

Update on 5P12-RANTES rectal gel

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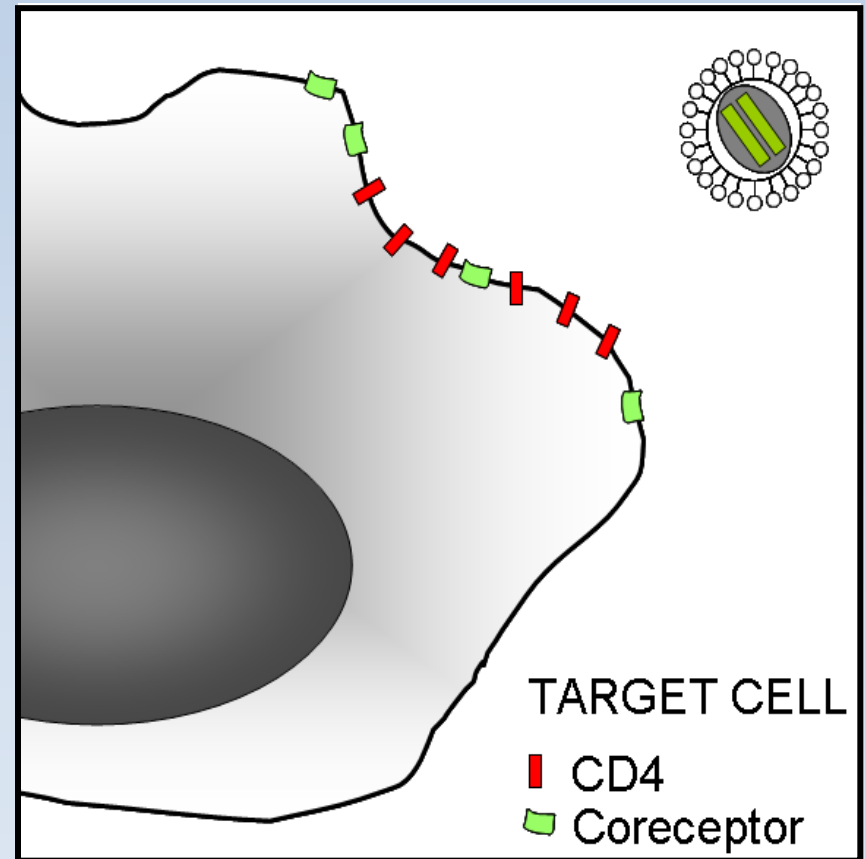
Mintaka Foundation for Medical Research

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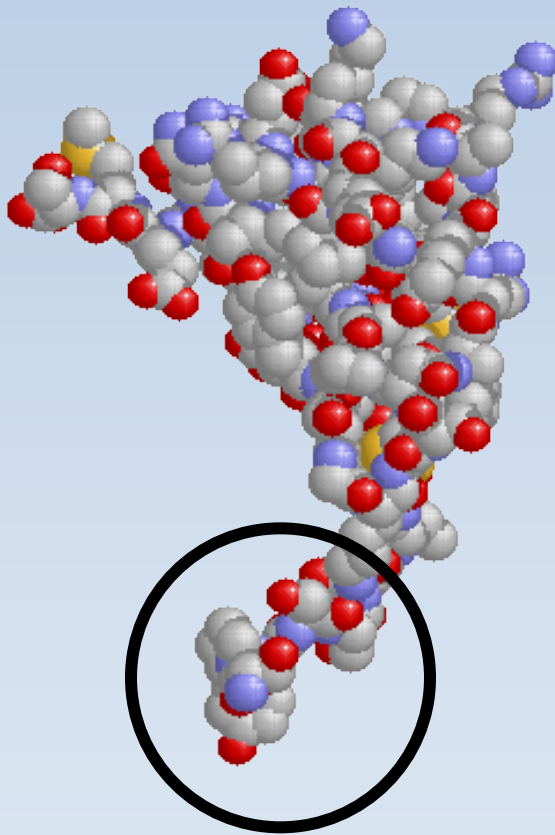


CCR5 is a valid target for microbicide development

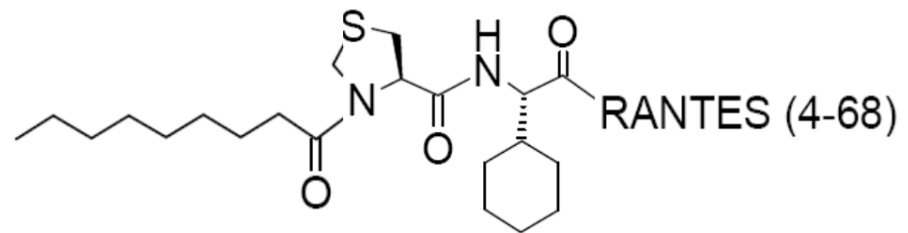
- HIV is almost completely dependent on CCR5 for person-to-person transmission
- People genetically deficient in CCR5 are healthy but almost completely resistant to HIV infection



