Published on *BSC-CNS* (https://www.bsc.es)

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Objectives

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Abstract:

Antibodies have been very extensively investigated for decades and therefore much is known about their sequence-structure-function relationship. The ability of accurately modeling the structure of antibodies stems from the recognition that the hypervariable loops only exhibit a limited number of main-chain conformations called "canonical structures". Most sequence variations in five of these loops only modify the surface generated by the side chains on a canonical main chain structure. The third loop of the heavy chain (H3) has a different behavior, and has revealed to be very difficult to model given its high variability in both length and structure. We applied a machine-learning approach combining sequence and structural related features to identify candidate loops as templates to build the structure of a target H3 loop. Models are subsequently ranked based on a score reflecting the likelihood of the presence/absence of specific interactions between the H3 residues and its structural environment. The method has led to a significant improvement in the prediction of the H3 region and the overall antigen-binding site.

We next analyzed how differences between antigen binding sites might be linked to their specificity. To this purpose, we developed a superposition free method for comparing the surfaces of antibody binding sites based on shape descriptors. We showed that similar antigen binding sites could be better detected based on shape descriptors than using traditional structure similarity metrics. Finally, we showed that a classification procedure based on this approach could be applied to derive information about the recognized antigen, representing a step towards the very elusive goal of predicting antibody specificity.

Short Bio:

Rosalba Lepore is currently a postdoctoral researcher at the Biozentrum University of Basel & SIB Swiss Institute of Bioinformatics. She has a background in molecular and computational biology and received a PhD in Life Sciences at Sapienza University of Rome. Her research activities include the analysis of evolutionary and structural properties of proteins using computational tools and bioinformatics. In 2016 she received a fellowship from Pasteur Institute and Fondazione Cenci-Bolognetti in Rome for a research project on the computational analysis of antibody-antigen recognition mechanisms.

Speakers

Alba Lepore, postdoctoral researcher at the Biozentrum University of Basel & SIB Swiss Institute of Bioinformatics

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