**Heterodimeric IL-15 Induces Effector Cell Activation and Trafficking to the Germinal Centers of SIV infected Macaques**

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**Background**

IL-15 stimulates the growth and activation of NK cells and cytotoxic lymphocytes. We have produced heterodimeric IL-15 (hetIL-15), the authentic form of IL-15 found in the circulation, and demonstrated that administration of hetIL-15 in macaques shows improved pharmacokinetics and pharmacodynamics compared to previous preparations of IL-15 without significant side effects. We have previously reported that therapeutic DNA vaccination together with pDNA encoding hetIL-15 in ART-treated macaques induces T cell responses able to control viremia after ART release.

**Methods**

Heterodimeric IL-15 (hetIL-15) was purified and tested in macaques upon subcutaneous (SC) administration. Phenotype and functional changes in lymphocyte subsets were monitored by flow cytometry and multiplexed confocal imaging (MCI).

**Results**

Treatment with hetIL-15 resulted in a significant increase of CD8+ effector T cells and NK cells with activated cytotoxic phenotype (Granzyme B). This expanded T lymphocyte population was distributed in the tissues and was also present in secondary lymphoid organs where an increased frequency of Ag-specific effector and total effector CD8 T cells could be observed by both flow cytometry and MCI. A subset of CD8 T cells present in lymph nodes expresses CXCR5, indicating that these cells are cytotoxic (Granzyme B) and actively proliferating (Ki67+) in response to hetIL-15.

**Conclusion**

We are exploring the potential of hetIL-15 as a viral reservoir reducing agent in ART-treated SIV infected macaques therapeutically vaccinated with DNA. Effective levels of hetIL-15 can be delivered without side effects. hetIL-15 treatment in combination with DNA vaccination enhances access to virus sanctuary areas (germinal centers) and is a promising HIV eradication strategy.