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Bioassays

Extending Protein Detection

Aptamer trio bests antibodies in quantifying protein over wide concentration range

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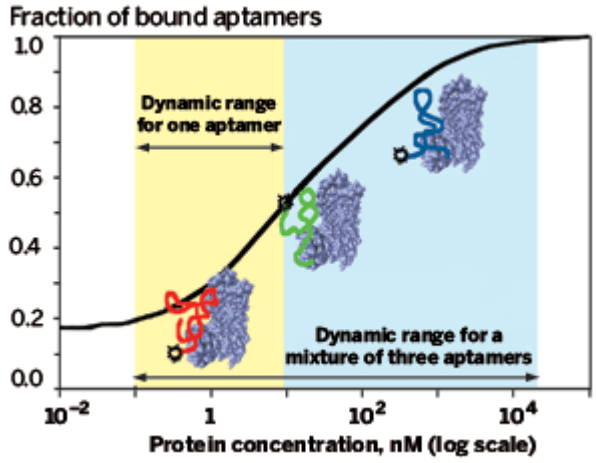
CONSIDERED BY MANY as antibody substitutes, aptamers are short DNA or RNA oligonucleotides capable of binding different classes of targets. Researchers at York University, in Toronto, have demonstrated that aptamers can do something antibodies cannot by using a trio of aptamers to detect a single target protein over a wide concentration range (*J. Am. Chem. Soc.* **2007**, *129*, 7260).



Teamwork Three aptamers, all of which bind specifically to the same protein target but with different dissociation constants, together can detect the protein over a wide concentration range.

That's important because protein concentrations can vary by several orders of magnitude during many physiological and pathological processes of interest to researchers and physicians.

Using three aptamers to target a protein, York chemistry professor Sergey N. Krylov and his team achieved a detection range of about five orders of magnitude. "Such analysis could not be realized with a single affinity probe," Krylov says.

Whether aptamer or antibody, every individual affinity probe is limited to detection ranges centered about its probe-protein dissociation constant. This constant is a rough indicator of the protein concentration that can be detected, plus or minus one order of magnitude, Krylov explains.

Although analysts have tried to use multiple probes to extend the protein concentration range that can be analyzed, that tactic has proven difficult to implement. For years, antibodies were the only type of affinity probe capable of binding to targets with sufficient specificity. For a multiple-probe system that can quantify proteins over a wide concentration range, all of the probes have to bind specifically to a common target protein, yet each probe must possess a distinct probe-protein dissociation constant. These are dual requirements that antibodies have yet to meet.

This is where aptamers come in. Krylov and his colleagues use a technique they developed in-house, kinetic capillary electrophoresis (KCE), to select aptamers from a large random library. As their aptamer target, they chose MutS, a protein involved in DNA repair. Earlier work by Krylov's team showed that KCE can serve as the means of identifying aptamers having a range of dissociation constants but a common specificity to MutS (*J. Am. Chem. Soc.* **2006**, *128*, 1410).

Preliminary studies of MutS aptamer probes in the presence of excessive amounts of protein-rich fetal bovine serum showed that the "selectivity of analysis is retained and other proteins do not interfere," according to Krylov. This suggests that such aptamer-probe systems could be valuable for monitoring specific proteins in biological fluids, he adds.

Krylov has set up a company called KCE Technologies to potentially hasten movement of this technology from the laboratory into clinical settings.

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