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P13-06. DARPin-based microbicide strategies to block HIV entry

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Background

Microbicide strategies against HIV must interrupt the critical cell-virus interactions that lead to infection, including envelope interactions with CD4, chemokine receptors, and C-type lectin receptors. We have recently identified a novel, highly specific approach to inhibit HIV infection using the Designed Ankyrin Repeat Protein (DARPin) technology [1]. DARPins are based on the principle of naturally occurring ankyrin repeat proteins, and binders can be selected against targets with high affinity and specificity from randomized libraries. These features, combined with a remarkable physical stability and relatively low cost production in procaryotes render DARPins extremely promising candidates for the selection of HIV inhibitors.

Methods

DARPin molecules specific for a HIV gp120 core stabilized in the CD4 bound state [2] were selected via ribosome display.

Results

Off-rate selection allowed the selection of DARPin binders with highly specific binding and antiviral activity against autologous as well as heterologous viral isolates.

Conclusion

Our initial proof of concept studies documented the selection of CD4-specific DARPins that are highly specific and efficiently prevent *in vitro* infection with a wide range of HIV as well as SIV isolates at nanomolar levels, without interfering with basic cellular functions [3]. We now report on the identification of gp120 specific DARPins with inhibitory activity.

References

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