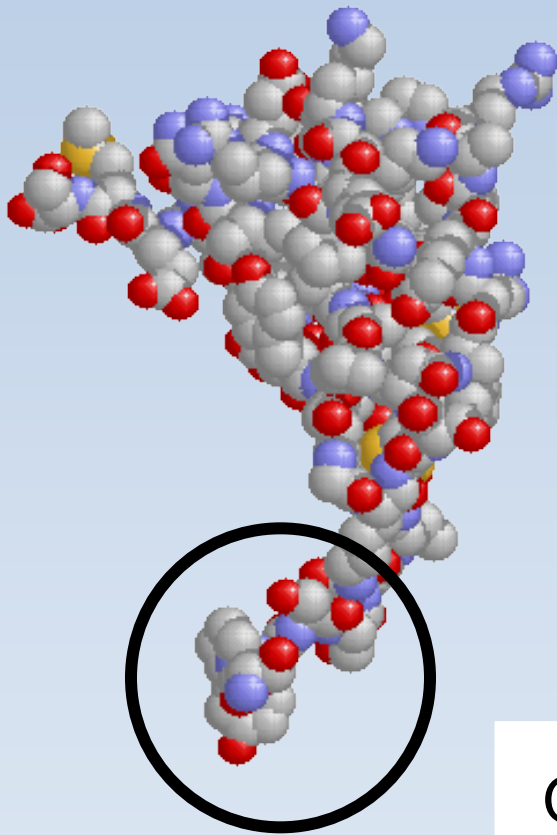
PSC-RANTES



- Highly potent in vitro (25 pM)
- Fully protects female macaques from viral challenge (1 mM)
- Production requires chemical synthesis
- CCR5 signaling activity



5P12-RANTES



- Highly potent in vitro (28 pM)
- Active in explant challenge experiments
- Fully protects female macaques from viral challenge (1 mM)
- Recombinant production possible
- No signaling activity on CCR5

Q-G-P-P-L-M-A-T-Q-S-RANTES(10-68)

Other key preclinical parameters

Good safety profile

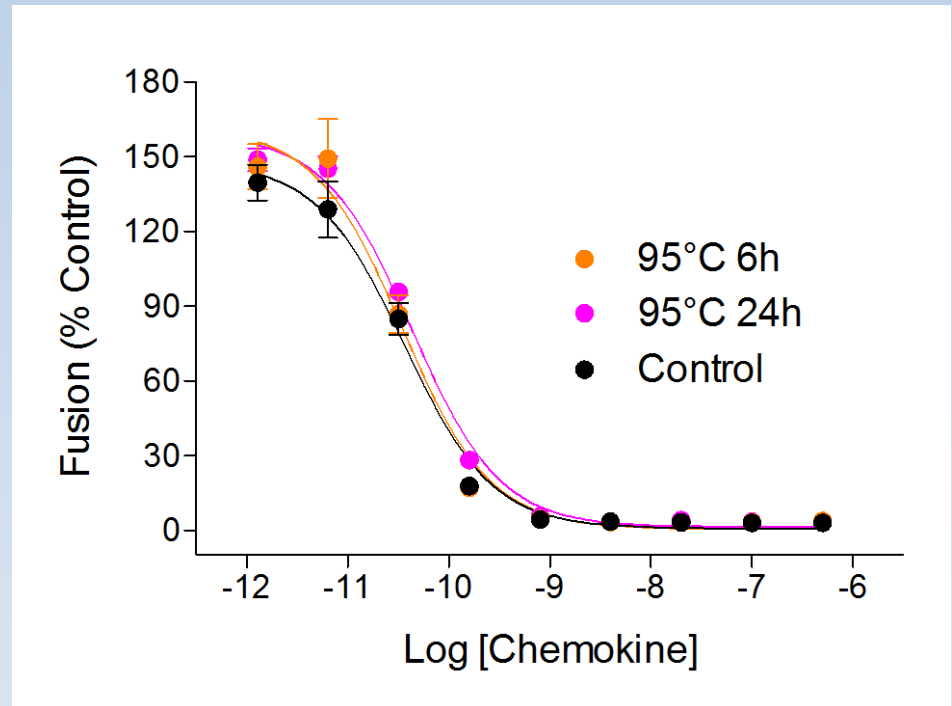
- *In vitro*
- *Ex-vivo* (explants)
- *In vivo* (macaques)

