

Characterization of antibody-antigen binding interactions aimed to develop an *In Vitro* Potency assay for *Strep A* vaccine

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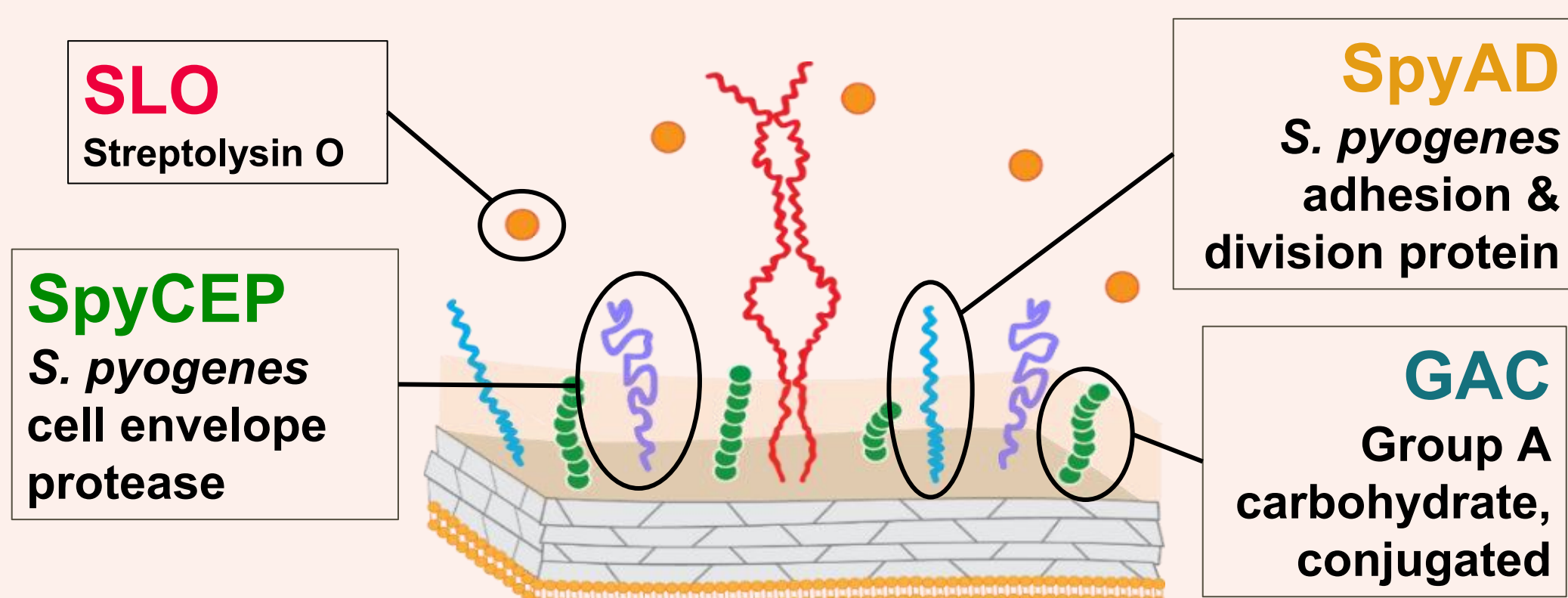
Introduction

Group A *Streptococcus* (GAS) is an important human pathogen, responsible for a significant and diverse global disease burden, from mild conditions such as **impetigo** and **pharyngitis**, to **life-threatening diseases** (ARF, RHD)

