Microsymposium

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Structure-based Vaccine Development (Structural Vaccinology)

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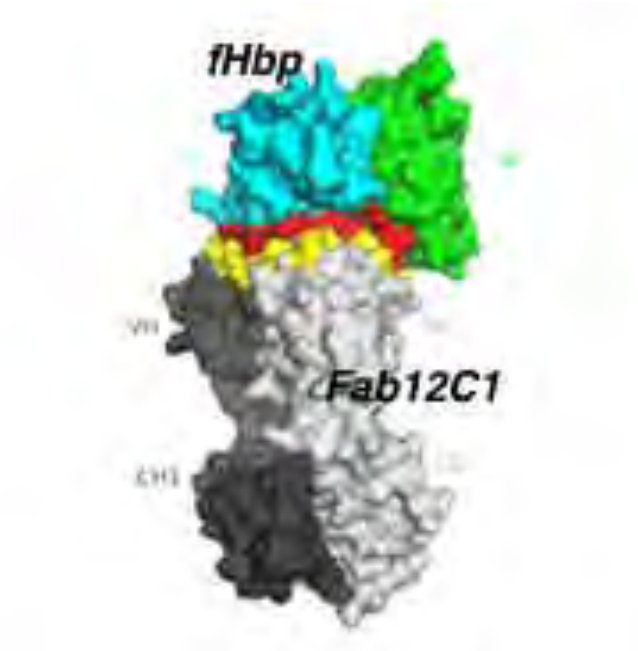
Structural biology is playing an increasingly important role in vaccine development, as it can facilitate the rational design of vaccines by allowing an atomic-level control of their antigenic and immunogenic properties. Several cases are now available that demonstrate the potential of structure-based methods for vaccine development. Here, I will present an overview of the insights we gained at Novartis Vaccines from studying two protein antigens of the recently approved vaccine against serogroup B meningococcus (MenB), and their impact for vaccine design and development. MenB causes severe sepsis and invasive meningococcal disease (IMD), particularly affecting young children and adolescents. In 2013, the first genome-derived vaccine, which targets MenB (4CMenB), was approved for use in Europe, and it is expected to become widely implemented in Europe beginning in 2014. The vaccine contains 3 previously unknown recombinant proteins discovered by genome mining. For one of the antigens, Factor H Binding Protein (FHBP), we recently generated a broadly protective chimera by a structure-based approach that consisted in grafting multiple immunodominant regions onto a single scaffold. Also, co-crystal structures of FHBP with Fabs from monoclonal antibodies provided insights into the molecular bases of the immune recognition and bactericidal activity. The structure of a second antigen, Neisserial adhesin A (NadA), a member of the Trimeric Autotransporter Adhesins (TAA), revealed a novel fold, while epitope mapping by Hydrogen-Deuterium Exchange Mass Spectrometry showed that in addition to being the receptor-binding domain, the head domain of NadA is also the target of a bactericidal monoclonal antibody. Overall, the structural information on the MenB antigens presented here provides important details on the pathogenesis and vaccine-induced immunity against meningococcus, and especially informs the engineering of improved immunogens by structure-based design.

[1] *Scarselli, M., Aricò, B., Brunelli, et al. Science Translational Medicine, 2011, 3(91), 91ra62.,* ***[2]*** *Malito, E., Faleri, A., Lo Surdo, P. et al. Proceedings of the National Academy of Sciences of the United States of America, 2013, 110(9), 3304–3309.,* ***[3]*** *Malito, E., & Rappuoli, R. Chemistry & Biology, 2013, 20(10), 1205–1206.*



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