Jacinto Lopez-Sagaseta, J Proteomics Bioinform 2016, 9:10(Suppl)
http://dx.doi.org/10.4172/0974-276X.C1.088

6th International Conference on
Structural Biology
August 22-23, 2016 New Orleans, USA

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Crystal structure of a human Fab in complex with a dominant antigen from *Neisseria meningitidis*

Anchored yet exposed to the outside moiety of the bacterial shell, Factor H binding protein (fHbp) is one of the main antigenic components of *Neisseria meningitidis*, one of the causative agents of *meningitis*, an infectious disease that can cause a fatal outcome or permanent disability within 24 hours of infection. Though there have been described up to three different variants of fHbp, it is fHbp variant 1 (fHbp-1), the subclass showing the highest prevalence amongst MenB strains, and also one of the actual components of Bexsero, the current licensed vaccine against serogroup B Meningococci (MenB). In order to define the structural basis that underlie the recognition of this highly immunogenic antigen and the broad strain coverage offered by Bexsero, we have determined the crystal structure of a complex between a human Fab and fHbp-1 at a resolution of 2.2 Å. The Fab has been originated from an immunization study that included a recombinant form of fHbp-1, and importantly, it is cross-reactive against all of them. The cross-reactive epitope spans along the c-terminal beta barrel of fHbp and encompasses residues that are highly conserved across the different fHbp variants. The hypervariable CDR3 loop of the heavy chain dominates the recognition of the antigen. This crystal structure represents the first evidence, at the atomic level, of the recognition of *Neisseria meningitidis* fHbp by a human Fab raised in an individual upon vaccination, and provides the basis behind the broad strain coverage of the current vaccine against MenB. In addition, the information gathered from this structure will be of high value for future structure-based antigen design.

Biography

Jacinto Lopez-Sagaseta has completed his PhD in 2007 and carried out Post-doctoral studies at the University of Chicago. His work has been focused mainly in the characterization of the endothelial protein C receptor and its interaction with the coagulation Factor VII. During his Post-doctoral research, he pursued structural studies on antigen recognition by NKT and MAIT cells. He has also worked on the structural elucidation of a potassium ion channel bound to an inhibitory ligand. In 2015, he was awarded a Marie Curie European Grant and joined the Structural Biology Unit of GSK Vaccines where he is carrying out studies in the context of structural vaccinology.

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