Sybody Platform: Fast access to conformation-specific synthetic nanobodies as research tools

Contributed by Roger Dawson

Today, hybridoma and display technologies are challenged to screen increasingly difficult disease-relevant target proteins to create desired binders. Discussions about how to eliminate limitations are omnipresent. Key areas include the target protein generation itself as well as intrinsic technical limitations during antibody screening.

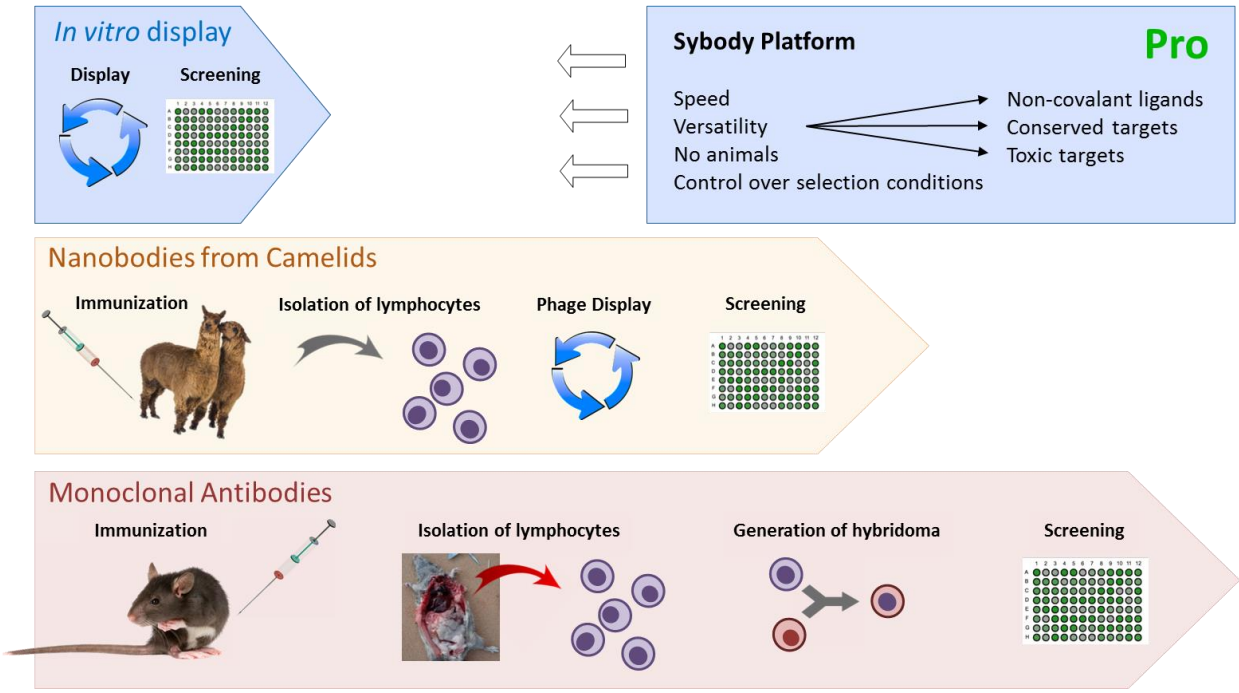
To create an advanced display platform – the so-called sybody platform – the Translational Protein Science (TPS) lab in TMo Chemical Biology strived at collaborating with the Seeger group at the University of Zurich right at the heart of one of the world's most successful spots for display technology development. The ideas for the project were awarded 750'000 ChF by the Swiss Federal Commission of Technology and Innovation (CTI). Two highly skilled and talented PostDoctoral Researchers were attracted - Dr. Iwan Zimmermann and Dr. Pascal Egloff who introduce 'shape design' to account for different target surfaces. Currently, the sybody platform features 3 differently designed synthetic libraries based on the very successful camelid single domain antibody scaffold also known as nanobody.

"The idea of sybodies focused on the most fundamental question during screening: how can we significantly increase effective library diversity and preserve biological key protein conformations even for the most difficult targets." explains Prof. Markus Seeger.

Essentially, a robust screening platform was created that combines ribosome display for maximum diversity and phage display to fish for only 'real' binders by the cooperative cancellation of selection bias. Using the latest *in vitro* tools to real-time monitor the selections, a fundamentally different understanding of how to use display technologies was realized. Selections were performed against 8 different membrane proteins and all of them provided hits from several families with binding affinities between 1-100 nM. For two Roche transporters, binders with the ability to even stabilize the inhibition-state were identified.

"Fast access to tool nanobodies with very specific properties is essential for the short timelines we have to deliver X-ray structures or setting up assays. The combination of high quality protein from our site and an excellent screening platform really pays off", stated Ralf Thoma Head of Protein Science.

The novel workflow allows parallel use of many more conditions than by previous display technologies. Selections are completed within 3 weeks after protein arrival. Cell surface receptors, membrane proteins and multi-enzyme complexes can be screened even in presence of non-covalent low affinity ligands that stabilize the target protein or trap it in the optimal conformation to elicit the desired biological response.


In vitro display
Display
Screening
Sybody Platform
Pro
Speed
Versatility
No animals
Control over selection conditions
Non-covalant ligands
Conserved targets
Toxic targets
Nanobodies from Camelids
Immunization
Isolation of lymphocytes
Phage Display
Screening
Monoclonal Antibodies
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Isolation of lymphocytes
Generation of hybridoma
Screening