his body, and there are at least three others that have appeared and have no identifiable function at all.

The DNA changes are accompanied by increasingly dramatic changes to his behavior and physical appearance. Meanwhile, the Emergency Medical Hologram formulates a treatment that requires deletion of any "new" DNA:

> EMH [on monitor]: I believe the answer lies in forcing his DNA to revert to its original coding. Once that occurs, his body should return to its former state.
>
> CHAKOTAY: How do we do that?
>
> EMH [on monitor]: We destroy all of the new DNA in his body. His cells will have to use the original coding as a blueprint. But the only way to destroy the mutant DNA is with highly focused antiproton radiation.

Echoing themes presented in *Star Trek: Enterprise* "Genesis" and "Unnatural Selection," the source of Paris's genetic illness is attributed to accelerated genetic evolution, in this instance triggered by travelling at infinite velocity:

> EMH: I've re-examined the data on Mister Paris' transformation, and I think I understand what's happening to him. The mutations we observed are natural.
>
> CHAKOTAY: Natural?
>
> EMH: The changes in his DNA are consistent with the evolutionary development of the human genotype observed over the past four million years. Increased brain capacity, the loss of vestigial organs.
>
> TUVOK: Are you saying Lieutenant Paris is evolving?
>
> EMH: That's my theory. The only difference between natural evolution and what happened to Mister Paris is that his changes took place over a twenty four hour period. Somehow, travelling at infinite velocity accelerated the natural human evolutionary process by millions of years. It's possible that Mister Paris represents a future stage in human development, although I can't say it's very attractive.
>
> CHAKOTAY: What do we do about it?
>
> EMH: I think my antiproton approach was correct. However, I'll need to intensify the treatment to restore his original DNA.

By tenuously connecting ideas about biological evolution with theoretical physics, this episode seems to imply that human evolution is directed towards a specific goal and normally occurs at a specific rate. It also suggests that DNA sequences are not simply the product of evolution but an evolutionary force that can be applied onto itself. Few of these can be taken any more seriously than traveling at "infinite velocity" can (or should be) taken.

The proposed treatment for this condition is impossibly complex: targeted destruction of mutant DNA sequences in every cell of affected subjects using antiproton radiation redirected from Voyager's warp core engines, which will in turn revert affected

subjects (now both Paris and Janeway) back to their human form. When the treatment is administered, it is comically unsophisticated and routine[77]:

> EMH: I've eradicated all traces of the mutant DNA from your system and restored your original genome. Congratulations. You're human again.
>
> JANEWAY: Thank you, Doctor.
>
> EMH: Captain, it'll take some time for your genetic codes to stabilize. I'd like you to remain in Sickbay for the next three days, just to be safe.

While traveling at infinite velocity may expose inhabitants of the Star Trek universe to unknown risks of genetic modifications, a similar risk is present when encountering alien life forms with vastly superior technological capabilities. This disparity in technological capabilities is on full display whenever members of the Federation encounter the Borg Collective, a powerful, technologically advanced pseudo-species comprised of cybernetic humanoids. The Borg function as a connected network of "assimilated" individuals from various species who have been modified into mechanized cyborgs. The process of assimilation into the Borg Collective requires significant physical changes such as cybernetic implants and the introduction of microscopic robotic machines called "nanoprobes" that regulate the cells of assimilated individuals. Individuals who have been rescued from the Borg and separated from the Collective require medical intervention to address the condition of having once been a member of the Borg Collective, and in these cases, a genetic resequencer is used.

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[77] An even more vague example of medically divine intervention to restore genetics can be found in Star Trek: Voyager "Vis a Vis" which involves a shapeshifting alien that moves between host bodies and leaving victims trapped in other bodies along the way. Upon defeating the alien, the Captain narrates, "While the alien intruder remains trapped in the body of his last victim, the doctor has found a way to return Tom, Steth and me to our own bodies." No additional explanation is given.

One example is mentioned in *Star Trek: Voyager* "The Raven" (1997) in which the character Seven of Nine, a former member of the Borg Collective, experiences hallucinations as part of an attempt to have her return to the Collective. Her hallucinations are triggered by a reactivation of dormant nanoprobes, and a genetic resequencer is used to alter the DNA of cells under the influence of nanoprobes:

> JANEWAY: What have you found, Doctor?
>
> EMH: Something most peculiar. This graphic represents the matter conversion data from Seven of Nine's last transport. If you'll notice, there's a high concentration of Borg organelles in the bone marrow and lymphatic tissue. The dormant nanoprobes in Seven of Nine's cells have reasserted themselves, taken over blood cell production and they're growing new Borg implants. Thirteen percent of the Borg technology I removed three weeks ago has regenerated in a matter of hours.
>
> CHAKOTAY: You said the nanoprobes in her bloodstream were dormant. What reactivated them?
>
> EMH: I don't know, but I've developed a way to stop the process. This hypospray contains a genetic resequencing vector. It should neutralize the nanoprobes.

Another proposed use of a genetic resequencer is to overcome the loss of cortical node, a cybernetic implant normally possessed by all members of the Borg Collective and critical in regulating vital functions:

> ICHEB: You took these scans of me when I left the Collective. By your own estimation I emerged from my maturation chamber before I was fully assimilated. As a result my physiology is less dependent on my implants.
>
> EMH: They still regulate many of your vital functions.
>
> ICHEB: What about my age? I'm younger, so it should be easier for my body to adapt to the loss.
>
> EMH: You're obviously too young to understand the risks involved.
>
> ICHEB: I understand the risks perfectly. If we continue to do nothing, Seven will die.
>
> EMH: And if we proceed with your idea, you could both die.

> ICHEB: According to my research, there's an eighty six point nine percent chance that Seven's implants will adapt to my node.
>
> EMH: Eighty-six
>
> ICHEB: Point nine.
>
> EMH: What about you? Without a cortical node, how will you regulate your implants?
>
> ICHEB: You should be able to compensate with genetic resequencing. This isn't suicide, Doctor. I believe it can work. All I ask is that you consider it.

Although it not explicitly stated, it is assumed from its name that the purpose of the genetic resequencer device is to modify genetic code, thus it is a tool for practicing genetic medicine. This assumption is confirmed by the genetic resequencer's appearance in a different context in the *Star Trek: Voyager* episode "Child's Play" (2000), as a tool used to create genetically engineered crops specially adapted to the ecologically devasted Brunali homeworld. It is also used to fake paternity in the *Star Trek: The Next Generation* episode "Bloodlines" (1994), discussed later.

