UNIVERSITÄT LEIPZIG

Medizinische Fakultät

Establishment of a computational vaccine development pipeline for emerging viral diseases – a case study on Lassa virus

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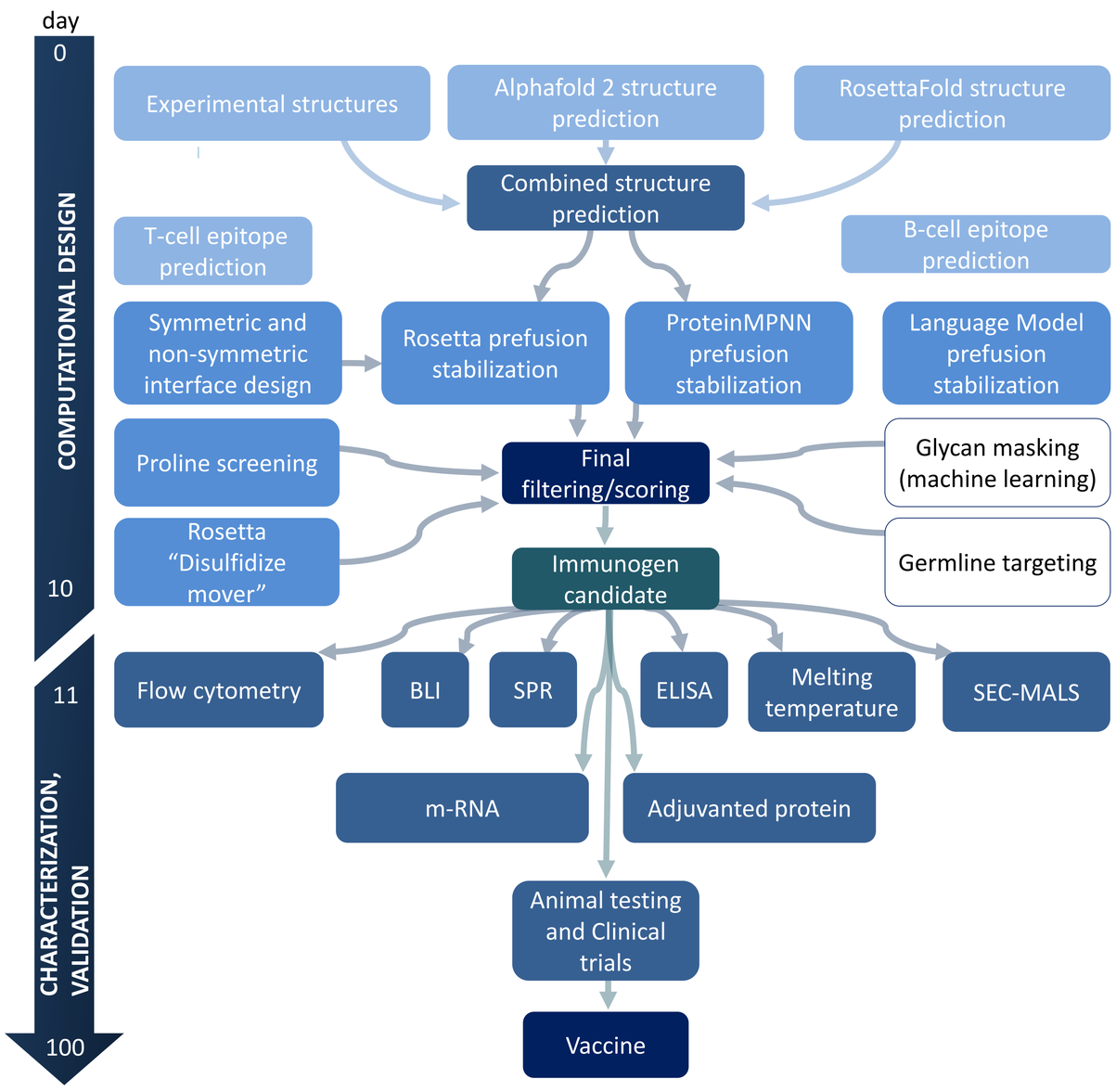
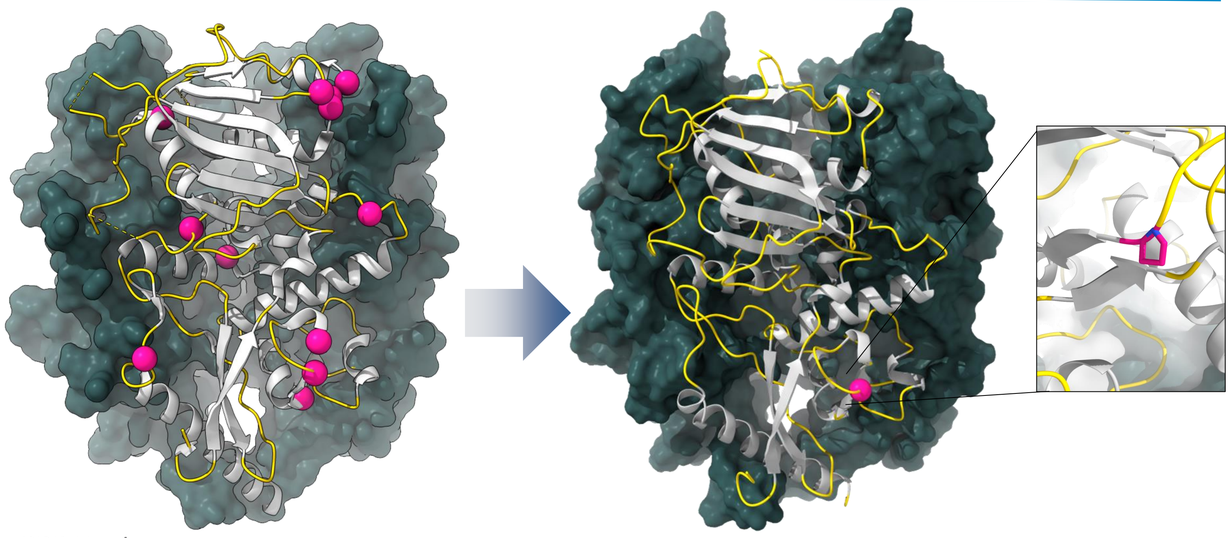
COMPUTATIONAL VACCINE DESIGN PIPELINE

