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Case ID:M17-013L Published: 4/14/2023

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Structure Assisted Directed Evolution of Multivalent Ligands

Nanotechnology needs organization and precise control, which is why DNA self-assembly into nanostructures has been a remarkable breakthrough. The challenges in creating nanostructures and also the opportunities lie in how to achieve self-sustained replication. This allows for the system to amplify itself in unlimited cycles, which is not enabled in current systems.

DNA nanostructures have many nanotechnology potential applications, an important one being the creation of multivalent ligands. Traditional methods for selecting ligands are cumbersome and involve finding a pool of ligands per epitope and then combining them using a linker to optimize the distance and orientations between multivalent ligands. Thus, it is time consuming and expensive to create multivalent ligands. However, multivalent ligands produce stronger binding and higher avidities, thus they are preferred for many applications.

Prof. Hao Yan at Arizona State University has developed a novel platform for self-replication of DNA nanostructures and uses this platform for effective DNA scaffold assisted evolution of multivalent binding ligands. The DNA scaffold, folded from a single stranded DNA, is positioned with random loops for developing multivalent ligands. Multivalent ligands with high affinity evolve on the predefined scaffold and are dominant in the selecting library after repeated affinity screening and PCR amplification. This one-pot, scaffold-optimization-free platform is both cost-saving and time-saving, making it very effective for ultra-high affinity multivalent ligands identification.

This novel platform to create multivalent ligands using evolvable DNA nanostructures opens up a whole new world of exciting opportunities for functional DNA nanotechnology.

Potential Applications

- Directed evolution of multivalent ligands
- o Potential therapeutic candidates
- o Research reagents and tools

o Diagnostics & probes for affinity capture
o Nanomechanical devices
o Catalysts
o Biosensors
o Drug delivery
Benefits and Advantages
Simplified methods for creating multivalent ligands
The ligands have high affinity and high specificity
• Low-cost – the DNA nanostructures enable multivalent ligand creation in a single SELEX
Multivalent ligands are free of linker or scaffold optimization
For more information about the inventor(s) and their research, please see <u>Dr. Yan's</u> <u>laboratory webpage</u>