JOHNNY HUARD (MAIN LECTURE)

_ Johnny Huard _

_ Henry J. Mankin Professor and Vice-chair for Musculoskeletal Cellular Therapeutics in the Department of Orthopaedic Surgery and in the Departments of Microbiology and Molecular Genetics, Pathology and Physical Medicine, Bioengineering, and Rehabilitation. Director of the Stem Cell Research Centre of Children’s Hospital of Pittsburgh. Deputy Director of the McGowan Institute for Regenerative Medicine, United States of America. _

“Development of biological approaches to improve muscle healing after injury”.

Muscle injuries are extremely common and have a high tendency to reoccur. Both limitations in force production and re-injury frequently are attributed to the development of regeneration-restrictive fibrotic tissue at the original site of injury. Gene therapy may prove useful for the development of techniques to improve the healing of muscle injuries. Transforming growth factor-beta 1 (TGF-b1) plays a key role in inducing the formation of fibrotic tissue that limits muscle healing after severe injury. Muscle Stem Cells have exhibited the capacity to differentiate into a myofibroblast-like lineage _in vitro_ and can contribute to scar formation after muscle injury _in vivo_. Various inhibitors of TGF- b1, including relaxin, decorin, gamma-interferon, and suramin can improve muscle regeneration and force production by limiting muscle fibrosis. Relaxin and decorin are molecules that can be expressed by cells and delivered to muscle via gene therapy techniques. Gamma-interferon, suramin and losartan represent drugs with other clinical indications, are potentially available for clinical use. However, due to the potential side-effects of these agents, further research must be performed in order to determine clinical safety. _Ex vivo_ gene therapy techniques may provide a method to deliver inhibitors of TGF-b1 to injured muscle. The proteoglycan, decorin, appears to be beneficial not only in reducing fibrosis, but also in improving muscle regeneration.
Delivery of MDSCs expressing decorin or a viral vector carrying decorin to injured muscle may help to improve long-term outcomes by reducing muscle fibrosis and, therefore, recurrence of injury. The proteins, myostatin and follistatin, has been shown to inhibit muscle growth and differentiation and represents good target to produce muscle hypertrophy and improved muscle strength. In this course, we will review the current knowledge concerning the use of gene therapy and tissue engineering applications based on muscle stem cells to improve the recovery of skeletal muscle after injuries and disease.