AIM: Improvement of pandemic preparedness by creation of a modular protein analysis and design pipeline that can be run within 7-10 days and a vaccine library that stores vaccines.



PROLINE DESIGN



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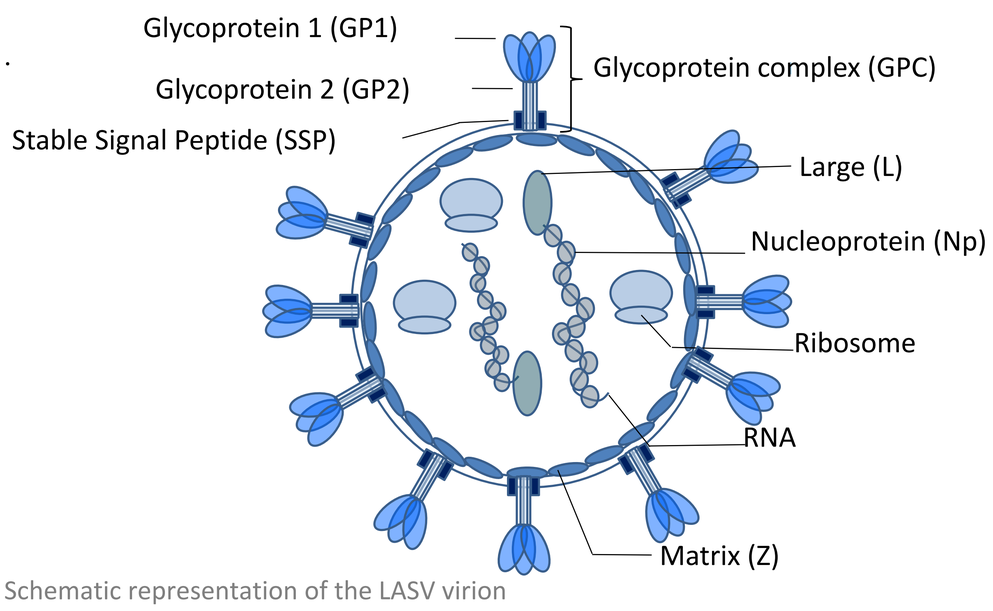
Prolines stabilize interdomain links by reducing the degrees of freedom and forcibly introducing turns. They are introduced by Protein MPNN at turns between two structured domains, at the end of helices or within long partially structured loops. We were able to identify twelve positions where the indtroduction of prolines could have a stabilizing effect

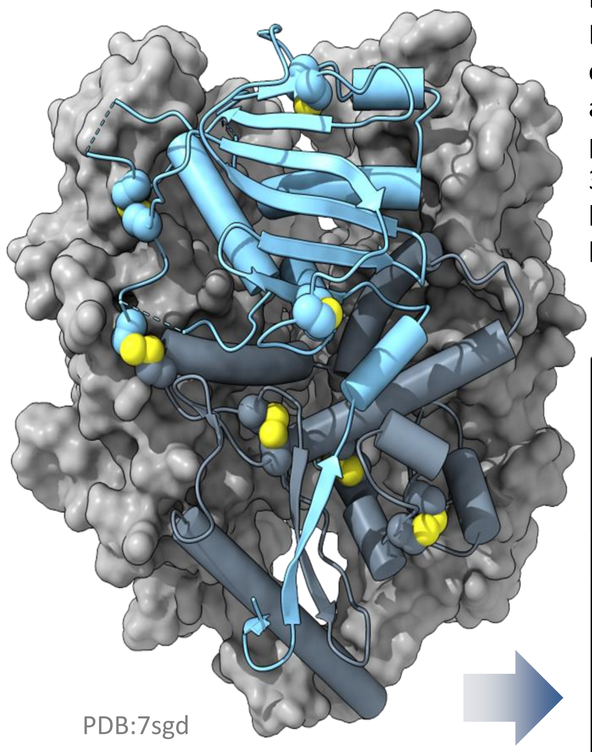
CASE: LASSA VIRUS

Lassa virus (LASV) is endemic to rodent populations (*Mastomys natalensis)* of western Africa. Spillover infections to humans and human to human transmission can occur and cause hemorrhagic fever, also referred to as Lassa fever. Infections can have a case fatality rate of up to 26% [1, 2] LASV entry into the host cell is mediated by the only viral surface protein, the Glycoprotein complex (GPC). It is the dominant immunogen and therefore a prime-target for vaccine induced immunity. It is comprised of the GP1, GP2 and stable signal peptide (SSP) and a Class I fusion protein and undergoes dramatic changes after attachment and cell entry [3].



Schematic representation of the LASV virion

DISULFIDE CHAIN LINK DESIGN



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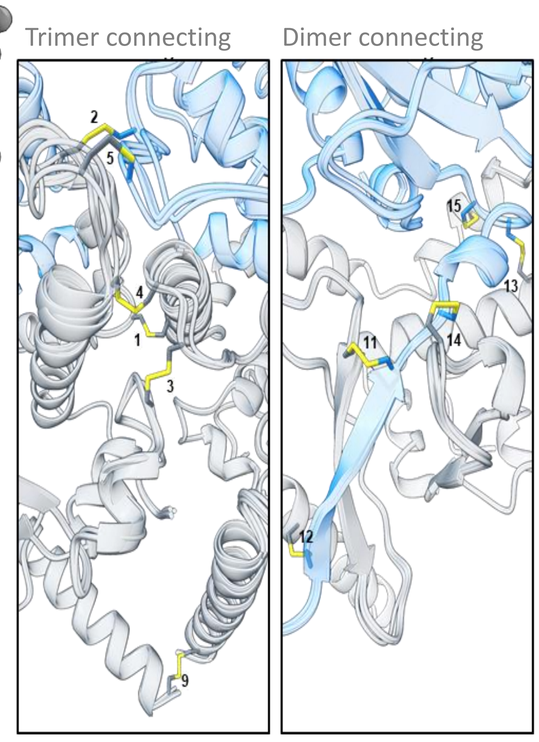
Disulfide bridges stabilize the wild type LASV Josiah GPC dimer. There are three conserved disulfide-bridges in each GP1 and GP2 domain. It was identified previously that the introduction of 207C–360C leads to a stabilization [4]. So far no homotrimer connecting disulfide has been identified.



We were able to identify nine GPC-trimer connecting and six GP1-GP2 connecting disulfide bridges with the Rosetta Disulfidize mover that could potentially be stabilizing.

CONTACT

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REFERENCES

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