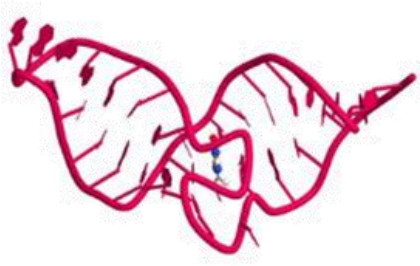
Selecting Aptamers to Small Molecules

At Aptamer Group (AG), we utilise state-of-the-art methods to select and identify aptamers that bind to specific small molecule targets.

The Issue

Small molecules have traditionally been off-limits to antibodies and other equivalent technologies, with relatively few examples in the market place. The accepted method is to prepare haptens; small molecule-protein conjugates. Although a useful tool in some areas, haptens do not represent species that exist in native biological systems. Also, the protein conjugate is chosen specifically for its ability to elicit an immune response and often antibodies recognise the conjugate, rather than the target molecule.



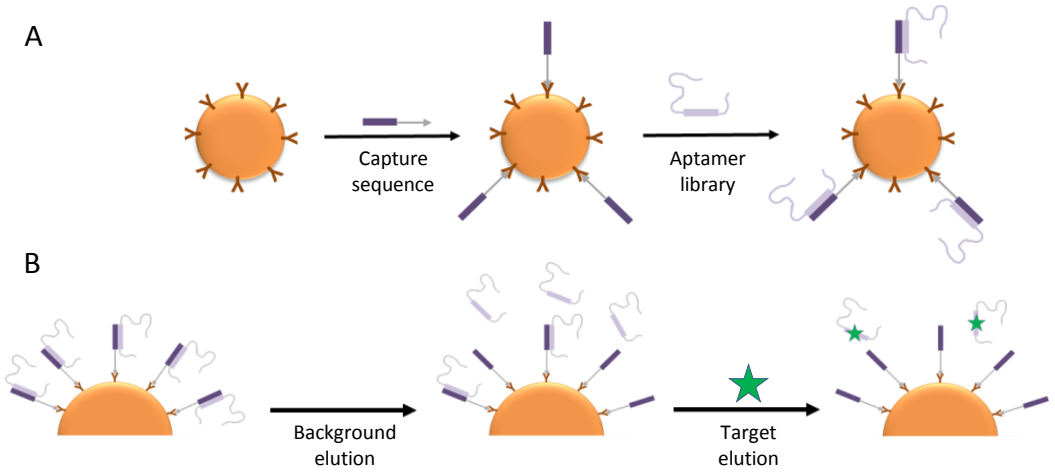
A small molecule binding aptamer.

The Solution

There is a need for alternative methods to detect and monitor small molecules, and aptamers are fast emerging as a powerful tool for a variety of systems. The small molecule specialists at AG select aptamers from an incredibly diverse library (≈10^{15} molecules). The library is systematically enriched until only aptamers with the required binding characteristics remain. Traditionally, aptamer selection methods immobilise the target to a surface. The requisite chemistry for immobilisation is not always beneficial to aptamer selection, as aptamers wrap around small molecules and immobilisation can disrupt this process. Small molecules may also lack the necessary functional groups to be immobilised and modifications can change their properties significantly.

Aptamer Group Displacement Method

Our displacement strategy selects against a target in solution so we are able to simulate biological conditions. Rather than immobilising the small molecule, the aptamers are bound to an immobilisation molecule with a predetermined affinity. When the small molecules are introduced to the system, any aptamer with a greater affinity for the target will be displaced from the immobilisation molecule and anneal to the target. This ensures that only aptamers with a minimum affinity for the target are selected; a stringency measure that is not possible with any equivalent technique.



A Immobilisation of aptamers to an immobilisation molecule.
B Background elution exposes the library to customer-defined conditions. The target molecule is introduced after.

Before each round of selection, the library is treated under customer-defined conditions to remove aptamers that recognize buffer and media components. This ensures that only aptamers specific to the target are liberated by the target and taken forward to subsequent rounds of selection. Selection is deemed successful when the ratio of target specific aptamers eluted relative to non-specific increases exponentially.

