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## Citation

Seung, E., A. Dugast, T. Dudek, H. Mattoo, V. Vrbanac, T. Tivey, T. Murooka et al. 2012. Neutralizing anti-HIV antibodies develop in a humanized mouse model of HIV-1 infection. *Retrovirology* 9(Suppl 2): P60.

## Published Version

doi:10.1186/1742-4690-9-S2-P60

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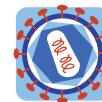
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POSTER PRESENTATION

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# Neutralizing anti-HIV antibodies develop in a humanized mouse model of HIV-1 infection

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From AIDS Vaccine 2012  
Boston, MA, USA. 9-12 September 2012

## Background

In BLT (bone marrow-liver-thymus) humanized mice, human thymocytes are educated by autologous human thymic tissue, resulting in functional human T cells capable of rapidly selecting for CTL escape mutations in HIV. In contrast, limitations to B cell maturation have been noted. But despite this, we show for the first time that HIV infected BLT mice can produce class-switched anti-HIV antibodies with neutralizing activities.

## Methods

Humanized BLT mice were generated by transplanting irradiated NOD-scid/IL2rgnull (NSG) mice with fetal thymus and liver fragments and then injecting them with autologous human CD34+ stem cells. BLT mice were then infected with HIV<sub>JRCSF</sub> and bled at various time-points. HIV neutralizing activity was measured using Tat-induced luciferase reporter TZM-bl cells.

## Results

Human transitional B cells were present in greater frequencies in BLT mice than adult humans. Most of these cells had a T1 phenotype in the blood and spleen. But despite this B cell maturation defect, class-switched IgG Abs against various HIV proteins were detected by Western Blot in HIV-infected BLT mice. Using ELISA to determine anti-p24 IgG Ab titers, Abs were present as early as 8 weeks post infection (p.i.), with peak Ab titers seen after 15 weeks. One infected mouse demonstrated a peak titer similar to that seen in a chronically infected human. Finally, plasma samples from infected BLT mice after 22 weeks p.i. demonstrated neutralizing activities against the challenge virus. Average IC<sub>50</sub> neutralizing

titers in these mice were similar to those from infected human samples.

## Conclusion

The ability of humanized BLT mice to generate functional humoral immune responses may be further improved by strategies to improve their B cell maturation, which will further improve the potential of these mice to become a model system to study candidate HIV vaccines and therapies.

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Published: 13 September 2012

doi:10.1186/1742-4690-9-S2-P60

Cite this article as: Seung et al.: Neutralizing anti-HIV antibodies develop in a humanized mouse model of HIV-1 infection. *Retrovirology* 2012 **9**(Suppl 2):P60.

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