Very high barrier to resistance

- So far not possible to generate viable escape mutants *in vitro*
- Maraviroc escape mutants are sensitive to 5P12-RANTES

Excellent intrinsic stability

- Extremely heat-stable
- Stable at vaginal pH
- Stable in the presence of human CVL
- Stable in the presence of human semen



Stability in rectal lavage samples
to be tested in the near future

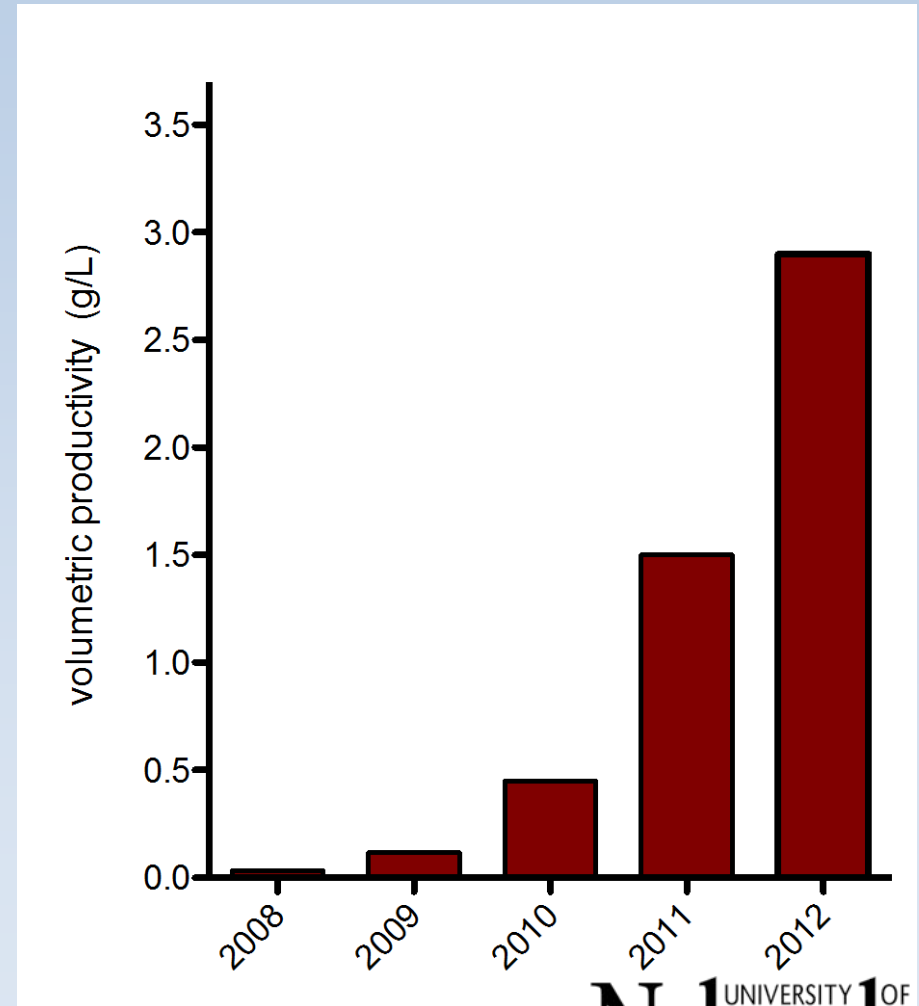
Pennies-per-dose can be envisaged

- cGMP proteins can be produced at high scale and low cost
- 5P12-RANTES expressed in *Pichia* yeast



Pennies-per-dose can be envisaged

- cGMP proteins can be produced at high scale and low cost
- 5P12-RANTES expressed in *Pichia* yeast
- Strain optimization
- Low cost, scalable purification process developed
- Final target cost: ~\$2 per gram



cGMP production is underway

Formulation

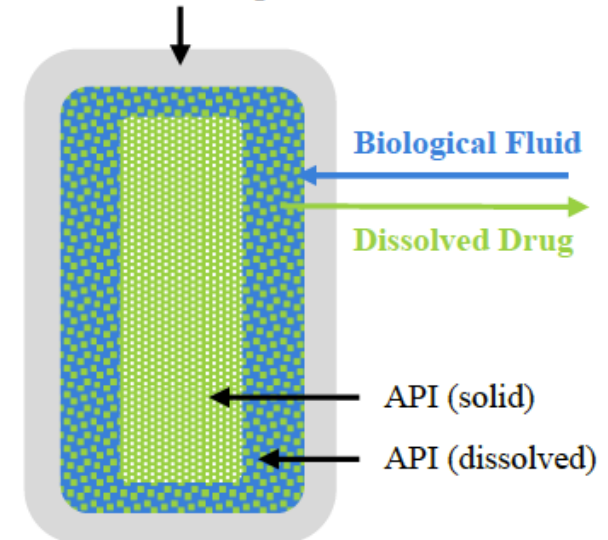
- Initial formulation strategy is isotonic HEC gel, pH 4.4
- Other formulation strategies are being pursued
 - Sustained release
 - Coital independence

Karl Malcolm

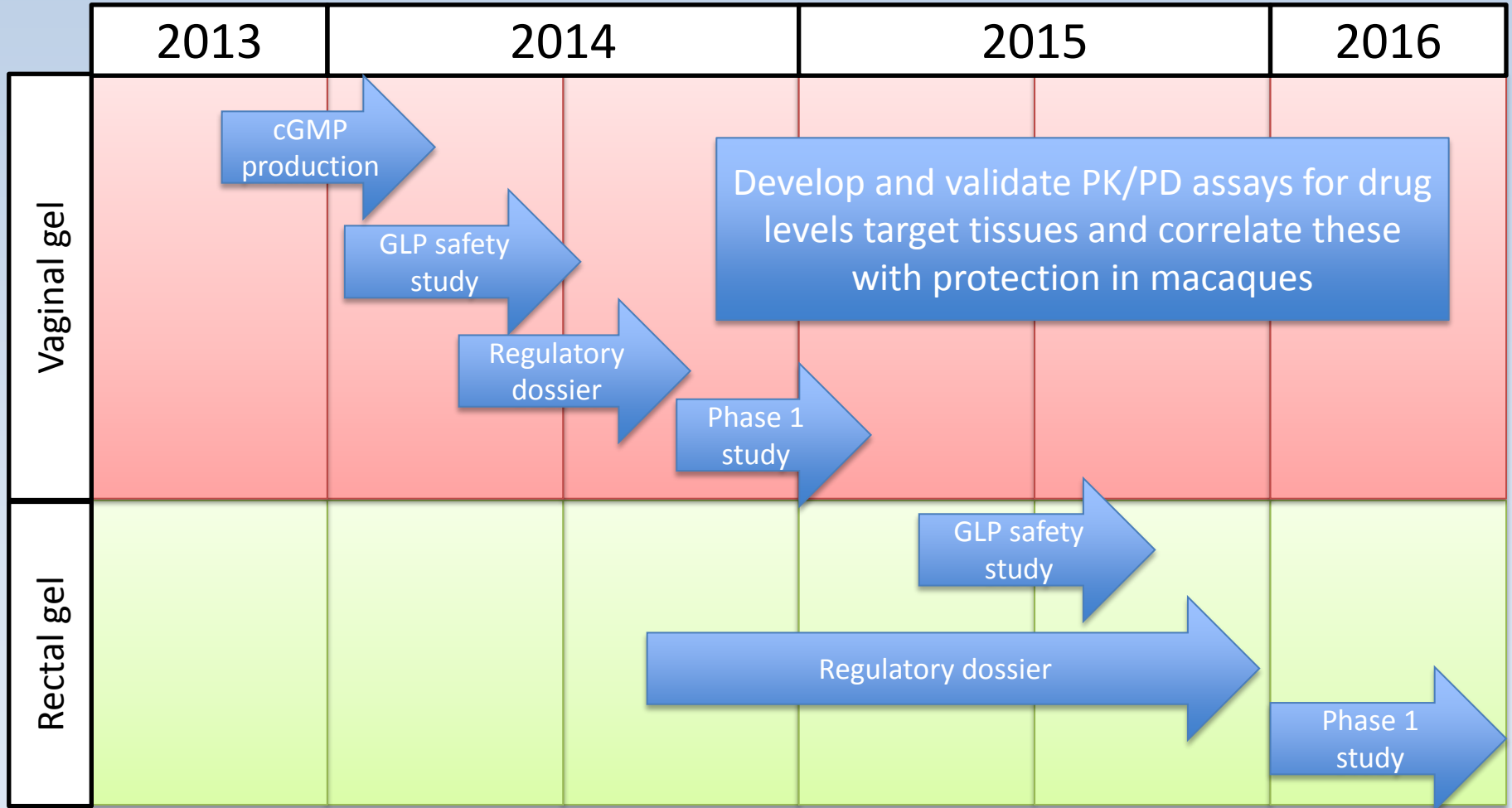
Ariane van der Straten



Thin film semi-permeable membrane



Projected timelines



Thank you for your attention!



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