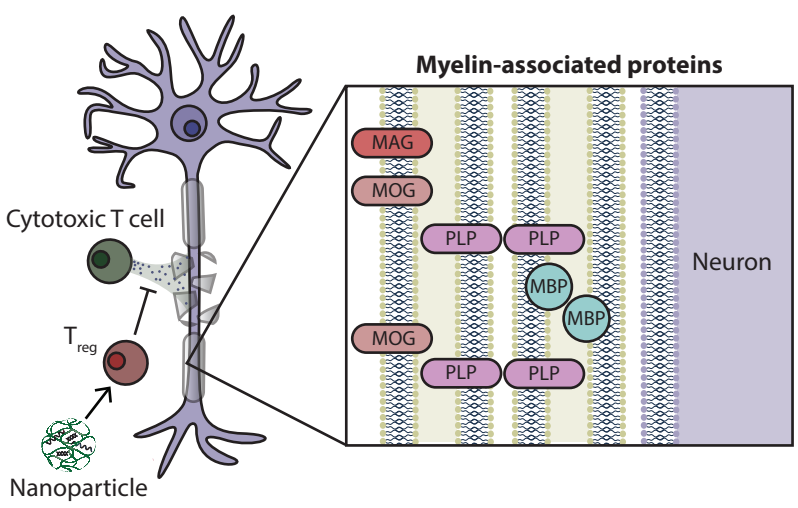
Tolerogenic RNA nanoparticles to treat multiple sclerosis

Julien Couture-Senécal[1] , Omar F. Khan[1,2]

[1]Institute of Biomedical Engineering, University of Toronto [2]Department of Immunology, University of Toronto

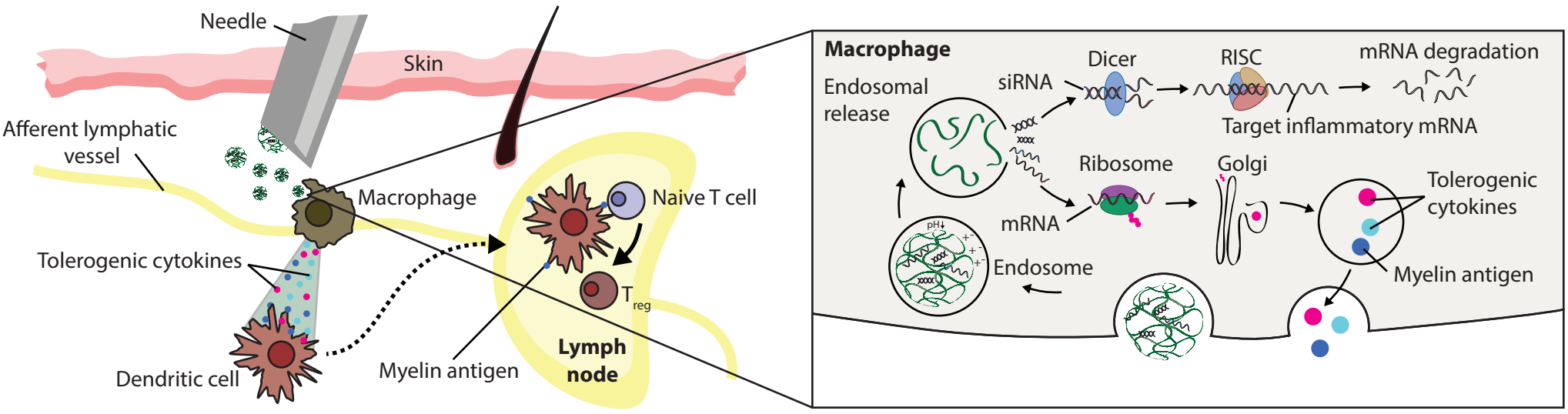
@juliencsenecal @OFKLab



Background

Canada has one of the highest prevalence of multiple sclerosis (MS), with about 77 000 people living with the disease. MS is an autoimmune disease of the central nervous system, in which immune cells attack myelin-associated proteins (e.g. MBP, PLP, MAG and MOG). The resulting demyelination of nerves leads to various neurological impairments. MS is characterized by the dysregulation of regulatory T cells (T_{regs}). Though there currently is no cure, T_{reg} therapy is a promising treatment to restore tolerance to myelin proteins. However, cell therapy has significant regulatory and manufacturing challenges, hence the importance of developing methods to induce T_{regs} *in vivo*. **My objective is to develop a nanoparticle capable of co-delivering RNA combinations for the treatment or prevention of MS**. I hypothesize that the combinatorial expression and silencing of cytokines facilitate the development of T_{regs} via the multigene control of antigen-presenting cells.

