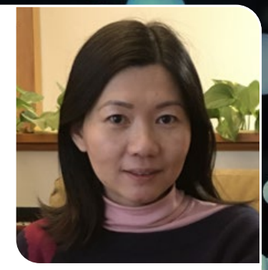
SPEAKER SPOTLIGHT:

Oligonucleotides – Analytical Considerations

Lying between traditional large and small molecules, oligonucleotides occupy a unique area within the global biologics market. The market is growing and many attribute this expansion to increased research activities conducted by pharmaceutical & biotech companies as well as research & academic institutions. There is a growing interest in adopting synthetized oligonucleotides, especially for diagnostic and clinical applications and there is a demand to develop advanced oligo therapeutics. The future looks promising, but challenges still remain.

Prior to our 7th Annual Peptides & Oligonucleotides Congress, we interviewed one of our highly distinguished speakers, Hong Jiang, Scientist and Group Leader, Biogen to discuss the interesting research done by her group and their recent findings.

Please note that the following responses are Hong's personal opinions and not that of Biogen.



Hong Jiang

Scientist & Group Leader, Analytical Development, **Biogen**

Hong is a scientist and group leader in Analytical Development at Biogen. Her current focus is analytical method and control strategy development for antisense oligonucleotides therapeutics. Before joining Biogen in 2016, she held positions at Wyeth BioPharma and Novartis Institutes for BioMedical Research, where she worked in protein drug formulation, small molecule drug metabolism, and method development to support both research and development in multiple modalities.

The field of oligonucleotides has grown over the past years. What key milestones do you think have contributed to this?

The approval and commercial success of a few oligonucleotide drugs in recent years obviously energized the field. More importantly, the recent success is the result of many years of effort by countless groups and persons working in basic research, pharmaceutical industry, and regulatory.

What is your role in Biogen?

I lead a small group of analytical scientists who work on analytical support for ASO and small molecule drug development. I support ASO development at different levels, including serving as the technical team leader or analytical lead for programs in clinical development, and as a subject matter expert in various areas.

Briefly describe what work you have done in oligonucleotides and what your team is involved in.

My team works on new method development, sample analysis for novel process development, impurity and degradation product identification, analytical control strategy development, drafting documents submitted to regulators, and responding to questions from agencies. Before I joined Biogen I worked with oligonucleotides for enzyme mechanism research and developed LCMS based oligonucleotide analysis to support mRNA therapeutics development.

What are some of your recent exciting findings?

My team recently made major improvements to our platform method for ASO purity and impurity analysis. This new method was successfully validated and used to analyze samples from Biogen's first ASO Process Validation campaign. My team also played a critical role in a novel liquid phase oligonucleotide synthesis process development. It is an exciting project due to its novelty, foreseeable impact, learning along the way, and the challenges we overcame.

What are some of the analytical challenges your team needed to overcome?

Accurate quantification of ASO impurities of low abundance remains a common challenge in the field. The main reasons for the difficulties are high number of impurities that are structurally similar to the full-length product (FLP) and diastereomers of FLP and impurities which complicate the chromatographic resolution of these species. Another set of challenges are related to the novel liquid phase synthesis project, and I hope that we can start sharing more detail sometime this year.

There are manufacturing constrains for oligos. In your opinion, why is it so challenging to manufacture them?

Current oligonucleotide manufacturing relies on column based solid phase synthesis process. Due to the large number of sequential reactions required to make oligonucleotides and the limited volume of each column, synthesis is time-consuming and expensive to scale up. The typical purification process involves liquid chromatography, which can also be expensive.

What do you think the future holds for oligonucleotides?

Of course, I think oligonucleotide therapeutics has a bright future. High specificity and generally low toxicity are among the advantages of oligonucleotide drugs. Due to the common polymeric structure of this type of drug, new modifications to improve drug properties and improvements in manufacturing processes are often broadly applicable to the field. A platform approach is well suited for development of oligonucleotide drugs, which will bring down the cost and shorten the time to market.