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## Humanized Mice for the Generation of HIV-1 Human Monoclonal Antibodies


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## **Humanized Mice for the Generation of HIV-1 Human Monoclonal Antibodies**

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**Background:** Despite the length of time HIV has been wreaking havoc on its victims, improvements in the prevention and treatment of HIV are needed. Anti-retroviral therapy can be effective but is expensive and not entirely accessible for people infected in third world countries. Several promising broadly neutralizing antibodies have been isolated from infected individuals; we propose that generating antigen specific human monoclonal antibodies using humanized mice further represents a promising approach to engineer prophylactic antibodies to reduce spread and infection of HIV.

**Methods:** Immunodeficient mice were engrafted with fetal liver and thymus (BLT) prior to infection with different HIV isolates. HIV infection of the mice was monitored by viral load and antibody response followed by ELISA using gp120, gp41 or gp120/CD4 complex as antigens. Approximately 8-12 weeks post infection, spleens were harvested and splenocytes fused with human fusion partner HMMA 2.5 to isolate antibody-expressing hybridomas. Lead clones were scaled and purified for testing in functional assays such as TZM-bl neutralization assays as well as ADCVI to determine neutralizing and cytotoxic ability of the antibodies. Antibody sequences were also determined for analysis.

**Results:** A robust, specific antibody response, of both IgG and IgA isotypes, was generated in response to HIV infection. Over 60 hybridomas were created that were not only immunoreactive with env antigens, but also had neutralization activity. Moreover, variable family usage was not limited and somatic mutation was clearly evident.

**Conclusions:** These findings suggest that humanized BLT mice are a novel source for well-characterized, stable human monoclonal antibodies to HIV.

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