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Oral presentation

Highly potent, fully recombinant RANTES analogues represent promising new candidate microbicides

Oliver Hartley*

Address: Faculty of Medicine, Department of Structural Biology and Bioinformatics, University of Geneva, Geneva, Switzerland
* Corresponding author

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Targeting CCR5 is a valid strategy for microbicide development. PSC-RANTES, a chemically modified variant of one the natural protein ligands of CCR5, is a potent HIV entry inhibitor that has shown significant activity in a macaque vaginal challenge model. PSC-RANTES itself is unlikely to be developed for clinical use as a microbicide, however, since (i) the production costs are likely to be too high for it to meet the needs of developing countries, and (ii) it strongly activates CCR5; if long-term use were to give rise to pro-inflammatory effects, this could counterbalance its inhibitory activities against HIV acquisition.

We have been using an innovative phage display approach to discover novel, potent, fully recombinant RANTES analogues which could be produced entirely by biosynthesis, and thus at a much lower cost than PSC-RANTES. The resulting molecules have been tested in vitro for anti-HIV potency, as well as their capacity to activate CCR5.

Among the new molecules that we have identified and tested is 5P12-RANTES, which (i) has comparable potency to PSC-RANTES in all tests conducted so far (ii) contains only natural amino acids and could therefore be produced could be produced entirely by biosynthesis, and (iii) has no detectable signaling activity on CCR5.

Highly potent, fully recombinant RANTES analogues such as 5P12-RANTES represent promising candidates for development as microbicides.