1.8m
New Strep A
infections per year

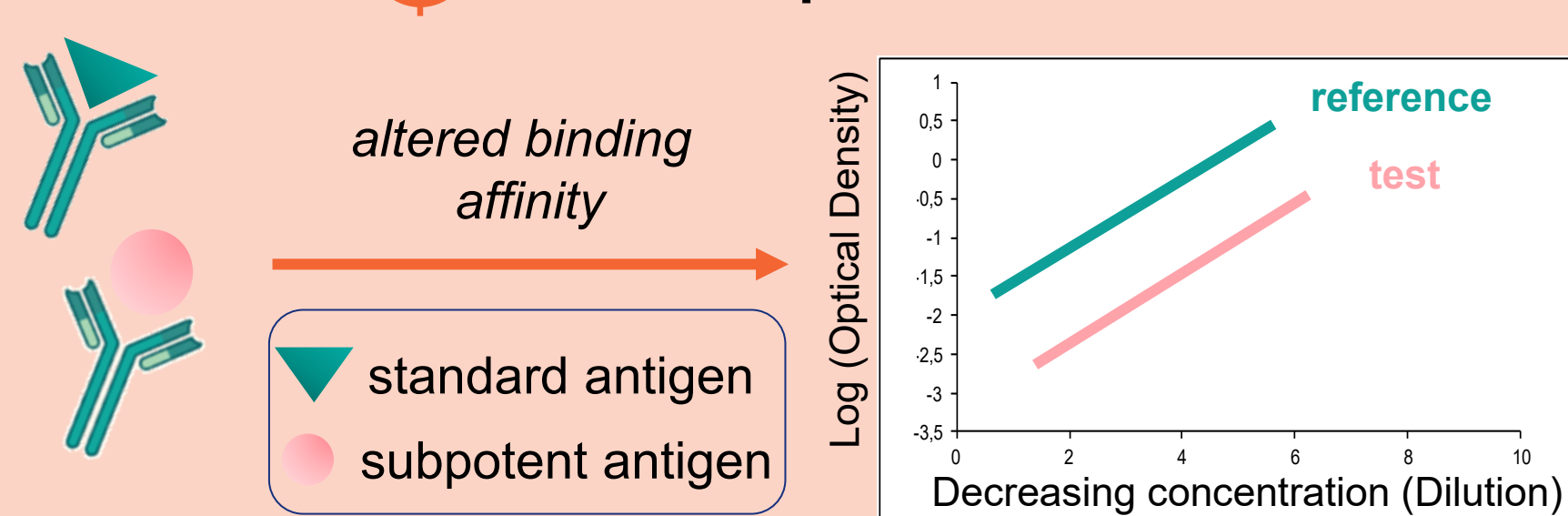
GVGH is currently developing a **4 component vaccine**, targeting multiple Strep A mechanisms of pathogenesis

500k
Annual deaths by
Strep A infections



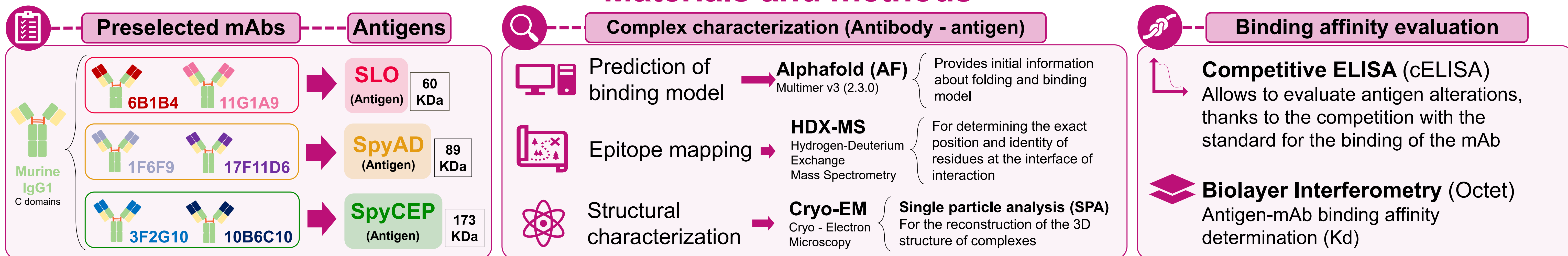
Objectives

Development of an **IVRP** (*In Vitro* Relative Potency assay)