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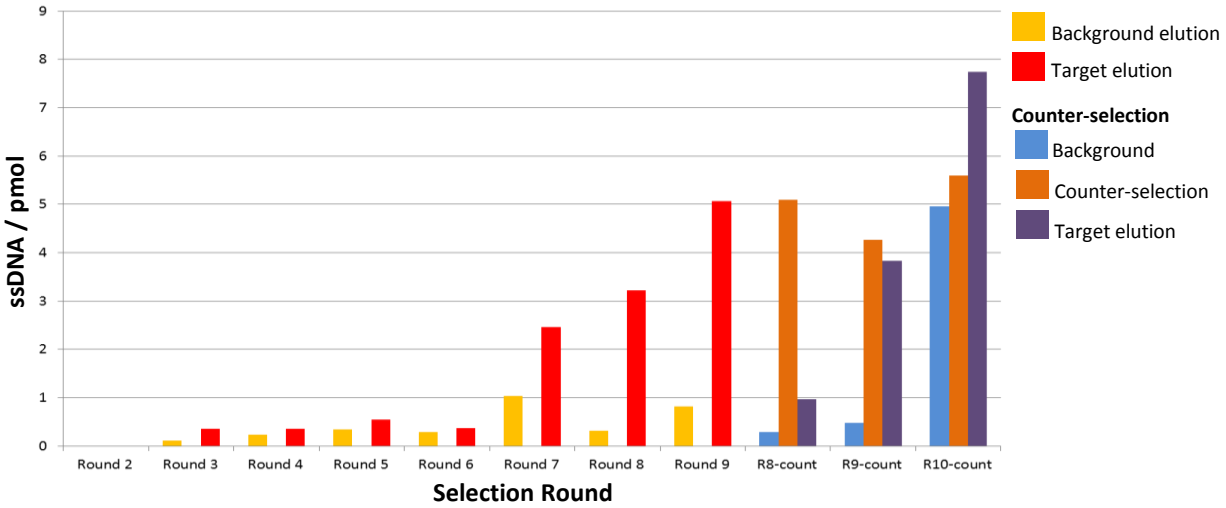
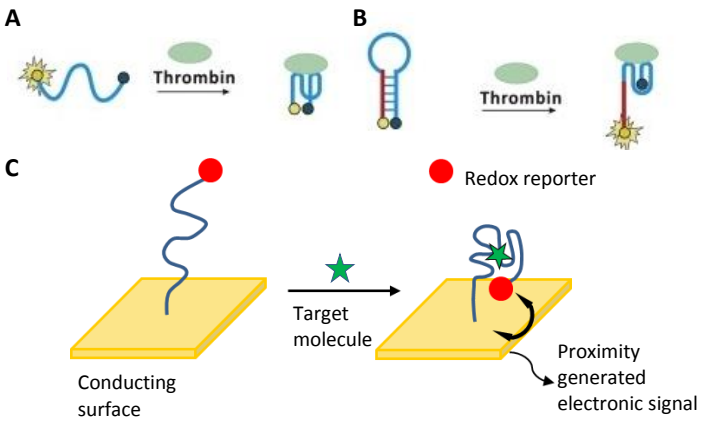


Case study showing the amount of ssDNA during the different rounds of aptamer selection.

Using a carefully designed counter-selection strategy, we are able to isolate aptamers with exquisite specificity. This means that we can differentiate between molecules differing by a single functional group. This specificity is essential for the development of effective biological assays.

Small Molecule Detection

Due to the displacement during small molecule binding, a structural switch is induced in the aptamers. Structure-switching is a phenomenon that can be exploited to great effect in a variety of detection methods. Our Aptamer Beacons platform and redox reporter systems (see diagrams) are just two possibilities that can be incorporated into detection systems.



A Change of aptamer conformation upon binding leading to loss of fluorescence (quenched)

B Change of aptamer conformation upon binding resulting in fluorescence

C Redox reporter system through proximity generated electronic signal

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