Co-receptor CCR5

In addition to its main receptor CD4, HIV uses C-C chemokine receptor 5 (CCR5) as a co-receptor to invade the host cell (see Fig. 1). Among other locations, CCR5 can be found on immune cells, such as T cells and macrophages, and plays a role in inflammatory reaction.

An estimated 1% of the European population carries a natural mutation, CCR5Δ32 (Fig. 2B), in both CCR5 alleles (paternal and maternal), resulting in the complete absence of CCR5 on the cell surface. Affected individuals are healthy and extremely resistant to HIV infection.

To date, the only confirmed cure of an HIV infection in 2008 was based on the CCR5Δ32 mutation. To treat his acute leukaemia, an HIV-positive patient (also known as the 'Berlin Patient') received a stem cell transplant from a donor, who was homozygous (both alleles affected) for the CCR5Δ32 mutation. Even today, after more than 10 years, the 'Berlin patient' is free from detectable HIV without receiving antiretroviral therapy.

One of the goals of our collaborative project is focused on the development of special gene scissors, such as the so-called TALENS (Fig. 2A) to switch off the CCR5 gene in the cells of HIV-infected patients and to protect the cells from infection by the virus. We can already successfully establish that in cell culture experiments (see Fig. 2C), and a clinical study is planned.

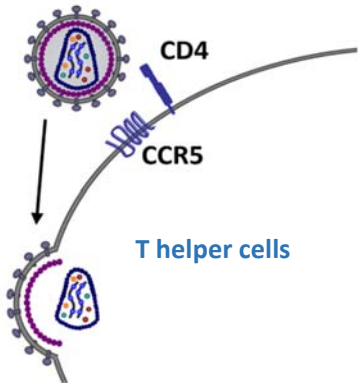

Figure 1: Most HIV strains require C-C chemokine receptor 5 (CCR5) as a co-receptor to invade the host cell

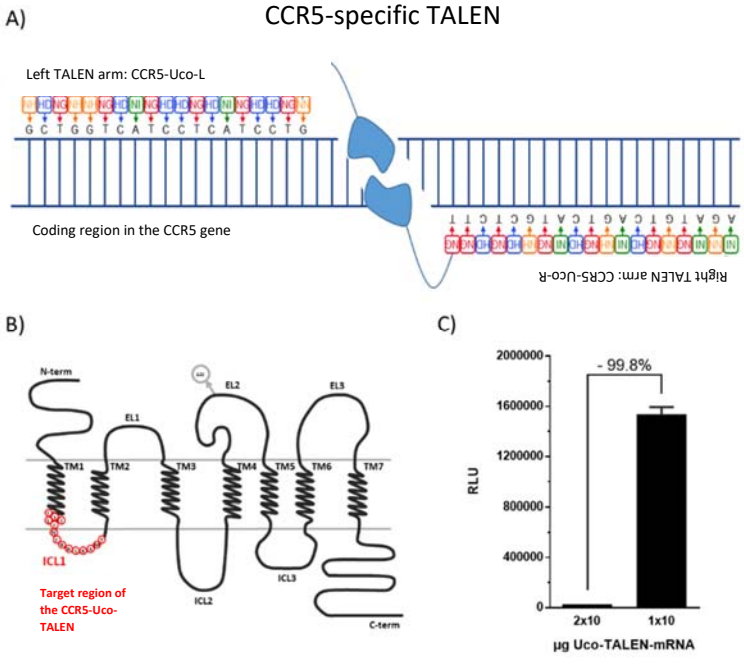

Figure 2: A) A CCR5-Uco-TALEN splices the coding region of the CCR5 gene, eliminating all functional receptors on the cell surface. C) The CCR5 knockout leads to almost complete suppression of HIV replication *in vitro*. [Mock et al., *Nucl Acids Res* 2015]