CHITOSAN THERMOGELS FOR LOCAL T LYMPHOCYTE DELIVERY FOR CANCER IMMUNOTHERAPY

Anne Monette[1,2,4,5], Caroline Ceccaldi[3,4,5], Sophie Lerouge[3,4,5], Réjean Lapointe[1,2,4,5]
1. Immuno-oncology laboratory of Réjean Lapointe; 2. Institut du cancer de Montréal (ICM);
3. École de technologie supérieure (ETS); 4. Université de Montréal; 5. Centre de Recherche du Centre Hospitalier de l'Université de Montreal (CRCHUM)

Introduction:

The success of systemic adoptive T cell transfer lies in the capacity of the antigen-experienced cytotoxic T lymphocytes (cTL) to access and persist within the tumour microenvironment. The mimicking of tertiary lymphoid structures (TLS) that promote a protective immune response against cancer can be achieved using an injectable biocompatible matrix releasing anti-tumour proliferating cTL. Prime candidates for this application are liquid, chitosan-based, biocompatible thermogels which rapidly gelify at physiological temperatures. Therefore, we aimed to fine-tune an injectable chitosan-based thermogel formulation that would provide an environment permitting the three-dimensional (3D) proliferation and release of cTL whose activation state can be influenced by the surrounding conditions. We have developed a novel formulation that is cytocompatible and injectable, and that has ideal mechanical properties and porosity for T cell encapsulation and growth. With such promising characteristics, we hypothesize that the injection of these cTL loaded hydrogels into the tumour microenvironment will provide a means for a continuous delivery of cTL towards the reprogramming of inflammation mechanisms and the reduction of tumour burden.

Materials and Methods:

Novel T-cell cytocompatible chitosan thermogels were prepared using combinations of gelling agents. Their rheological properties, mechanical strengths, pH, osmolality, and morphology were evaluated. Three formulations were selected for human T cell encapsulation. Biocompatibility was assessed using live/dead staining and fluorescent microscopy. Thermogel- and supernatant-derived T cells and tumour infiltrating lymphocytes (TIL) were immunophenotyped over time using flow cytometry.

Results and Conclusion:

We have optimized thermogel formulations supporting the encapsulation of cTL *in vitro*. Flow cytometry and microscopy demonstrate which novel thermogel formulation is best suited for cell viability, proliferation, and escape over time, along with the maintenance of cTL cellular phenotype and an activation status that can be influenced by surrounding conditions. Our injectable 3D lymphocyte cultures may serve to complement current adoptive cell transfer immunotherapies.