Appendix

Modified DNA aptamer technology

Fujitsu Laboratories Singapore

Aptamers

- Antibodies are best known for their roles in the immune system which defends our body against foreign bodies like bacteria and viruses. They have been used for the past few decades as diagnostic reagents and therapeutic agents

- Like antibodies, aptamers have molecular recognition property. However, aptamers are non-protein in nature, simpler in structure and therefore potentially less immunogenic than antibodies

- Aptamer is oligomer of ribonucleotides, RNA, which is known to bind specifically to protein targets with high specificity and affinity in a manner similar to monoclonal antibodies

- They are short stretches of nucleic acid, the very same basic entity that makes up the genetic material in our body. They are able to bind target molecules such as DNA and proteins with high specificity and affinity

- Aptamers also demonstrate the stability and non-immunogenicity of small molecule drugs giving aptamers the benefits of both monoclonal antibodies and small molecule drugs without many of the disadvantages exhibited by each of these therapeutic modalities

- Unlike monoclonal antibodies, aptamers are manufactured by chemical synthesis by which its production is reproducible, predictable and cost-effective.

- Key benefits of RNA aptamers:
    - Discriminate recognition and enhanced selection capability for variety of targets
    - Engineered completely in a test tube (in vitro)
    - Readily produced by chemical synthesis (compared to biological expression)

    - Improved reproducibility

Proprietary Fujitsu Methodology - Modified DNA Aptamer Development

- RNA aptamers are known for their instability and difficulties in chemical synthesis. Therefore, Fujitsu focused on the more stable DNA aptamers, rather than RNA aptamers at the beginning of their technology development. This is Fujitsu's modified DNA aptamer technology, and it will provide the following additional features as compared to RNA aptamers:
    - Improved chemical stability
    - Cheaper to produce
    - Possess desirable storage properties

- Fujitsu has established a cutting-edge methodology to develop modified DNA aptamers with various amino acid side chains to enable high affinity molecular probe
- The process enables higher interaction with fluctuated protein molecule by introducing more interaction points
- This will allow for high quality aptamers to be developed by introducing many chemical residues for inter- and intra-molecular contact points

Key Features/Benefits of Modified DNA Aptamers

- Fujitsu's methodology enables optimisation in the aptamer development process as compared to the currently available antibody research
- It is possible to display up to sixteen types of side chains at a time based on Fujitsu's original "block coding method"
    - An encode table composed of side chain information and two-base sequence of DNA is written
    - Modified dimers in the table are synthesised individually as substrates for random library preparation
    - Side chain is identified based on the backbone DNA sequence and the encode table
- The ability to generate a high number of side chains with combinatorial technique will enable the creation of a larger variety of molecular structures (more than 10^{14})

- The development process is carried out in vitro (in test tube) and is therefore free from biological immune system’s tolerance problems
- Modified DNA aptamers of a unique sequence can be synthesised in an order of up to 1 gram in routine processes

Workflow to Develop Modified DNA Aptamers