

## **Bioconjugated Cellulose Nanocrystals for Immunotargeting**

The proposed research represents a multi-disciplinary collaboration between a polymer chemist (Dr. Roman) and a molecular biologist (Dr. Lee). We propose to attach antibodies, specifically anti-E-selectin, to the surface of nanometer-sized, rodlike particles of cellulose, termed cellulose nanocrystals, and investigate the ability of the thus formed bioconjugates to block adhesion molecules of activated endothelial cells and thus ameliorate vascular inflammation. If successful, the proposed research will provide a novel therapeutic approach for diseases involving vascular inflammation, such as brain injury, diabetes, rheumatoid arthritis, and many types of cancer.

The main hypothesis for the proposed research is that cellulose nanocrystals are ideally suited as nanoscale drug carriers in targeted drug delivery applications. Our hypothesis is based on the following properties of cellulose nanocrystals:

- (1) Cellulose nanocrystals have a size range between 50 and 200 nm with the majority of the rodlike particles between 100 and 150 nm long. This size range is expected to be too large for removal from the blood stream by the renal system (i.e. the kidneys) but still small enough that the rate of clearance from the blood stream by the mononuclear phagocytic system (MPS) is delayed.
- (2) Being entirely composed of polysaccharide molecules, cellulose nanocrystals are highly hydrophilic in nature. A hydrophilic surface has been shown to impede adsorption of opsonin proteins, a critical step before phagocytosis during removal of nanoparticles from the blood stream. Thus, cellulose nanocrystals are expected to have an inherent prolonged blood circulation half-life as compared to hydrophobic particles.
- (3) Cellulose can be degraded by reactive oxygen and nitrogen species, such as those used by phagocytes to break down the phagocytosed material. Cellulose nanocrystals are therefore expected not to accumulate permanently in the MPS organs (e.g. liver and spleen).

- (4) The surface chemistry of cellulose nanocrystals is governed by hydroxyl groups, which can be easily converted into other functional groups for covalent and non-covalent binding of targeting and/or drug moieties to the surface of the nanoparticles.

The specific objectives of the proposed research are:

- (1) To develop novel nanoparticles bioconjugated with specific ligands for immunotargeting. We propose to conjugate cellulose nanocrystals with anti-E-selectin monoclonal antibody to selectively target adhesion molecules overexpressed on the surface of activated vascular endothelium.
- (2) To determine the targeting ability/efficiency of bioconjugated cellulose nanocrystals. Specific binding of fluorescently labeled cellulose nanocrystal bioconjugates on activated brain microvascular endothelium will be analyzed by fluorescence microscopy.
- (3) To determine the ability of bioconjugated cellulose nanocrystals to ameliorate vascular inflammation in animal cell cultures.
- (4) To determine the ability of bioconjugated cellulose nanocrystals to ameliorate brain inflammation in experimental animals.