New linker for affinity resins boosts binding capacity

Protein A chromatography is an essential step in most commercial antibody/mAb purification processes. It is immobilized on chromatography resins to specifically capture and thus purify antibodies. The actual binding capacity is usually much lower than the theoretical one, due to steric constraints. To remediate this problem, our researchers have developed a new rigid protein linker that ensures ideal accessibility of binding surfaces and thus boosts binding capacity and yields of affinity resins.

IP RIGHTS
EP application from
2024

Patented linker opens up hidden binding sites

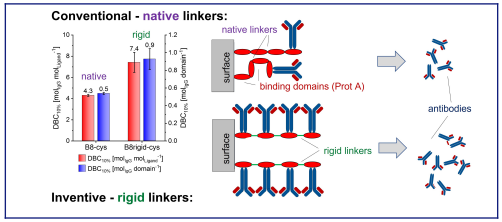
The clonable, rigid protein linker can be easily introduced into existing Protein A other affinity ligand constructs, thereby boosting yields and productivity. Existing antibody/mAb purification protocols will likely not have to be altered for resins with the inventive rigid linker. We assume that a moderate development effort by an industry partner could bring the technology to market readiness.

01 rigid inter-domain linker enhances the accessibility of individual Protein A binding sites

02 simple way to boost binding capacity of a Protein A resin 1.5 to 2-fold

03 can be combined with other capacity-optimizing strategies (e.g. multiple domains, point mutations)

04 Potential to reduce costs and increase productivity in downstream platform processes



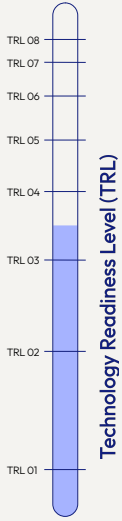
Left: Dynamic binding capacity (DBC) for resin with 8 polymerized B-Domains of Protein A (B8-cys) containing native linkers or the inventive rigid linkers.
Right: schematic representation of the effect of rigid spacing of Protein A subunits for an optimized antibody/mAb binding capacity.

CHALLENGE

Affinity chromatography is industrially relevant. E.g. protein A resins are commonly used commercial antibody purifications. This step often becomes a bottleneck for manufacturing due to generally low binding capacities. One underestimated factor affecting binding capacity is that many binding sites of the immobilized Protein A ligand are not accessible to the relatively large antibodies. Since Protein A resin is expensive, increasing its binding capacity can directly lower antibody/mAb productions costs.

INNOVATION

Our team of inventors from the Technical University of Munich have developed a new, rigid protein linker for affinity resins. It serves to ideally space out binding surfaces, which drastically increases e.g. antibody capture in antibody downstream processing. So far, a more than 50% increase in antibody capture per molar amount of Protein A could be achieved, as compared to a standard flexible linker. This directly translates into faster and cheaper industrial downstream processing. Our technology can easily be combined with other capacity-optimizing strategies such as domain multiplication or affinity-increasing point mutations.



01 Basic principles observed · **02** Technology concept formulated · **03** Experimental proof of concept · **04** Technology validated in lab · **05** Technology validated in relevant environment · **06** Technology demonstrated in relevant environment · **07** System prototype demonstrated in operational environment · **08** System complete and qualified

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