The practice of genetic medicine is not limited to members of the Federation in the *Star Trek* universe. In the *Star Trek: Voyager* episode "Scientific Method" (1997), the crew of Voyager experiences an outbreak of mysterious diseases caused by unseen medical experimenters. These invisible alien researchers perform a variety of experiments on unaware experimental subjects, some of which undergo genetic modifications. Commander Chokotay, for example, experiences rapid aging because of modifications to sequences of DNA that regulate metabolism. Neelix also has his genes altered to express the phenotype of his Mylean great-grandfather. Closer inspection of both Neelix and Chakotay's DNA show anomalies on their DNA, eventually determined to be genetic markers placed by the alien researchers:

EMH: There seems to be some kind of contaminant on the base pair sequence. It didn't show up on the first scan. I need a closer look.

TORRES: I'm going to maximum magnification. What do you see?

(An alien bar code.)

EMH: I'm not exactly sure.

TORRES: Well, what does it look like?

EMH: See for yourself.

TORRES: I'm no microbiologist, but that doesn't look like it belongs there.

EMH: Believe me, it doesn't. I've never seen it. This level of sub-molecular technology is well beyond anything Starfleet has developed.

TORRES: What are those markings? Some kind of alien writing?

EMH: I wish I knew. They might help us determine where it came from.

The activities of the aliens should not be considered genetic medicine per se, as they do not seek to treat a condition. Instead, these activities might more accurately be considered examples of genetic medical research, in this case causing instead of treating disease. On the other hand, the Federation's attempt to eliminate the cause of the disease by removing the genetic tag could be considered a type of genetic medicine. The Emergency Medical Hologram suggests this can be accomplished through a "neuraleptic [sic] shock":

EMH: The key to the aliens' control is the genetic tags. I believe a neuraleptic shock would disable them. Unfortunately, it would be rather painful.

SEVEN: Will the crew recover?

EMH: Yes, they will. The hard part will be administering the shock to everyone simultaneously.

Another example of genetic medicine used to reverse the effect of prior genetic modification appears in the *Star Trek: The Next Generation* episode "Bloodlines" (1994).

In this episode, Captain Picard meets Jason, identified through genetic testing as Picard's biological son. Later in the episode, it is revealed that Jason is not in fact Picard's son, and that Jason's genetic code was resequenced to fake his identity by an extortionist Ferengi named Bok:

> PICARD: You know as well as I do, Bok...he's not my son.
>
> Bok is stunned by Picard's words... as is Jason...
>
> PICARD: I know what you did... Miranda Vigo is Jason's mother... but, I am not his father... it only appeared as if I were because you resequenced his DNA...
>
> The Ferengi are as surprised to hear this as Jason is.
>
> PICARD: But your technique was flawed...Jason began to suffer from a neurological disorder... when my ship's Doctor investigated its cause, she discovered what you'd done...
>
> Bok can't believe his plan is unraveling before his eyes...
>
> TOL (despondent): Now he'll never pay the ransom...

Note that once again, an effort to modify genetic material backfires, introducing a neurological condition which reveals the ruse and threatens the health of the subject of the genetic resequencing. Fortunately, a treatment is devised which leverages genetic medicine to correct the errors introduced by the genetic resequencing:

> Picard and Jason make their way toward the Transporter room. Jason carries a SHOULDER PACK with all his belongings in it.
>
> JASON: Doctor Crusher said I'm responding well to the treatment... she thinks the damage is going to be completely reversed...
>
> PICARD: I'm glad to hear it...

In summary, Star Trek's references to genetic medicine use to treat non-hereditary conditions consist of the following relevant episodes:

- Two cases used to correct transporter accidents (*Star Trek: The Next Generation* "Rascals," 1999, and *Star Trek: Voyager* "Tuvix," 1996)
- One reference to it being used to address accelerated evolution caused by travelling at infinite velocity (*Star Trek: Voyager* episode "Threshold," 1996)
- One case used to reverse the effects of Borg assimilation (*Star Trek: Voyager* "The Raven," 1997)
- A case of removing genetic tagging by alien medical experimenters (*Star Trek: Voyager* episode "Scientific Method," 1997)
- One instance of reversing the effects of genetic disguise (*Star Trek: The Next Generation* episode "Bloodlines," 1994)

Genetic Medicine as Advanced Technology

Less substantive references to gene therapy within the *Star Trek* universe represent the technological capability with a sort of reverence worthy of high respect and admiration, while simultaneously treating it as routine. The following looks at minor references to genetic medicine within *Star Trek* and show how they fall within this contradictory framework.

An example of gene therapy being cited as the epitome of medical sophistication occurs in the *Star Trek: Voyager* episode "Innocence" (1996). In this episode, the Emergency Medical Hologram touts the capabilities of sickbay using genetic resequencing as an impressive example of their medical capabilities:

> EMH: Ah, visitors! Welcome to sickbay. I'm the Chief Medical Officer.
>
> JANEWAY: This is First Prelate Alcia of Drayan Two.

> EMH: It's an honor to meet you. We don't often receive such distinguished guests here, unless there's been some sort of accident. I'm sure nothing unfortunate will happen to you on your visit here, but if it did you can rest assured you will find yourself in very capable hands. We are fully equipped to provide a wide variety of treatments here from removing a splinter to re-sequencing the base pairs in a strand of DNA, and our research facilities are the most advanced in Starfleet.
>
> ALCIA: Very impressive.

Note the intentionally high contrast between the trivial procedure of splinter removal and genetic resequencing, and the suggestion that only the most advanced facility in Starfleet would be capable of the latter procedure.

This reverence for genetic medicine appears again from the same character, the EMH, in *the Star Trek: Voyager* episode "Fury" (2000). As an artificial life form, the EMH doesn't have a given name (aside from EMH or simply "The Doctor). To become more human-like, he is encouraged by a colleague to consider taking a name, and is inspired by medical innovators of the past:

> EMH: Ah. Pyong Ko.
>
> KES: Excuse me?
>
> EMH: You encouraged me to choose a name, remember? Pyong Ko was a twenty first century surgeon who discovered the genetic sequence for inhibiting cancer cells. It heralded a new chapter in Earth's medical history.
>
> KES: That's a perfect name, Doctor.
>
> EMH: Then again, I'm also considering Schweitzer, Jarvik, Pasteur. There are so many options, each with its own merits.
>
> KES: Why don't you give it some more thought? You don't have to decide right away.

