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Ion-pair chromatography analysis of large mRNA

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Messenger RNA (mRNA)-based therapeutics is of great interest in the field of vaccination as a safe and efficient alternative to traditional live virus or protein-based vaccines. Unlike these traditional vaccines, mRNA that is engineered to carry specific genetic information is injected and delivered into cells where the antigen is synthesized. Previous research has shown promising results on using mRNA to stimulate immune response and several mRNA vaccines are currently being evaluated in clinical trials. RNA stability is one of the most challenging issues that need to be solved because RNA may degrade during process, formulation and storage. Therefore, analytical methods to characterize RNA are required to measure integrity of RNA molecules. One degradation process involves formation of smaller fragments from large RNA. Separation of RNA by size is useful for this type of degradation analysis. Compared to electrophoresis, ion-pair chromatography provides better robustness and compatibility with MS detector. In addition, it is possible that the mechanism of separation under LC condition is different compared to electrophoresis. Therefore, LC can be used as an orthogonal method to electrophoresis. Existing LC analysis of RNA is more focused on oligonucleotides. However, LC analysis of larger RNA, such as mRNA, becomes critical due to its potential applications in vaccines. In this talk, method development using ion-pair chromatography for larger RNA, up to 6000 nucleotides, will be discussed. The result using triethylamine acetate as ion pair reagent with different organic modifiers will be included. A MS compatible ion-pair chromatography method using triethylamine and hexafluoroisopropanol in the mobile phase will also be presented.

Biography

Tian Lu is a Senior Scientist at Merck and Co., in Vaccine Analytical Development. She is currently involved in method development for HPLC and CE to support new vaccine development. She obtained her PhD degree in Analytical Chemistry. Her research interest includes development of stationary phases for chromatography and new substrates for laser desorption/ionization mass spectrometry.¬¬

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