University of Basel
Department Biozentrum

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BIOZENTRUM
The Center for Molecular Life Sciences

Basel Computational Biology Seminar

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Parameters and determinants of responses to selection in antibody libraries

The sequences of antibodies from a given repertoire are highly diverse at few sites located on the surface of a larger scaffold. The scaffold is often considered to play a lesser role than these highly diverse sites in controlling binding affinity and specificity. To gauge the impact of the scaffold, we carried out quantitative phage display experiments where we compare the response to selection for binding to four different targets of three different antibody libraries based on distinct scaffolds, with different levels of somatic mutations accumulated through affinity maturation, but harboring the same diversity at randomized sites. We find that the library of antibodies built around our only scaffold devoid of somatic mutations systematically outcompetes the other two. To quantify this effect, we define a library's selective potential as the variance of selection enrichments according to a log- normal model. We thus propose that naïve antibody scaffolds have a higher selective potential than maturated ones, likely as a consequence of a selection for this potential over the long-term evolution of germline antibody genes.
I will also present preliminary results about parallel work on another model protein, the serine protease trypsin, whose function has been also mainly described from a structural and biochemical perspective as essentially restricted to its active site. Following a conceptually similar combination of large-scale experiments and statistical analysis, we study how its catalytic function is encoded all over its sequence, beyond its active site.

Date: Monday, May 2, 2022

Time: 16:15 h – 17:15h

Location: Biozentrum U1.197 and live stream via Zoom

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