While Pyong Ko is a fictional character, the other names under consideration by the EMH are intended as recognizable references to nineteenth and twentieth century medical innovators: medical missionary Albert Schweitzer, Robert Jarvik, inventor of the

artificial heart, and Louis Pasteur, father of bacteriology and discoverer of principles of vaccination. That the EMH chose to elevate Pyong Ko above the others suggests that the writers imagined the potential of genetic medicine to be exceedingly important, as a tool for curing cancer that would also influence medicine more broadly, "heralding a new chapter in Earth's medical history." Pyong Ko is also specifically described as a twenty-first century physician, perhaps revealing the high level of optimism around genetic medicine felt by the screenwriters in the period leading up to turn of the century.

The *Star Trek: Deep Space Nine* "Tears of the Prophets" (1998) contains a similar optimistic reference to the potential of genetic medicine. In this episode Dax and Worf seek to have a child together despite being incompatible species. Using genetic medicine ("resequencing enzymes"), Dr. Bashir makes interspecies conception possible, to his own amazement:

> Dax and Bashir are walking down the corridor.
>
> BASHIR: According to the DNA scans I took this morning, the ovarian resequencing enzymes I've given you are working.
>
> DAX: You mean Worf and I can have a baby?
>
> BASHIR: It looks that way.
>
> (a beat)
>
> I have to say, I didn't expect such positive results so quickly. It's quite amazing, actually.
>
> Dax can't hide her joy at the news. Dax impetuously throws her arms around Bashir and gives him a warm hug. Bashir is a little taken back, but he returns the embrace.
>
> DAX: Thank you, Julian.
>
> BASHIR: It's all part of being a doctor.

A reference to genetic medicine's use in organ transplant appears in the *Star Trek: Enterprise* episode "A Night in Sickbay" (2002), which uses gene transfer technology to create an organ compatible for inter-species transplant:

> ARCHER: What are you doing?
>
> PHLOX: My treatment was effective, at least partially. His immune system is stabilising but his pituitary gland was severely damaged. It's all but disintegrated. Bring me the small grey cage on the second shelf. The one with the blue top.
>
> ARCHER: What's in here?
>
> (Phlox is wheeling in a large transparent tank.)
>
> PHLOX: A Calrissian Chameleon. Fill this for me.
>
> (He hands a shower head to Archer.)
>
> PHLOX: I'll need to alter its DNA to avoid rejection but its pituitary gland should be compatible with your dog's.
>
> ARCHER: You're going to perform a transplant from a lizard?
>
> PHLOX: Unless you have a better suggestion. It's a shame, actually. The chameleon secretes a rare toxin that's very useful in treating respiratory infections. She's the last one I have.

These examples are relatively minor references to genetic medicine, but they suggest that the writers believe genetic medicine is a complex technology that will have a profound impact on medicine. Interestingly, these minor asides are perhaps the most optimistic of all the examples identified. That is, when genetic medicine is put at the center of a storyline, it is often portrayed as dangerous, unethical, or posing detrimental risk to humanity. In contrast, when it is mentioned briefly, as in these examples, it is portrayed as a useful capability worth showcasing or celebrating. This contrast is brought into focus with the Star Trek: Enterprise episode "Dear Doctor" which is dedicated to exploring the ethical side of genetic medicine and explored in the next section.

Ethics of Genetic Medicine and Evolution in “Dear Doctor”

Many of the aforementioned examples of genetic medicine in the Star Trek universe introduce or explore an ethical dilemma presented by genetic medicine technology, but perhaps no other episode explores the ethical considerations of genetic medicine more than the *Star Trek: Enterprise* episode “Dear Doctor” (2002). This episode centers on whether it is appropriate to use genetic medicine to heal if it also means artificially changing the potential evolutionary trajectory of a species. This episode confronts ideas about genetic medicine opposes or threatens the natural course of evolution, and so it deserves special attention here.

In this episode, the crew of the Enterprise visits a planet inhabited by two intelligent humanoid species, the Valakians and the Menk. The Valakians are a more advanced species than the primitive Menk, but both species peacefully coexist, with the Valakians providing food, shelter, and security to the Menk. The Valakians are affected by a planet-wide plague, and they seek out assistance from the Enterprise. The Menk are unaffected by the plague.

Doctor Phlox investigates the disease, and his research determines that the Valakian people are suffering from a genetic disease:

> ARCHER: I've just gotten a call from the director of the clinic. He's eager to hear if you've made any progress. Doctor?
>
> PHLOX: I've developed a medication to ease the symptoms of the disease, but
>
> ARCHER: But?
>
> PHLOX: This epidemic isn't being caused by a virus or bacteria. The proteins that bind to their chromosomes are deteriorating. Their illness is genetic. It's been going on for thousands of years, but the rate of mutation has accelerated over the last few generations. Based on my projections, the

> Valakians will be extinct in less than two centuries. I wish I had better news.
>
> ARCHER: What about a cure?
>
> PHLOX: Genetic abnormalities on this level are very difficult to reverse.
>
> ARCHER: But not impossible.
>
> PHLOX: No. I still believe the Menk immunity could be the key to a cure. I plan to study them in more detail.
>
> ARCHER: Take all the time you need.

While researching a cure, Phlox is exposed to Menk culture and is surprised to learn they are not as primitive as he originally thought. Increasingly, Phlox grows to appreciate the Menk people and their culture and admits to having initially underestimated their abilities.

Phlox develops a cure for the Valakian genetic disease, but his newfound understanding and appreciation for the Menk leads him to conclude that treating the Valakian's genetic disease would be unethical. His reasoning is that treating the Valakian would evolutionarily disadvantage the Menk by interfering with forces of natural selection:

> ARCHER: A cure, Doctor. Have you found a cure?
>
> PHLOX: Even if I could find one, I'm not sure it would be ethical.
>
> ARCHER: Ethical?
>
> PHLOX: We'd be interfering with an evolutionary process that has been going on for thousands of years.
>
> ARCHER: Every time you treat an illness, you're interfering. That's what doctors do.
>
> PHLOX: You're forgetting about the Menk.
>
> ARCHER: What about the Menk?