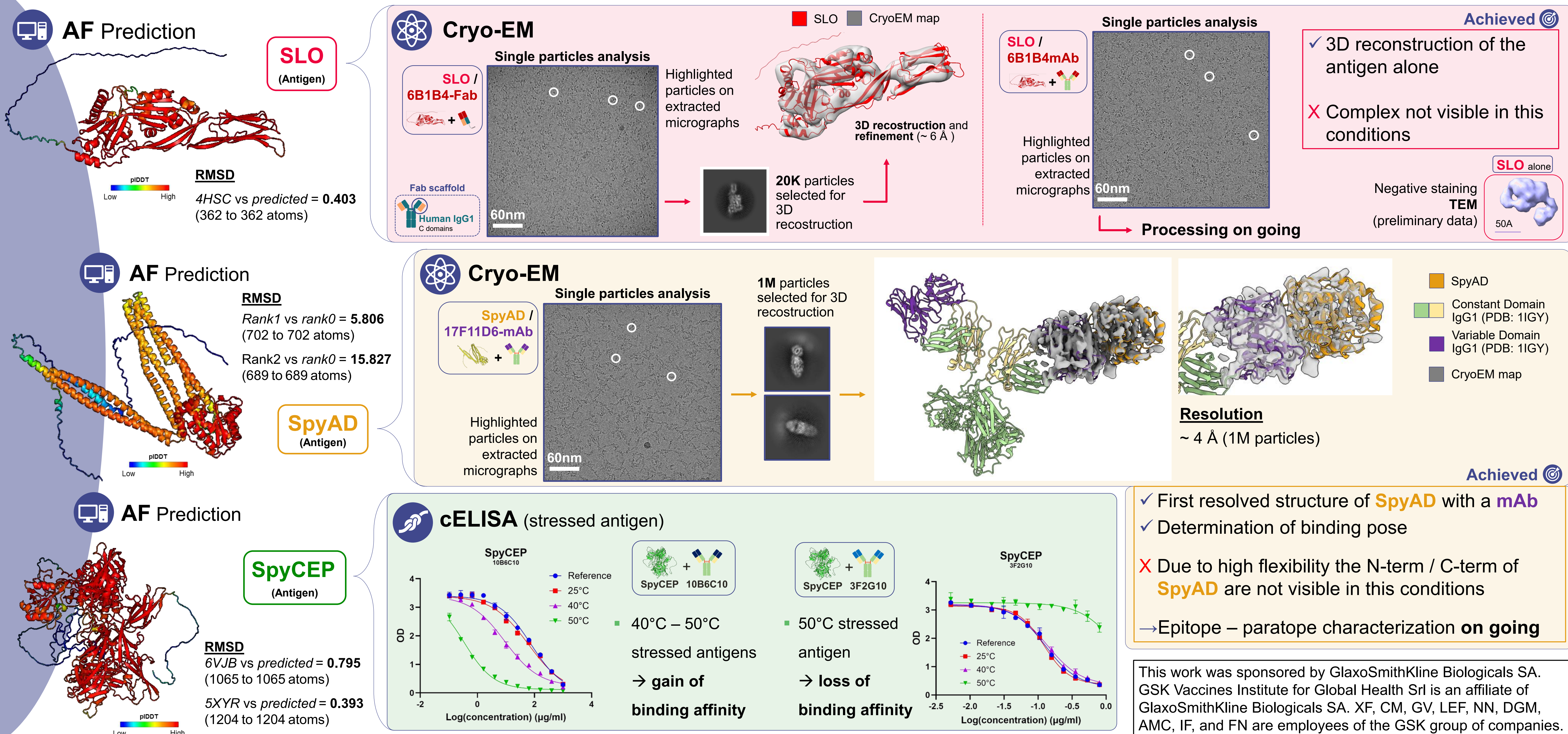


- To **evaluate** the **efficacy** and the **long-term stability** of the novel StrepA vaccine candidates
- To **correlate** **in vitro potency** of an antigen with **in vivo immunogenicity**
- To **replace** the use of **in vivo** with **in vitro** assay

Materials and methods



Results



Conclusions

- Reconstructed a **6 Å resolution map** of the **SLO** antigen.
- The **cryoEM 3D map** confirm the preliminary evaluation by **Negative Staining** and **AF prediction**.
- The **4 Å map** of the **SpyAD** and **17F11D6-mAb** complex helps with the characterization of the interaction.
- The determination of the binding model could drive the selection of the most suitable mAb for the **IVRP**.
- Our data suggest **10B6C10-mAb** recognize a **linear epitope** while **3F2G10-mAb** a **conformational epitope**. The result could be confirmed via the **structural characterization** of the two complexes mAb-SpyCEP.

Next Steps

- Cryo-EM** experimental conditions optimization to observe **SLO** in complex with **6B1B4 mAb**
- Epitope mapping** via **HDX-MS** to complement the structural data determined via **Cryo-EM**
- Binding characterization** of mAbs via **Octet** / **cELISA** with thermally stressed antigen
- Binding characterization** of mAbs via **Octet**
- Cryo-EM structural characterization** of the two complexes **SpyCEP+3F2G10** / **SpyCEP+10B6C10**