

Research

Glycotherapeutics

If we are to realize the therapeutic potential of stem cells, controlling lineage-specific decisions is paramount. The Glycotherapeutics Group is focused on determining how elements of the extracellular matrix within the stem cell niche, and most particularly heparan sulfate sugars, protect, hold and present crucial growth factors to embryonic and adult stem cells, thus controlling intracellular signaling cascades and ultimately cell fate decisions. These sugars are not randomly synthesized, but contain specific domains that couple active molecules together.

Using methods developed in our laboratory we purify growth factor-specific heparan sulfate variants and characterize their activity, *in vitro* and in numerous animal models. We are investigating a method by which we can reverse engineer their structure and allow them to be biochemically synthesized "on demand". Several of these heparan sulfates offer unique therapeutic advantages for tissue repair. A major focus of our translational program is the question of how bone marrow stromal stem cells respond when challenged by various heparan sulfate-growth factor combinations, both *in vitro* and in various wound-healing models. Most recently, *in vivo* bone fracture models have been successfully treated by heparan sulfate therapy, resulting in increased bone regeneration.

Following on from these exciting results, A*STAR's Exploit Technologies is helping us to patent and develop our growing portfolio for commercialization. Furthermore, with the help of commercial partners we are seeking to further strengthen our ability to biochemically synthesize these novel molecules, a first step in exploiting this technology. Most recently, we have begun pre-clinical animal trials using a combination of HS and implantable hydroxyapatite to improve the healing of critical-sized bone defects.