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Gene Engineering an HIV Resistant Immune System

We have a major effort in the laboratory to gene engineer an HIV resistant immune system. This work is done in collaboration with Prof. Karl-Heinz Krause (UNIGE, Geneva, CH) and Prof. Michael Pepper (University of Pretoria, South Africa).

For generating HIV resistant CD4+ T-cells, we have developed an optimized microRNA for down-regulating the HIV co-receptor CCR5. Using this microRNA we have gotten first-proof-of pre-clinical concept data that gene engineering HIV resistant CD4+ T-cells constrains HIV replication in vivo using humanized mice (functional cure). Briefly, we introduced the microRNA to CCR5 via lentiviral-based transduction into CD34+ cells and transplanted these gene-engineered CD34+ cells into the liver of new-born mice. 12 weeks later the humanized mice were infected with replication competent HIV.

We found that humanized mice expressing >50% of gene engineered CD4+ had HIV RNA copy numbers less than 5.000/µl – HIV-infected patients with such a low number of HIV RNA have a very protracted course of their HIV disease and in fact do not need any combined anti-retroviral treatment.

We are now working for identifying a 2nd anti-HIV target and getting all procedures/lab manipulations ready for a phase I clinical trial.