PHLOX: I've been studying their genome as well, and I've seen evidence of increasing intelligence. Motor skills, linguistic abilities. Unlike the Valakians they appear to be in the process of an evolutionary awakening. It may take millennia, but the Menk have the potential to become the dominant species on this planet.

ARCHER: And that won't happen as long as the Valakians are around.

PHLOX: If the Menk are to flourish, they need an opportunity to survive on their own.

ARCHER: Well, what are you suggesting? We choose one species over the other?

PHLOX: All I'm saying is that we let nature make the choice.

ARCHER: The hell with nature. You're a doctor. You have a moral obligation to help people who are suffering.

PHLOX: I'm also a scientist, and I'm obligated to consider the larger issues. Thirty-five thousand years ago, your species co-existed with other humanoids. Isn't that correct?

ARCHER: Go ahead.

PHLOX: What if an alien race had interfered and given the Neanderthals an evolutionary advantage? Fortunately for you, they didn't.

ARCHER: I appreciate your perspective on all of this, but we're talking about something that might happen. Might happen thousands of years from now. They've asked for our help. I am not prepared to walk away based on a theory.

PHLOX: Evolution is more than a theory. It is a fundamental scientific principle. Forgive me for saying so, but I believe your compassion for these people is affecting your judgment.

ARCHER: My compassion guides my judgment.

PHLOX: Captain.

ARCHER: Can you find a cure? Doctor?

PHLOX: I already have.

Phlox's ethical position of not intervening to modify the genetics of the Valakian people conflicts with Captain Archer's desire to intervene to treat disease. The argument

against using advanced technologies and medicine to change the course of nature is not an uncommon topic explored in *Star Trek.*[78] Interestingly, in this scenario it is the scientist that has chosen not to intervene to eliminate disease, arguing that natural forces should be permitted to run their course. Phlox's position is rationalized using science itself and the consideration of "larger issues" rather than being based on an opposition towards medically interfering with natural disease. This suggests that genetic medicine, and the consequences of using genetic medicine, requires a different calculus than other technologies to determine what is acceptable medical intervention and what constitutes improper or unnatural directed evolution.

Ultimately, Archer decides to embrace Phlox's recommended course of action, despite it being against his principles:

> ARCHER: I'm going down to the Valakian hospital.
>
> PHLOX: Sir, it would go against all my principles if I didn't ask you to reconsider what I..
>
> ARCHER: I have reconsidered. I spent the whole night reconsidering, and what I've decided goes against all my principles. Someday my people are going to come up with some sort of a doctrine, something that tells us what we can and can't do out here, should and shouldn't do. But until somebody tells me that they've drafted that directive I'm going to have to remind myself every day that we didn't come out here to play God.

Consistent with *Star Trek*'s overwhelming distrust towards genetic engineering and genetic medicine, this episode again lands on the side of opposition to using gene-modifying technologies in favor of letting nature take its course. The cure for the

[78] For examples of *Star Trek* space-faring civilizations choosing nature over technological advancement, see *Star Trek: The Next Generation* "Up the Long Ladder," *Star Trek: Deep Space Nine* "Paradise" and the film *Star Trek: Insurrection*.

Valakian genetic disease is explicitly withheld by Enterprise crew, and the Valakians are left to their own fate.

Perhaps most troubling about this episode's conclusion is that the argument against using genetic medicine because it could disturb nature is exceedingly broad and potentially always applicable. In this case, the existence and potential future evolutionary development of the Menk is used to justify withholding a cure for disease for an entirely different species *because* it happens to share environmental and evolutionary forces. The Menk were not at risk of becoming extinct or needing special protections; They merely risked delayed potential evolutionary development over the next millennia. The Valakian, however, faced almost certain extinction within a fraction of that time frame.

Applying this same logic to the use of genetic medicine in the real world, we might conclude there is never a satisfying use case, since any heritable genetic changes would affect the environment and therefore evolution. Changes could, one might argue, be to the detriment of other species who otherwise might have occupied the environmental niche and given selective advantages. If one incorrectly views evolution as a kind of "progress" towards a certain goal (sentience, technological development, etc.) then one might similarly prioritize species who appear to be on an "upward" evolutionary trajectory. This is problematic because it reframes the discussion around how genetic medicine fails to preserve a "natural" state, rather than addressing its potential in eliminating disease and alleviating suffering. Of course, until genetic medicine causes heritable changes to the genome, this is an irrelevant point. The fact that the ethical conclusion posed by "Dear Doctor" is to not intervene and let natural forces play out suggests that when these technologies are available and humanity is faced with similar

choices, there may likely be strong resistance to their use based on similar understanding of evolutionary processes and ideas of evolutionary progress.

Star Trek's Critical View Towards Genetic Medicine

Much of *Star Trek*'s depictions of genetic medicine and genetic engineering are highly critical of this technology, going as far back as *Star Trek: The Original Series*. The premise of "Miri" (1968) centers on a civilization in chaos resulting from genetic research into life extension gone wrong. The recipients of genetic enhancement are depicted as literal despotic tyrants, as is Khan in "Space Seed" (1969). In this episode we also learn that genetic engineering was the primary cause for Earth's final World War (the "Eugenics War"). Clearly the writers were more fearful of how this technology might be improperly used than interested in exploring its beneficial potential.

The same negative sentiment persists decade later with *Star Trek: The Next Generation* and the subsequent series. *Star Trek: The Next Generation* episodes "Unnatural Selection" (1989) and later "Genesis" (1994) tell tales of man-made disasters resulting from genetic modification. The episode "Too Short a Season" (1988) centers on an aging and ailing Admiral Jameson who abuses alien genetic medicine, causing his death. In *Star Trek: Enterprise* "Cold Station 12" (2004), genetic engineering is referred to as something that could "destroy a race." The *Star Trek: The Next Generation* episode "The Masterpiece Society" depicts a flawed civilization built upon foundations of a genetically engineered population, its genetic engineering practices being the target of Captain Picard's displeasure.

