University of Zurich[UZH]

High-Throughput Binder Selection Facility
Department of Biochemistry, University of Zurich, Switzerland

HT-Platform providing Innovative Next-Generation Binder Discovery

Obtaining high-quality and reliable affinity reagents remains a major challenge for many scientific projects. Frequently, commercially available antibodies fail to behave as advertised or only work for a subset of samples. To tackle this issue, Prof. Andreas Plückthun and his team established the **High-Throughput Binder Selection Facility (HT-BSF)** at the University of Zurich, focusing on the high-throughput generation of specific and reliable protein binders, the so-called **DARPins** (Designed Ankyrin Repeat Proteins). These small (~18kDa) and extremely stable repeat proteins exhibit very beneficial biophysical properties and have already been used in a variety of applications both in-house and by numerous collaboration partners: amongst others, DARPins have been successfully employed in advanced microscopy, pull-downs, immunohistochemistry, for co-crystallization, as intracellular biosensors, and even have been therapeutically validated. An important characteristics of these multipurpose binders is that they recognize structural rather than linear epitopes, resulting in high specificity and selectivity between closely related isoforms or in detecting e.g. posttranslational modifications.

Combining these binders with other in-house developed technologies we created a streamlined and robust pipeline, consisting of parallel **Ribosome Display selections** and various **semi-automated high-throughput screenings and validations.** Extensive method development allowed us to optimize the normally laborious and time-consuming discovery process with regards to its efficiency and sample capacity. Considering essential aspects like functional binder validations while decreasing the pipeline's time and cost requirements, we can perform simultaneous selections against 94 targets and subsequently screen and validate several thousand binders in parallel for their binding and biophysical characteristics.

Running standard assays with carefully designed adaptations facilitates predictions of the quality and properties of candidates at early stages of the screening process. This allows us to promptly provide high-end binders to our international cooperation partners, improving existing and enabling novel, so far unfeasible applications. The selected DARPins do not just cover a variety of different target families but also meet the high quality criteria important for challenging scientific projects: monomeric binders that specifically recognize different, non-overlapping epitopes at their targets with high affinities, thus allowing also applications requiring sandwich recognition.

If you are interested in learning more about our facility and in conducting collaborative studies, please contact Dr. Jonas Schaefer, Head of HT-BSF, at j.schaefer@bioc.uzh.ch. More information on the HT-BSF can be found at www.bioc.uzh.ch/ht-lab. For free reprints of publications highlighting the potential of the DARPin technology, please visit www.bioc.uzh.ch/plueckthun.