ItPS Seminars

31st Gen 2025 3pm CEST

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Engineering Nanobodies for Biotechnological Applications

Tailoring proteins to suit specific applications will improve their use in biosensors, as well as in many other biotechnological applications. This is, however, an important challenge in biomolecular engineering. In response, researchin my group focuseson developing rational engineering strategies to improve the properties of proteins. To do that, we are combining new computational and artificial intelligence tools with molecular biophysics. Among the large set of proteins of biotechnological relevance, nanobodies stand out due to their versatility and simplicity. Derived from camelid single-domain antibodies, these minimalistic antibodies offer antigen-binding capabilities very similar to canonical antibodies, but at a fraction of their size. Nanobodies have thus found widespread application inbiosensors, but also inimmunotherapy, imaging and drug delivery. Aiming to expand the implementation of nanobodies in biosensors and other biotechnologies, we have focused on improving their biophysical properties. In particular, we have developed an approach to engineer the conserved scaffold region of nanobodies,enhancing their stability, solubility, and ease of production. In addition to improving the biophysical properties of existing nanobodies, we have also succeeded at introducing new functionalities.

More specifically, we have developed new nanobody variants capable of undergoing conformational changes upon binding of their antigen. These receptors thus support conformational signaling, enabling more direct signal transduction and facilitating the development of reagent-less biosensors.Leveraging this, we have developed a biosensor for the hormone chorionic gonadotropin, a biomarker used to monitor the development of pregnancy. This work showcases our ability to engineer the properties and functional versatility of nanobodies, and potentially other proteins. Optimizing nanobodies rationally will facilitate the development of new biosensors supporting continuous measurements, but also their implementation in other biotechnologies.

For example, improving nanobody stability will facilitate their use as therapeuticagents; and increasing their production yield in recombinant protein expression systems will facilitate their industrial production.In addition, the high similarity between nanobodies for different antigens will facilitate the expansion of our approach to other nanobodies against drugs, hormones and biomarkers.

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