In Star Trek it's often the bad guys who embrace genetic modification technologies. A prominent advocate of genetic medicine, Dr. Arik Soong, is a criminal;

He makes his case for using genetic medicine to relieve suffering from a prison cell in the *Star Trek: Enterprise* episode "Borderland" (2004). In *Star Trek: Deep Space Nine* episode "In the Cards" (1997) Dr. Giger, a typical mad scientist, and Weyoun, a cloned servant of the enemy Dominion forces, discuss their shared interest in genetic engineering. *Star Trek: Insurrection's* Son'a people resort to genetic engineering to preserve their appearance after committing treason and being banished from their life-giving homeworld. The Borg's nanoprobes modify genetic material to assimilate their subjects as shown in Star Trek: Voyager "The Raven" (1997).

Similarly, the recipients of genetic medicine are portrayed as social outcasts, as in the genetically enhanced characters in "Doctor Bashir, I Presume" (1997). "Statistical Probabilities" (1997) and "Chrysalis" (1998). The Augments, the genetically enhanced "children" of Dr. Soong, are portrayed as rogues on the run from authority in the *Star Trek: Enterprise* episode "The Augments" (2004).

Even potentially useful or medically defensible depictions of gene therapy are often portrayed critically. *Star Trek: Voyager* "Phage" (1995), "Lifesigns" (1996), "Resolutions" (1996), "Coda" (1997), and "Faces" (1995) tell of a struggling and suffering Vidiian species that could be cured with Klingon-derived genetic medicine, but the normally altruistic Voyager crew willfully chooses not to help. The Emergency Medical Hologram can make genetic modifications to B'Elanna's unborn child that would decrease medical risk, but he refuses, deeming them medically unnecessary *in Star Trek: Voyager* "Lineage" (2001). The *Star Trek: Enterprise* episode "Dear Doctor" (2002) tells of a doctor who has developed a cure for a genetic disease that affects the entire Valakian race, but chooses not to give them the cure so as to not disrupt nature.

These examples of critical attitudes towards genetic engineering and genetic medicine appear to be the dominant portrayal within the Star Trek universe, presumably reflecting the fears and uncertainties held by the writers about this emerging technology and its uncertain direction.

Analysis and Plausibility of *Star Trek*'s Depictions of Genetic Medicine

Evaluation of *Star Trek*'s depiction of technologies heavily depends on the perspective of the critic. On the one hand, Star Trek is responsible for introducing a sizable lay audience to challenging ideas, concepts, and possibilities that probe the limits of a mainstream TV audience's tastes and standards. Occasionally, it even reaches the threshold of being genuinely thought-provoking or even inspiring.[79] On the other hand, critics have mocked Star Trek for its melodramatic plotlines, TV western-in-space formula, and over-reliance on technobabble and nonsensical onscreen visuals intended to look technologically sophisticated.[80] Viewers with a background in science, technology, computer-science, and those who are familiar with more sophisticated (e.g., literary) science fiction are especially likely to notice where *Star Trek* falls short in terms of

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[79] Private space industry pioneers Elon Musk and Jeff Bezos have both cited Star Trek as an influence, and both have made cameos in the series either in person or mentioned by name. At the 2014 MIT AeroAstro Centennial Symposium, Musk commented on his inspiration: "When I was a kid I'd just consume, like, all science fiction and fantasy, you know, movies, books, anything at all, even if it was really schlocky. So, in terms of sort of key influences, I mean I certainly like Star Trek, because that actually shows like more of a Utopian future, like it's not, like, things aren't horrible in the future. It's like there's so many bloody post-apocalyptic futures, like okay can we have one that's nice? Just a few. So I like that about Star Trek."
https://www.youtube.com/watch?t=1h18m10s&v=4DUbiCQpw_4&feature=youtu.be&ab_channel=ElonMuskSoundBites

[80] Called "Okudagrams" in scripts, *Star Trek*'s high-tech looking onscreen graphics are named for Star Trek technical advisor Michael Okuda and often contain in-jokes, recognizable references, or nonsensical text visible only upon close inspection.

scientific accuracy. For the purposes of this analysis, I am not going to comprehensively categorize the overwhelming inaccuracy of *Star Trek's* representation of genetic medicine, beyond acknowledging that it is scientifically flawed in its presentation due to being generally vague, fabricated (e.g., "rybo-viroxic-nucleic sequences"), and conflating unrelated scientific concepts (e.g., theoretical physics and biological evolution).

Instead, I'm going to highlight a few ways that Star Trek's depiction of genetic medicine seems to reflect or align with the modern science. Briefly, I will review the following through the context of real-world medicine: the use of viral vectors in genetic medicine, the similarity of the fictional genetic resequencer to CRISPR-Cas9 gene editing, RVN therapy and RNA-based drugs, the use of T-cells in immunotherapy, and *Star Trek*'s treatment of transgenic medicine.

Viruses and Viral Vectors

Perhaps most striking is the number of examples of genetic medicine in *Star Trek* that involve viruses, either as a cause of genetic changes or employed as part of a treatment. As of this writing, both FDA-approved gene therapies (Luxturna and Zolgensma) use viral vectors in order to carry genetic material into cells.

As speculated earlier, the presence of gene-delivering viruses in *Star Trek* may have something to do with the elementary understanding that viruses can carry genetic code, but it is also curious that as early as 1966 *Star Trek* was implicating "a chain-reaction of viruses" as the mechanism for which the Life Prolongation Project's genetics section sought to extend life in the *Star:Trek: The Original Series* episode "Miri". Although it's probably nothing more than an uncanny coincidence, it was in the very

same year (1966) that scientist Edward Tatum first speculated that a virus might be used to transfer genes into cells.[81]

Given the use of viruses as vectors for gene delivery, it's reasonable to think that future applications of genetic medicine will consider viruses an essential component. Future uses of genetic medicine may include patient-doctor discussions about viruses, to determine ineligibility for example, through detection of pre-existing antibodies to a viral vector being considered in treatment. Doctors might discuss side-effects such as viral shedding following treatment, and use viral transfection rates as means to quantify the efficacy of a gene therapy dose. In short, viruses seem to play both a large role in *Star Trek*'s depiction of genetic medicine and the evolution of real-world applications.

DNA Resequencing and Similarities to CRISPR-Cas9 Gene Editing

The fictional device of a "genetic resequencer" reappears with the *Star Trek* universe and seems to describe a device that can modify DNA of animals, humans, and plants. Whereas the currently FDA-approved gene therapies rely on gene transfer delivery to cells, they do not reorganize or edit existing DNA.

Recent advances in chemistry, however, suggest that it may be possible to directly modify DNA through a chemistry-based "cut and paste" technique called CRISPR-Cas9 editing. This technique allows for precise targeted cutting of DNA molecules, and the precise insertion or deletion of DNA sequences (or entire genes) *in vivo.* On the surface, this seems to resemble the genetic resequencer in that it can directly change the genetic coding of subject.

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[81] E. L. Tatum, "Molecular biology, nucleic acids, and the future of medicine." *Perspect. Biol. Med*. 10, 19–32. 1966.

CRISPR gene-editing technology is fraught with bioethical considerations as it has the potential to modify the human genome with heritable changes. As such, its intended use in humans is controversial, with the United States National Academies of Science, Engineering, and Medicine (NASEM) concluding in 2017 that human genome editing is not permissible at present, but that it might be considered in the future for certain diseases.[82]

Biochemists Jennifer Doudna and Emmanuelle Charpentier won the 2020 Nobel Prize in Chemistry for their work in developing CRISPR-Cas9 gene editing.[83]

RVN and its Similarities to RNA-based Therapeutics

In the *Star Trek: Enterprise* episode "Rascals," members of the crew experience changes in gene expression as the result of insufficient adult rybo-viroxic-nucleic (RVN) sequences that purportedly regulate DNA gene expression. Although RVN is fictional, some clues suggest similarities to RNA that are worth exploring. First, RVN is distinguished from DNA, but specifically refers to a nucleic sequence, suggesting it may be the product of transcription like RNA (I will assume "rybo-viroxic" is mostly technobabble since the "ribo" prefix typically denoting ribose is misspelled, and "viroxic" appears to be a portmanteau of "virus" and "toxic"). Secondly, RVN seems to facilitate gene expression; those affected by RVN deficiency are unable to express genes associated with adult phenotypes. This gives us enough information to compare the proposed treatment of exogenous RVN to that of RNA-based therapeutics.

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[82] Brokowski C (April 2018). "Do CRISPR Germline Ethics Statements Cut It?". The CRISPR Journal. 1 (2): 115–125. doi:10.1089/crispr.2017.0024. PMC 6694771. PMID 31021208.

[83] The Nobel Prize in Chemistry 2020. NobelPrize.org. Nobel Media AB 2021. Mon. 15 Feb 2021. https://www.nobelprize.org/prizes/chemistry/2020/summary/

As of this writing there are nine FDA approved RNA drugs consisting of RNA molecules.[84] Five of these therapies are single-stranded anti-sense RNA molecules that bind to mRNA to modify gene expression. The other three therapies block gene expression through RNA interference or by binding to a target molecule. These could be considered a type of gene-modifying medicine, functioning as an intermediary between genetic coding protein synthesis, although these do not meet my initial definition of genetic medicine because they do not contain genetic coding sequences.

The fictional RVN and RNA-based therapeutics are similar in that they both seek to treat disease by replacing an intermediary molecule involved in the translation of DNA into proteins. A major difference, however, is that the changes in gene expression affected by the individuals in "Rascals" likely consisted of many hundreds of genes, whereas current therapeutic uses of RNA therapies is monogenic in scope, limited to targeting individual mRNA molecules with very specific mutation types amenable to that form of treatment.

T-cells and Genetically Modified Cell Therapies

The Star Trek: The Next Generation episode "Genesis" features an infectious disease that causes the crew to devolve to an evolutionary ancestor. The origin of this outbreak is worth briefly examining since it specifically references the use of T-cells. In this episode, the doctor introduces a synthetic T-cell to a patient in order to fight the infection "naturally" using the patient's own immune response. (Note: This is not an instance of genetic medicine in Star Trek, but rather the premise for the outbreak, which

[84] Kim, Young-Kook. "RNA Therapy: Current Status and Future Potential." Chonnam medical journal vol. 56,2 (2020): 87-93. doi:10.4068/cmj.2020.56.2.87

is later treated with genetic medicine). It's interesting that the authors would specifically mention T-cells and their ability to trigger immune responses, because this does parallel current forms of genetically modified cell therapies.

As mentioned in the prior section "Major Milestones in the Development of Gene Therapies," Kymriah was approved for the treatment of pediatric and young adult patients with a form of acute lymphoblastic leukemia, and Yescarta was approved for treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy. Both therapies were FDA approved in 2017, and both consist of genetically modified autologous chimeric antigen receptor T-cells (CAR-T). These cells target specific antigens expressed on the cell surfaces of leukemia and lymphona cells. T-cells are an important component of the immune system responsible for killing cells infected by pathogens. Treatments that leverage the body's natural immune response to fight diseases are part of the emerging field of immunotherapy (specifically immunoncology in the case of cancer).

There are a few similarities between "Genesis" and the immunotherapies in the real-world. In *Star Trek,* the T-cell is referred to as "synthetic." While the technologies do not exist to create truly synthetic cells, real-world CAR-T treatments involve complex intracellular engineering to allow greater replication and longer persistence once transplanted into patients.[85] CAR-T cell therapies are also genetically modified using the patient's own cells, which gives the patient's immune system abilities they would not otherwise possess.

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[85] National Cancer Institute. “CAR T Cells: Engineering Patients’ Immune Cells to Treat Their Cancers.” U.S. National Institutes of Health (NIH). Accessible Feb 14, 2020. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells

The Star Trek: Enterprise episode "Borderlands" also makes a specific mention to the use of a T-cell to "render Sharat Syndrome a thing of the past." Unlike "Genesis" from ten years earlier, this reference specifically says that the treatment is a DNA-based modification of a human T-cell, even more closely reflecting the science of CAR-T therapies that would be approved more than ten years following its airing.

Transgenic Medicine

A number of Voyager episodes discuss the use of Klingon DNA to treat the Phage, particularly *Star Trek: Voyager* “Resolutions” (1996), “Coda” (1997), and “Faces” (1995). The suggestion that a cure for a gene-altering virus might arise from harnessing the genome of a different (and exotic) species is an interesting nuance worth briefly addressing. Transgenic species are those created through the artificial insertion of genetic material from one species to another. Unlike in traditional breeding, transgenesis doesn’t require that the two species be closely related. Transgenic species were first created in the mid-1970s and have been routinely used in medicine to create genetic models of disease (e.g., knockout mice and oncomice).[86] Researchers also create transgenic species that express green fluorescent protein (GFR), a protein originally isolated from the jellyfish *Aequorea victoria* as a marker to label cells of interest. Transgenic cell cultures are routinely used by the biopharmaceutical industry to biomanufacturer therapeutic proteins.[87] But despite over forty years of transgenic use in

[86] Nishu Nishu, et al. Chapter 23 - Transgenic animals in research and industry, Animal Biotechnology (Second Edition), Academic Press, 2020, Pages 463-480, https://doi.org/10.1016/B978-0-12-811710-1.00021-5.

