Retrovirology

Poster presentation

P03-02. SCID-hu mice generate HIV specific human immune responses after gp96 vaccination

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Background

NOD.SCID common gamma chain (NSG) knockout mice have no functional adaptive immune system of their own and readily accept human CD34+ hematopoietic stem cell xenografts (SCID-hu). These SCID-hu represent a unique opportunity to study human adaptive immunological responses in a small rodent animal model. We have previously developed a cell based vaccine system utilizing a secreted form of heat shock protein gp96 along with HIV gag protein (293-gp96Ig-HIVgag).

Methods

Day 1 neonatal NSG mice were sub lethally irradiated and transplanted with 10^6 human CD34+ hematopoietic stem cells intrahepatically. The pups were fostered, allowed to engraft and weened at 28 days. SCID-hu mice were vaccinated i.p. with 106 293-gp96Ig-HIVgag cells or 293 cells on days 0, 14 and 28. On day 33 the mice were sacrificed, spleen and peritoneal cavity cells (PEC) were harvested. 2×10^5 cells were plated in triplicate, stimulated for 20 hours with 20 μg/ml of SLYNVATL, HIV gag peptide, for an IFN-γ ELISPOT assay.

Results

Flow cytometry analysis of peripheral blood in pre-vaccination animals revealed human engraftment (mCD45 vs. hCD45) ranging from 4%–7%. Post vaccination analysis of the spleen indicated human engraftment ranging from 16–20%, PECs from SCID-hu after gp96 vaccination were primarily of human origin (90%–95%). SCID-hu vaccinated with 293-gp96Ig-HIVgag i.p. generated an HIV specific immune response. 293-gp96Ig-HIVgag vaccination generated an average of 778 spots per 2×10^5 cells plated whereas mice vaccinated with 293 cells alone generated an average of 88.5 spots per 2×10^5 cells plated ($p < 0.05$).

Conclusion

We conclude that SCID-hu mice are able to mount a human HIV-specific immune response after gp96 vaccination. Given the high cost of nonhuman primate models SCID-hu further represent an innovative way to study human immunological responses in a small animal model.