Cationic Polymers based on Fructose and Galactose Moieties for Nucleic Acids Delivery

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Cationic polymers and glycopolymers were synthesised using the RAFT technique. Combining cationic polymers with glycopolymers has great potential in targeted nucleic acid delivery.[1,2] However, many obstacles prevent the use of cationic glycopolymers as vectors including low success in nucleic acid delivery and high toxicity of the cationic polymer. This project aims to investigate RAFT synthesis of cationic glycopolymers with galactose or fructose carbohydrates, their binding ability with their specific lectins and with negatively charged nucleic acids.

The cationic polymer poly(2-(dimethylamino)ethyl methacrylate) (PDMAEMA) was synthesised using RAFT polymerisation. The galactose monomer, 2-(2',3',4',6'-tetra-O-acetyl-β-D-galactosyloxy)ethyl methacrylate (AcGalEMA), and the fructose monomer, 1-*O*-methacryloyl-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (1-*O*-MAiPFru)[3], were polymerised with PDMAEMA to form cationic glycopolymers. Chain extension was confirmed using proton nuclear magnetic spectroscopy (NMR) and gel permeation chromatography (GPC). Gel permeation chromatography was also performed to determine the polydispersity index (uniformity) of the polymers.

The protected glycopolymer blocks were modified by deacetylation of the galactose block and acid deprotection of the fructose block. Characterisation of the modified cationic glycopolymers was achieved using proton nuclear magnetic spectroscopy for confirmation of deacetylation/deprotection, and dynamic light scattering to determine the sizes of the diblock copolymers. The zeta potential (ionic charge) of the diblock copolymers was recorded.

Aggregation assays between the cationic glycopolymers and plant lectins were assessed. The galactose-containing glycopolymers were conjugated with peanut agglutinin lectin and the fructose-containing glycopolymers were conjugated with lectin from *Ulex europaeus*. The assays were analysed using dynamic light spectroscopy and ultraviolet-visible spectroscopy. Complexation of the cationic glycopolymer with small interfering RNA (siRNA) was accomplished. The size of the resulting polyplex was recorded with dynamic light spectroscopy. The zeta potential was measured and compared to the zeta potential measurement before complexation with siRNA.

Results indicated that RAFT polymerisation was successful in producing diblock polymers of controlled weight and uniform size. The cationic glycopolymers were partially successful in deacetylation/deprotection and highly successful in binding to their specific lectins. The cationic glycopolymer complexed with siRNA; however, further research into the appropriate *N:P* ratio is necessary. In conclusion, RAFT polymerisation is a suitable technique for the synthesis of cationic glycopolymers for use in nucleic acid delivery. The cationic block of the polymer is able to complex with nucleic acids while the glycopolymer block is able to bind to specific lectins. Further research into carbohydrates specific binding and further modifications to increase nucleic acid delivery efficiency would be beneficial.

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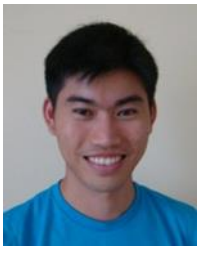

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Research interests: Reversible deactivation radical polymerisation; functional polymer; nucleic acids delivery; glycopolymer; polymeric scaffolds