[87] Houdebine LM. Production of pharmaceutical proteins by transgenic animals. Comp Immunol Microbiol Infect Dis. 2009 Mar;32(2):107-21. doi:

medicine and medical research, transgene use in humans to address genetic diseases remains experimental, although with speculated potential. A possible use of transgenics might be to replace faulty or mutant genes in humans with replacement genes takes from other species. Another potential use is creating transgenic organs for transplant.[88] In the Voyager episodes discussing the use of Klingon DNA to treat the Phage, we see the real-world potentiality of transgenic medicine acknowledged, despite its continued experimental status.

Concluding Remarks and Future Directions

In conclusion, this research shows the ways that Star Trek's past portrayal of genetic medicine compares to the emerging practice and application of this technology. In this section I will briefly comment on the major findings and observations and suggest potential directions for future researchers.

Utility of an Expanded Definition of Genetic Medicine

As this research shows, Star Trek has indeed addressed some of the central ideas and explored the possibilities of genetic medicine in over the past five decades since it first aired. But as the examples show, many of these do not easily fall within a simple definition of gene therapy. In a universe of fantastic possibilities, where aliens procreate by reanimating corpses and evolution is accelerated when travelling at infinite velocity, it

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10.1016/j.cimid.2007.11.005. Epub 2008 Feb 19. PMID: 18243312; PMCID: PMC7112688.

[88] For an example of transgenic tissue creation in the Star Trek universe, see Star Trek: Enterprise “Similitude” in which a Lyssarrian Desert Larvae (a "mimetic simbiot") is used to clone tissue to address head trauma sustained in an accident.

makes little sense to apply rigid, real-world inspired boundaries on what constitutes "genetic medicine." This challenge of determining if a fictional description of a real-world technology meets a certain criterion is further complicated by Star Trek's reliance on technobabble and the outright exclusion of relevant scientific details.

This research suggests it is more valuable to embrace a loose definition of "genetic medicine," when evaluating science fiction through reality's lens. This is necessary to calibrate reality against the anything-is-possible framework imposed by science fiction. As my research shows, Star Trek's contribution and treatment comes into greater focus using a broad definition of “genetic medicine” and a reassessment of what constitutes "medicine."

From Genetic Enhancement to Treatment

In the *Star Trek* universe, it is suggested that following the Eugenics Wars there was a ban on all genetic engineering, including genetic medicine, and that genetic medicine was eventually permitted centuries later but only under tightly controlled circumstances. Gene modification for the purposes of curing disease was therefore virtually indistinguishable from gene enhancement for super-human strength or intelligence. Why is this? Shouldn't curing disease be uncontroversial? Why would Star Trek focus on the extreme and most controversial applications of genetic engineering technology (enhancement) rather than a noncontroversial and most likely first real-world use (addressing disease)?

A possible reason for grouping these together is to illustrate how ambiguous the distinction between "medicine" and "enhancement" is, or could be if allowed to proceed. As bioethicist Lee Silver warns, the foot-in-the-door for genetic enhancement may come

from relatively uncontroversial applications like treating disease. But once opened, we might see increasingly less medically necessary applications as we slide down a slippery slope towards eventual genetic enhancement. Perhaps Star Trek's willingness to jump to extreme uses is intended to force viewers to look past the more immediate and uncontroversial uses, extrapolating out to face what comes next. It also likely makes for more interesting and imaginative dramatic television.

Critical Attitudes Dominate

As previously noted, Star Trek's portrayal of genetic medicine, and genetic engineering in general, is predominantly negative. Genetic modification is depicted as the source of war, despotism, disease, and disaster. Genetic engineering is a tool used by enemies, criminals, the immoral, and the mad. Those who receive genetic modifications (especially enhancement) are ironically portrayed as broken, troubled individuals and outcasts. Medical professionals express some discomfort in using this technology, even in relatively justifiable or noncontroversial settings, such as eliminating disease. When it is used to eliminate disease, its side effect is multi-generational disfigurement.

A few minor examples of positive attitudes towards genetic medicine exist, but they are brief and fleeting. Instead, *Star Trek*'s portrayal is remarkably consistent and clear: the ability to modify genetics, be it for medical purposes or otherwise, is a Pandora's box that is best left unopened.

Future Directions

This research describes the ways that *Star Trek* portrayed genetic medicine over the past five decades, much of it critical. As real-world applications of genetic medicine

inevitably become a reality, it will be interesting to see if contemporary attitudes as evidenced by ongoing *Star Trek* series change. My research suggests that Star Trek writers relied on contemporaneous medical breakthroughs and best-guess extrapolations to imagine an uncertain future, being inspired by the science of the real-world. Future researchers might investigate the relationship between *Star Trek*'s imagined future and the actual future than came to be. Lastly, more work can be done ascertaining how *Star Trek*, with its global multi-decade reach, has influenced medical innovations in the other direction, by inspiring scientists to develop technologies that mirror fiction, bringing to reality *Star Trek*'s futuristic visions.

Definition of Terms

Adenovirus: any of a group of DNA viruses first discovered in adenoid tissue, most of which cause respiratory diseases.

Adeno-associated virus (AAV): a small virus that infects humans and some other primate species, is not currently known to cause disease, and causes a mild immune response. Used as viral vector for gene therapy.

Autologous: refers to cells or tissues obtained from the same patient.

Cell therapy: therapy in which living cells are injected, grafted or implanted into a patient. For example, immunotherapy uses CAR T cells to fight cancer cells via cell-mediated immunity

Chromosome: a long thin structure containing DNA found in the nucleus of most living cells and carrying genetic information in the form of genes.

Deoxyribonucleic acid (DNA): any of various double-helix-shaped nucleic acids located in cell nuclei that are usually the molecular basis of heredity, carrying genetic information in the cells of plants and animals

Episomal DNA: A segment of DNA that can exist and replicate either autonomously in the cytoplasm or as part of a chromosome, mainly found in bacteria.

