

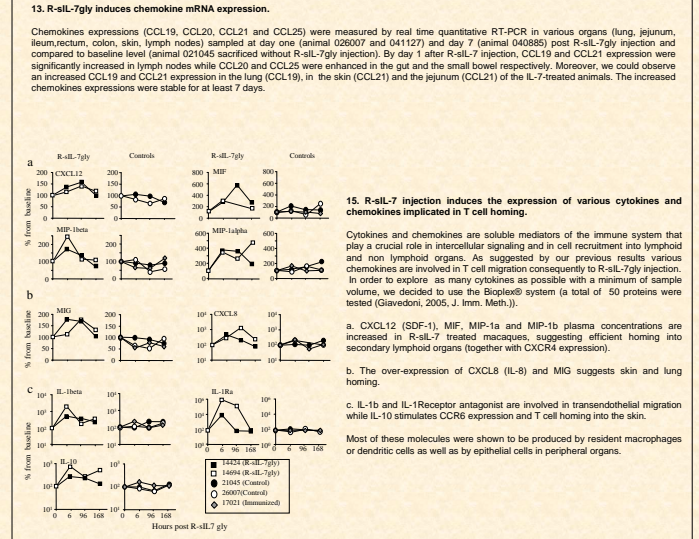
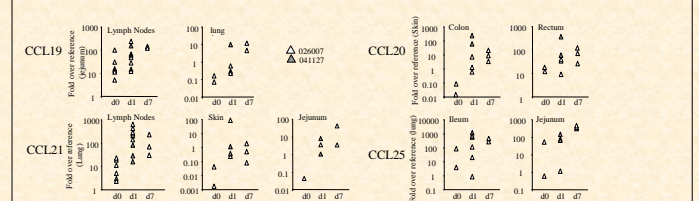
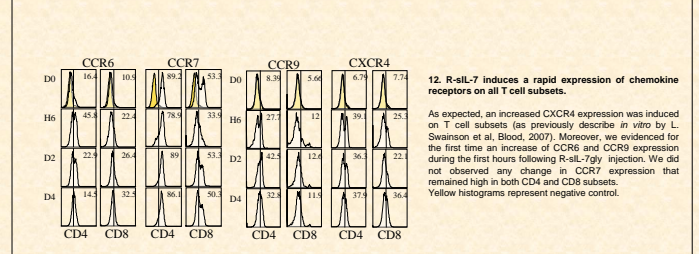
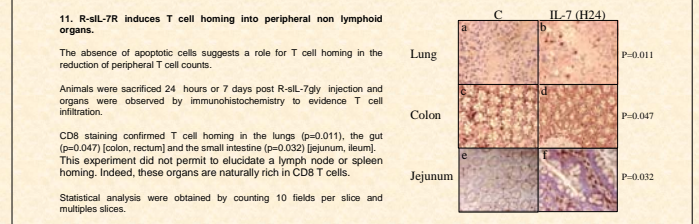
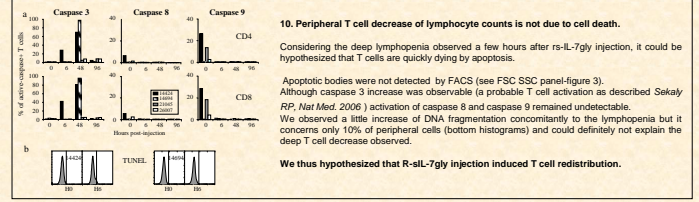
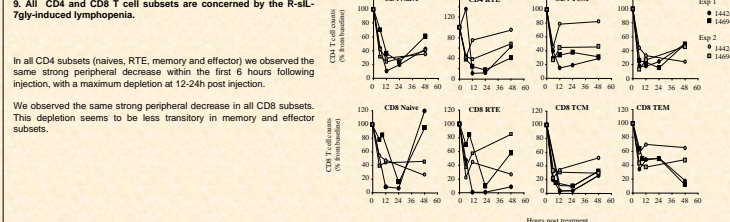
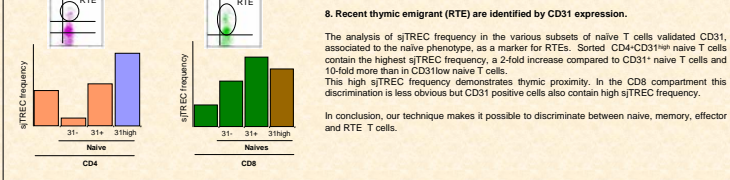
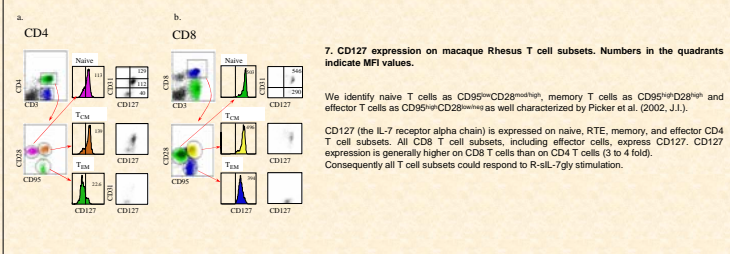
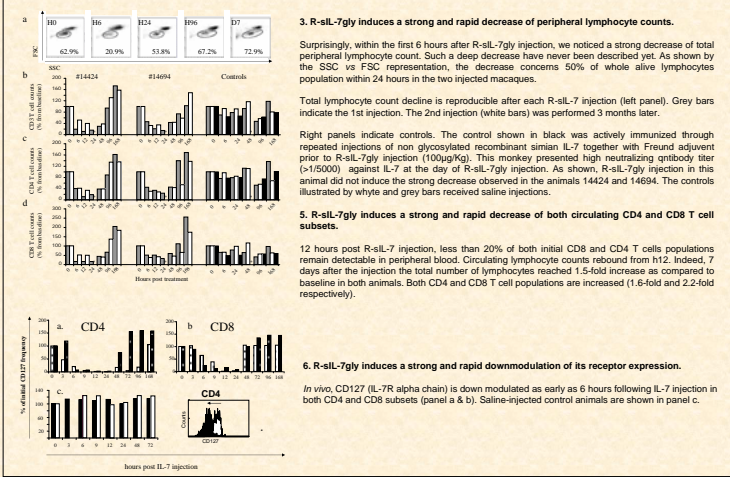
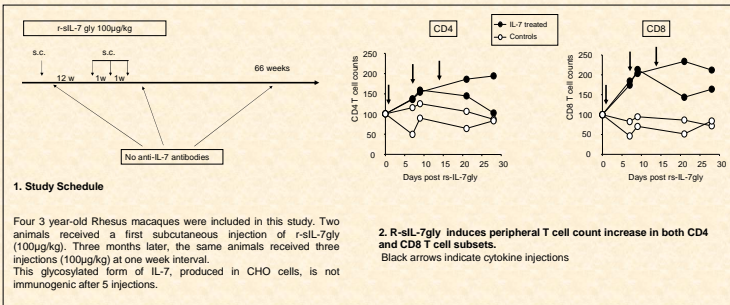
Early T cell homing following recombinant simian glycosylated IL-7 injection in Rhesus macaques

