Collaborative Partnerships with Oak Ridge National Laboratory for the Discovery of Functional Charged Macromolecules

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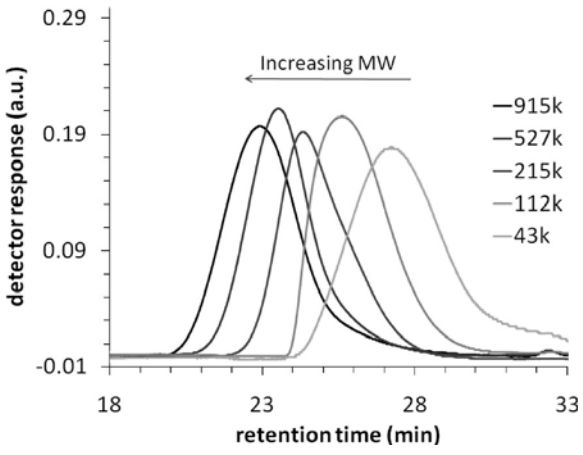
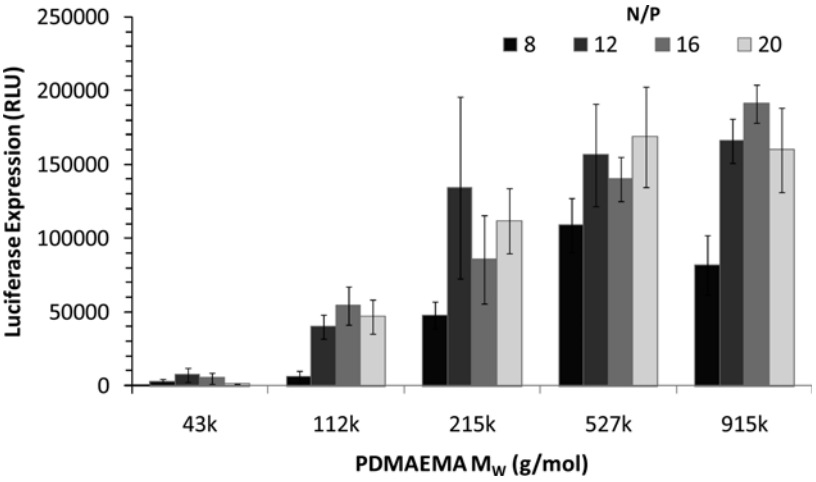
User Proposal Titles

(1) Hydrogen bonding influence of urea-functionalized carbon nanotubes with complementary polymer matrices (Sean M. Ramirez), **(2)** Aqueous size exclusion chromatography for the characterization of ion containing polymers for gene delivery (John M. Layman), **(3)** RAFT polymerization of acrylic monomers for block copolymer architectures (summer internship for Rebecca H. Brown), and **(4)** Synthesis of ionenes in the presence of ionic liquids (Sharlene R. Williams)

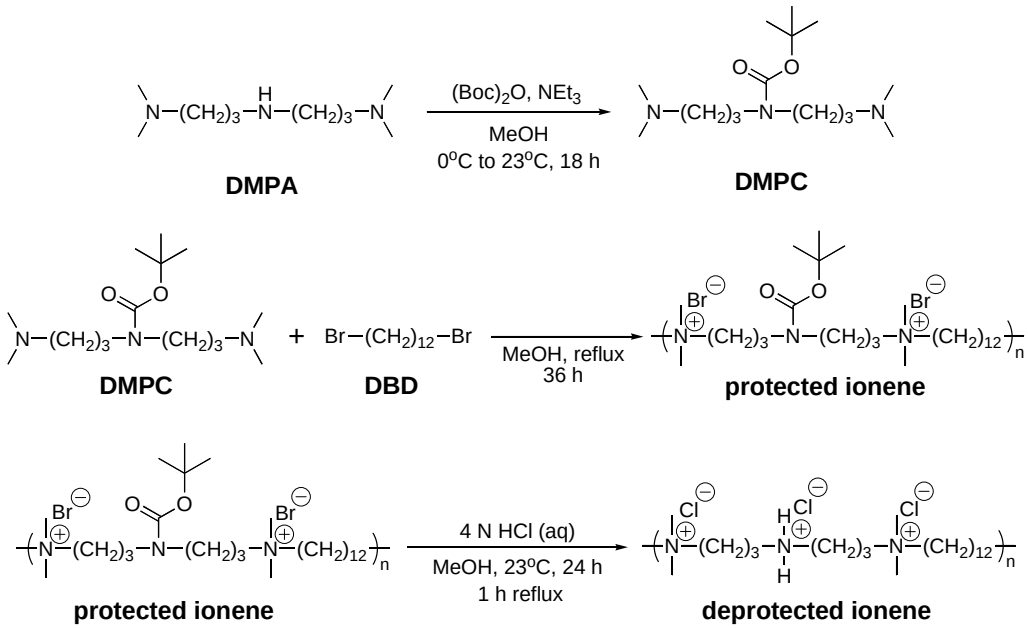
Research Achievements

Non-viral gene delivery agents, such as cationic polyelectrolytes, are attractive replacements to viruses due to the absence of potential immunogenic risk and the ability to tune their macromolecular structure. Although non-viral vectors possess numerous design advantages, several investigators have shown that transfer efficiencies are considerably lower when compared to viral vectors. Our work aims to fundamentally understand the underlying structure-property relationships involved in polycation-mediated gene delivery. The molecular weight was determined using absolute molecular weight detection, and the control of molecular weight over a broad range is depicted. The molecular weight of PDMAEMA was found to have a dramatic influence on transfection efficiency, and luciferase reporter gene expression increased as a function of increasing molecular weight. However, cellular uptake of polyplexes was determined to be insensitive to molecular weight. Collectively, our data suggested that the intracellular fate of the polyplexes, which involves endosomal release and DNase resistance, is more important to overall transfection efficiency than barriers to entry, such as polyplex size. User collaborations with ORNL CNMS provided key experimental parameters to the determination of the absolute molecular weight measurements of these vectors, and the following figure depicts the role of molecular weight on the transfection efficiency for a series of cationic polyelectrolytes.





ORNL CNMS collaborations also involved investigations of the polymerization of cationic ionenes in ionic liquid monomers. The use of ionic liquids offers versatility in the solubility and ultimate performance in electro-active devices. Ionenes consist of cations within the polymer backbone as opposed to pendant as described above for gene therapy vectors. The following synthetic scheme illustrates the synthesis of functional ionenes, and the preparation of these novel monomer families in ionic liquid solvents will be described in more detail.



Future Work

Our current collaborative efforts are focused on the introduction of nucleobase intermolecular interactions between MWCNTs and various polymer matrices, and collaborations involve the characterization of functionalization efficiency. In addition, ionene synthesis continues with a focus on the introduction of imidazolium cations to the ionene architecture in an attempt to provide favorable interactions with complementary ionic liquids.

References

Layman, J. M., Long, T.E., et al. *Biomacromolecules* **2009,** *in press.*