Rosemary Nyamboya, J Proteomics Bioinform 2017, 10:8(Suppl)
DOI: 10.4172/0974-276X-C1-0101

Evolution of immunoglobulin's through studies of structure and function of IgE and IgM

Rosemary Nyamboya
King's College London, UK

IgM is the first class of antibody to appear during phylogeny and ontogeny, and is also the only class produced by all species of jawed vertebrates. It is the first immunoglobulin isotype produced in the primary immune response and therefore plays a pivotal role in front line host defence against pathogens. Despite its crucial role, it is surprising that very little is known about its detailed molecular structure and receptor interactions, a knowledge that is fundamental to understanding the role of IgM in human diseases. On the other hand, the structure of IgE, the main class of antibody which mediates allergic reactions, has been well studied. The crystal structure of IgE-Fc showed that the molecule is acutely bent between the Cε2 and Cε3 domains. And the IgE-FcεRI complex structure revealed the extent of the further conformational changes involved in both IgE and its receptor upon binding. These conformational changes have been shown to result in a high affinity interaction. Structural studies of IgE have proved crucial in mapping receptor interactions, to inform mutagenesis for functional studies and engineering effector functionality, as well as drug discovery. A structural framework is urgently required to underpin the current research activity in the functions of IgM and interplay between its Fc receptors. The hypothesis of this study is that IgM and IgM-receptor interactions also involve conformational changes. The key question is whether IgM displays the acutely bent Fc structure that was discovered in IgE-Fc, and whether conformational changes play a role in its functions. A new IgE-Fc biosensor designed by the sortase mediated liagtion technique further confirmed these conformational changes. The next step is to design a sensor using IgM-Fc to assess the disposition of the Cμ2, Cμ3 and Cμ4 domains and its implications for the IgM B cell receptor. Site specific labeling will be achieved by a mutation in Cμ2 to attach a maleimide–fluorophore at the N-terminus, and sortase ligation at the C-terminus of the molecules by the sortase trans-peptidation method.

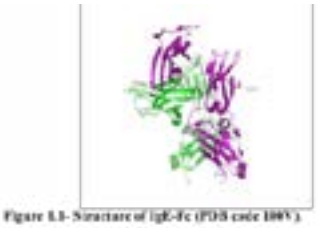

Figure 1.1- Structure of IgE-Fc (PDB code 1H9V).

IgE structure with the Cε2 domain bent back against Cε3 and Cε4 domain. Chain A: green; Chain B: magenta (Wan et al., 2002).

Biography

Rosemary Nyamboya is a final year PhD student working in the Randall Division of Cell and Structural Biophysics at King's College London under the supervision of Professor Brian Sutton. She is graduated from Kenyatta University, Kenya, in Master of Science in Microbiology. Her Master's thesis versed on the antibiotic resistance and on plasmid profiles of pathogenic bacteria found in wastewaters of Nairobi, Kenya. Prior to beginning the PhD program, she worked as an Embryologist at Agha Khan Hospital in Kenya. From this work and her project, she has developed an interest in understanding medical health complications, studying their origin of treatment and prevention. Her current work focusses on the use of bioinformatics and biophysical tools to understand the structure of IgE and IgM with the long term aim of developing new affordable therapeutic drugs for asthma and allergy.

rosemary.nyamboya@kcl.ac.uk

Notes: