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Single domain antibodies in bio-sensing

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Introduction

Heavy chain antibodies (HCAbs), naturally occurring in camelids and elasmobranch cartilaginous fish, lack the light chains of conventional Abs; these structures possess certain features that facilitate their splitting to stable, soluble and easily manipulated single-domain (sdAbs) formats to deliver a variety of derivatives. Owing to a high lucrative market, academic spin-offs were fast to capitalize on the new moieties, with a few products currently in clinical trials from the Belgian Ablynx (www.ablynx.com) on the camelid source (Nanobodies®) and the US GenWay Biotech (www.genwaybio.com) on the shark source. Meanwhile, GlaxoSmithKline acquired Domantis to get hold of its human-derived sdAbs.

Following the proof-of-concept, sdAbs have started to intrigue the scientific community as the new Ab-based tools [1-3]. They are easily expressed in microbial systems (E. coli, yeasts, and fungi) from a single gene requiring no post-translational modifications; development times are shorter and the fermentation condition scalable. The single domain nature facilitates molecular manipulation and formatting [4-7], although effector functions can be only recruited indirectly and to a lesser success than

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in conventional Abs [8,9]. The unique, however, physicochemical and pharmacokinetic properties of sdAbs match the requirements of many biomedical applications and offer several advantages over conventional Ab technology for immunotherapy, drug delivery, imaging and diagnostics.

The affinities of sdAbs are comparable or superior to those of conventional Ab derivatives [1-3]. The fast retrieval of high-affinity and target specific sdAbs provides a rich pool for intracellular signalling molecules, protein-protein interactions and cancer biomarkers. They can be fused with fluorescent proteins to produce chromobodies that can be utilized in single-molecule localization with super-resolution imaging techniques [10,11]. As they can be engineered to induce conformation changes or to discriminate between conformational variants [12], sdAbs may be proven a beneficial research tool for monitoring protein expression, translocation, and subcellular localization.

Since Spinelli et al. [13] showed that sdAbs bind to copper ions, a new tool became available for biosensor development. A critical advantage derives from the rugged nature of these moieties that allows for harsh engineering and endows a considerable extension in the shelf-life of the device. The ability of sdAbs to recognize cryptic epitopes [14] may open new avenues for environmental detection, especially in assessing pollution impact in the cellular or sub-cellular level and endocrine disruption mechanisms. The development of immunosensors using conventional Ab fragments has been proven challenging due to the low affinities expressed in the presence of binders; the option of producing multi-sensors using a series of high avidity bi-specific or trivalent sdAbs that can be accommodated in nanometer space [15] may certainly enhance the simultaneous detection of many compounds with a single instrument. The high solubility and low aggregation potential of sdAbs [1-3] could reduce the use of reagents during measurements, while in situ regeneration of the sensor might be further facilitated for uses in long-term monitoring.

Notwithstanding, the small sdAbs size may not be suited for random coupling to solid surfaces unless advanced engineering produces formats that would permit directional immobilization. For example, a prostate specific antigen sdAb was successfully immobilized on a surface plasmon resonance transducer by carbodiimide coupling to provide detection limits that were significantly lower than those of similar fragmented Ab platforms [16]. The fusion protein retained the ability to self assemble onto solid surface into a square lattice structure with the sdAb pointing outwards from the protein lattice surface into the solution. This monomolecular protein lattice could be exploited as a sensing layer in various biosensor setups. In related research, different constructs were immobilized onto commercial and custom-built sensor surfaces by metal chelation, biotin-streptavidin interactions or covalent coupling [17]. For the first time, the intrinsic stability was presented as an important biosensor design factor, showing experimentally that higher intrinsic stability offers higher resistance to harsh environments.

In conclusion, sdAbs could be proven advantageous for maximizing protein loading to lower detection limits, reducing steric hindrance to decrease noise

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levels and optimizing biomolecular interactions to increase sensitivity. Still, immobilization on the transducer platforms might be proven quite tricky, possibly necessitating new self-assembly methods and 'click' chemistry techniques.

References

1. Muyldermans S (2013) Annu. Rev. Biochem., 82: 775-797.
2. Siontorou CG (2013) Int. J. Nanomedicine, 8: 4215–4227.
3. Chakravarty R, Goel S, Cai W (2014) Theranostics, 4: 386-398.
4. Dumoulin M, Conrath K, Van Meirhaeghe A, et al., (2002) Protein Sci., 11: 500-515.
5. Coppieters K, Dreier T, Silence K, et al., (2006) Arthritis Rheum., 54: 1856-1866.
6. Harmsen MM, Van Solt CB, Fijten HPD, et al., (2007) Vet Microbiol., 120: 193-206.
7. Roovers RC, Laeremans T, Huang L, et al., (2007) Cancer Immunol. Immunother., 56: 303-317.
8. Nguyen VK, Desmyter A, Muyldermans S (2001) Adv. Immunol., 79: 261-296.
9. Nguyen A, Reyes AE 2nd, Zhang M, et al., (2006) Protein Eng. Des. Sel., 19: 291-297.
10. Rothbauer U, Zolghadr K, Tillib S, et al., (2006) Nat. Methods, 3: 887-889.
11. Caussinus E, Kanca O, Affolter M. (2012) Nat. Struct. Mol. Biol., 19: 117-121.
12. Klooster R, Eman MR, le Duc Q, et al., (2009) J. Immunol. Methods, 342: 1-12.
13. Spinelli S, Frenken LG, Hermans P, et al., (2000) Biochemistry, 39: 1217-1222.
14. Stijlemans B, Conrath K, Cortez-Retamozo V, et al., (2004) J. Biol. Chem., 279: 1256-1261
15. Backmann N, Zahnd C, Huber F, et al., (2005) Proc. Natl. Acad. Sci. USA,102: 14587-14592.
16. Pleschberger M, Saerens D, Weigert S, et al., (2004) Bioconjug. Chem., 15: 664-671.
17. Saerens D, Frederix F, Reekmans G, et al., (2005) Anal Chem. 77: 7547-7555.

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