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Abstract: IL-7 plays a crucial role in T cell homeostasis, it sustains both thymocytes and lymphocytes proliferation and survival. Previous studies in macaque models have demonstrated that exogenous IL-7 induces the expansion of naive and memory peripheral T cell population 7 days after injection. Here we report for the first time a strong effect of R-sIL-7gly on T cell homing *in vivo*. We evidenced a strong decrease of total circulating T cell count (up-to 80%) as early as 9 hours post R-sIL-7gly administration. This phenomenon concern all T cell subsets including Recent Thymic Emigrants. Concomitantly, we observed all T cell subsets up regulate chemokine receptors (such as CXCR4, CCR6 and CCR9 but not CCR7) and that an increase of several chemokines was detectable. All these observations evidence that R-sIL-7gly induces a reorganization of T cell pool, probably inducing a massive homing.



Conclusions

Injection of non immunogenic recombinant glycosylated simian IL-7 to healthy Rhesus macaques leads to sustained increase of circulating T cell numbers in both CD4 and CD8, RTE, naive, memory and effector subsets.

However, we here evidenced for the first time that R-sIL-7gly induces, immediately after injection, a strong and rapid peripheral lymphopenia. This T cell depletion is probably a consequence of both chemokine receptor over-expression on T cells (CXCR4, CCR6 and CCR9) and up-regulation of chemokine/cytokine secretion (CXCL12, CXCL8, IL-10, IL-1β, IL-1Ra, MIP-1βeta, MIP-1α, MIG), leading to enhanced T cell homing out of circulating blood. Our observations evidence a new property of IL-7 that induces a strong and rapid T cell reallocation in lymphoid organs and various peripheral organs such as gut, lung and skin. As IL-7 is naturally produced in these organs and sequestered there on heparan sulfates, we hypothesize that this homing process is necessary to maximize the effect of the injected molecule by stimulating T cell localization where the cytokine concentration is maximal.