Mechanism



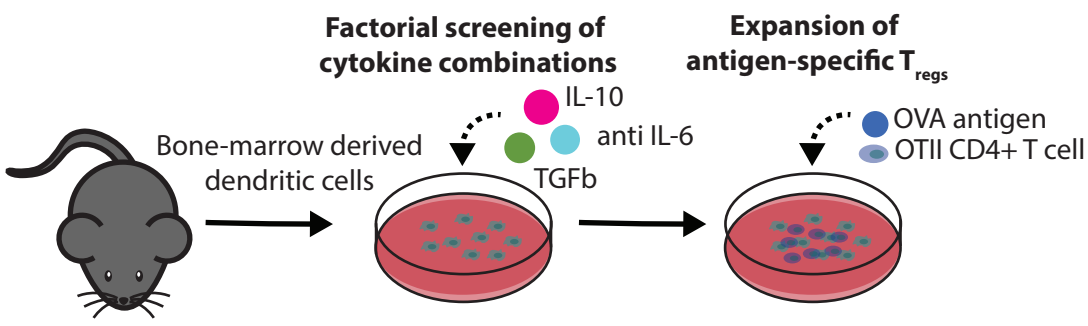
Hypothesis

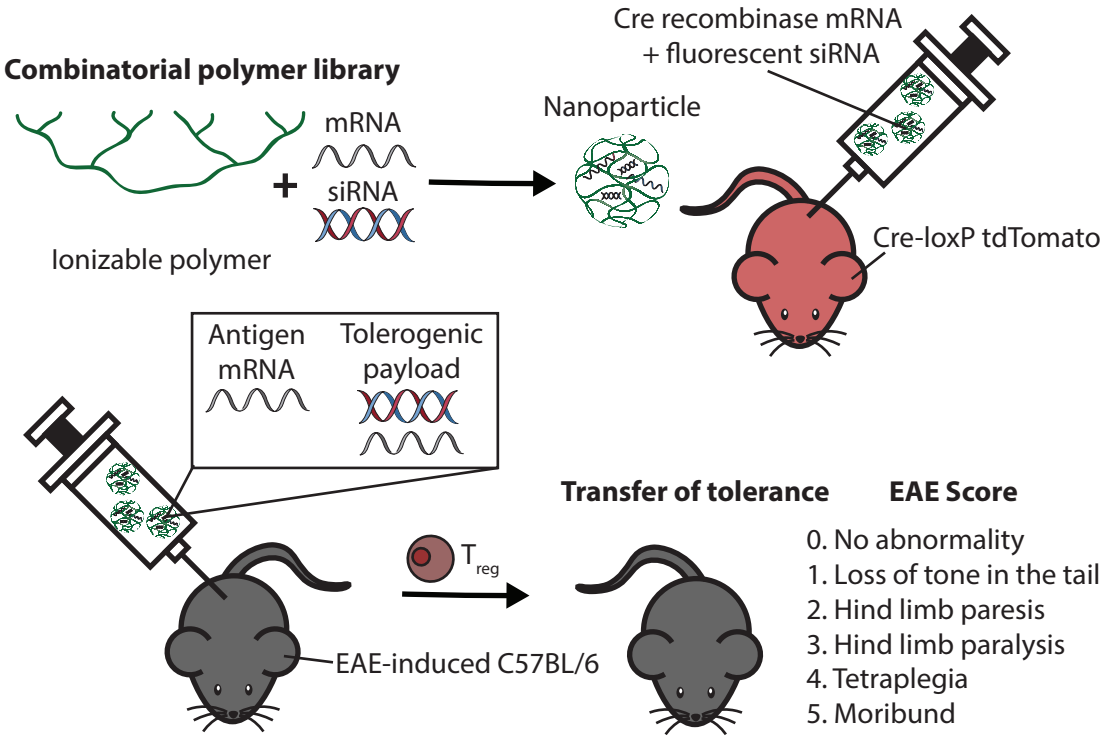
1. Expression of tolerogenic cytokines and silencing of inflammatory factors induce T_{regs} by modulating the phenotype of dendritic cells.

2. Our novel nanoparticle is non-reactogenic and efficiently delivers RNA combinations to antigen-presenting cells *in vivo*.

3. Delivery of tolerogenic nanoparticles to experimental autoimmune encephalomyelitis (EAE) mice induces immune tolerance.

Methods





Outcome

1. The identification of fate-specifying cytokines and the related RNA payload that induces tolerogenic dendritic cells and T_{regs} *in vitro*.

2. An optimal formulation that transfects antigen presenting cells *in vivo* with high efficiency and low reactogenicity.

3. A clinically deployable treatment that improves EAE disease score and induces antigen specific T_{regs} *in vivo*.

Significance

This research hopes to determine whether tolerogenic RNA nanoparticles can treat or prevent complex autoimmune diseases such as MS. This technology is unique in its ability to co-deliver multiple types of RNA. Its versatilty makes it applicable to other autoimmune diseases, since the antigenic and tolerogenic RNA payloads can be easily tuned to control different aberrant genes.

Acknowledgments

This research is part of the University of Toronto's Medicine by Design initiative, which receives funding from the Canada First Research Excellence Fund (CFREF). JCS is also funded by the Wildcat PhD Fellows Award.