Eugenics: the science and belief system associated with improving the genetic quality of a human population through selective breeding of groups believed to contain desirable genetic characteristics and exclusion of groups judged to be inferior. Often criticized on moral grounds.

Ex vivo: taking place outside of an organism, as in experiments or measurements done on tissue removed from an organism.

Gene: a unit of heredity comprised of a sequence of nucleotides forming part of a chromosome which is transferred from a parent to offspring and determines some characteristic of the offspring.

Genetic determinism: the idea or set of beliefs that that most human characteristics are determined or controlled by an individual's genes.

Gene expression: the process by which information from a gene is used in the synthesis of a functional gene product, often proteins.

Gene editing: the use of biotechnological techniques to make changes to specific DNA sequences in the genome of a living organism

Gene sequencing: the process of determining the order of nucleotides of DNA comprising a gene.

Gene therapy: the direct insertion of genes into cells to replace defective genes in the treatment of genetic disorders or to provide a specialized function

Genetic engineering: the direct manipulation of an organism's gene using biotechnology to change the genetic makeup of cells, including transfer of genes within or across species.

Genetic enhancement: the genetic engineering of humans for reasons beyond treating disease, such as to change physical appearance, alter metabolism, improve physical capabilities, or improve memory or intelligence.

Genome: an organism's complete set of DNA, including all of its genes.

Hematopoietic stem cell (HSC): the stem cells that give rise to other blood cells.

In vivo gene therapy: gene therapy in which gene transfer is performed on whole, living humans as opposed to a tissue extract.

Nucleic acids: molecules composed of nucleotides which encode and store genetic information of every living cell of every life-form. DNA and RNA are nucleic acids.

Optogenetics: biological control of a cellular process through the insertion of a gene encoding a light-sensitive protein

Promoter: a binding site in a DNA chain at which RNA polymerase binds to initiate transcription of messenger RNA by one or more nearby structural genes

Protein expression: see gene expression.

Recombinant DNA: A molecule of DNA that combines genetic material from multiple sources using laboratory methods, resulting in sequences that would not otherwise be found in the genome.

Ribonucleic acid (RNA): a nucleic acid present in all living cells whose main function is to carry instructions from DNA for controlling the expression of proteins.

Transcription: the process of constructing a messenger RNA molecule using a DNA molecule as a template with resulting transfer of genetic information to the messenger RNA

Transduction: the process by which foreign DNA is introduced into a cell by a virus or viral vector, as in gene therapy

Transfection: the process of deliberately introducing nucleic acids into eukaryotic cells.

Translation: the final step in gene expression where proteins are synthesized following the process of transcription of DNA to RNA

Star Trek canon: The set of all canonical material in the Star Trek universe. The official

Star Trek website defines canon as comprising the television series The Original Series, The Next Generation, Deep Space Nine, Voyager, Enterprise, Discovery, Picard, and Short Treks, as well as the feature-length films in the franchise.

Viral capsid: the protein shell of a virus which encloses genetic material

Viral vector: a genetically engineered virus designed to deliver genetic material into cells as part of gene transfer

Appendix 1.

Themes Identified Following Keyword Analysis

The following list contains the categorized themes identified following keyword analysis. Most of these themes are considered out of scope for this research but because they are indirectly related they may provide areas of additional focus for future researchers.

- genetic identification
- genetic engineering
- genetic medicine
- genetic enhancement
- cloning
- non-inherited genetic disease
- evolutionary genetics
- genetic testing
- genetic determinism
- genetic disease
- bioweapons
- gene-as-identity
- genetic memory
- organ creation/donation/transplant
- assistive repro tech
- interspecies hybridization/ compatibility
- genetic heredity
- genetic anxiety
- eugenics/selective breeding
- gene activation
- genetic diminishment
- genetic trait
- genetic diagnostics
- genetic disguise
- DNA-as-data
- DNA-as-commodity
- genetic ethics
- DNA complexity
- genetically engineered crops
- personalized genetics
- genetic screening
- genetic accidents
- genetic discrimination
- DNA-as-individual

Appendix 2.

Star Trek and Genetic Medicine: Recommended Works

The following is a list of Star Trek works directly referencing genetic medicine.

1. *Star Trek: The Original Series* “Miri” (1966)
2. *Star Trek: The Original Series* “Space Seed” (1967)
3. *Star Trek: The Next Generation* “Too Short a Season” (1988)
4. *Star Trek: The Next Generation* “Unnatural Selection” (1989)
5. *Star Trek: The Next Generation* “The Masterpiece Society” (1992)
6. *Star Trek: The Next Generation* “Rascals” (1992)
7. *Star Trek: The Next Generation* “Bloodlines” (1994)
8. *Star Trek: The Next Generation* “Genesis” (1994)
9. *Star Trek: Deep Space Nine* “In the Cards” (1997)
10. *Star Trek: Deep Space Nine* "Tears of the Prophets" (1998)
11. *Star Trek: Voyager* “Phage” (1995)
12. *Star Trek: Voyager* “Faces” (1995)
13. *Star Trek: Voyager* “Tuvix” (1996)
14. *Star Trek: Voyager* “Threshold” (1996)
15. *Star Trek: Voyager* “Lifesigns” (1996)
16. *Star Trek: Voyager* “Resolutions” (1996)
17. *Star Trek: Voyager* “Coda” (1997)
18. *Star Trek: Voyager* “Doctor Bashir, I Presume” (1997)

19. *Star Trek: Voyager* “Statistical Probabilities” (1997)

20. *Star Trek: Voyager* “The Raven” (1997)

21. *Star Trek: Voyager* “Chrysalis” (1998)

22. *Star Trek: Voyager* “Fury” (2000)

23. *Star Trek: Voyager* “Lineage” (2001)

24. *Star Trek: Enterprise* “Dear Doctor” (2002)

25. *Star Trek: Enterprise* “A Night in Sickbay” (2002)

26. *Star Trek: Enterprise* “Borderland” (2004)

27. *Star Trek: Enterprise* “Cold Station 12” (2004)

28. *Star Trek: Enterprise* “The Augments” (2004)

29. *Star Trek: Enterprise* “Terra Prime” (2005)

30. *Star Trek: Enterprise* “Affliction” (2005)

31. *Star Trek: Enterprise* “Divergence” (2005)

32. *Star Trek: Insurrection* (film) (1998)

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