Michael H Heggeness et al., J Tissue Sci Eng 2017, 8:3 (Suppl)
DOI: 10.4172/2157-7552-C1-036

Quiescent pluripotent stem cells capable of expressing *SOX2*, *OCT4*, *KLF4* and *c-Myc* reside within peripheral nerves in adult mammals and can differentiate into cells of all 3 germ layers

Michael H Heggeness and S Yang
University of Kansas School of Medicine, USA

Preliminary evidence from our laboratory has documented a large population of quiescent stem cells within peripheral nerves. In response to nerve injury, or stimulation with the cytokine BMP2, these cells proliferate and generate populations of pluripotent stem cells, expressing Sox2, Klf4, Oct4 and c-Myc (verified by double stain immunohistochemistry and by real time PCR). These 4 markers are the transcription factors that confer embryonic pluripotency (Cell 126: 663, 2006). We call them Nerve Derived Pluripotent Stem cells, or NEDAPS cells. The cells are readily induced to form tissues from all 3 germ layers. We hypothesize that these cells are central to a previously unknown universal pathway for tissue repair. Nerves are nearly ubiquitous in the body, from the cornea of the eye to every hair follicle. Thus, we believe that nerve injury, and the consequent proliferation of these stem cells, is occurring following essentially any injury. We propose that this is a previously unknown universal pathway for healing.

We will show data documenting the induction and successful culture pluripotent cells from three mammalian species, and demonstrate their directed differentiation into osteoblasts, endothelial cells, primitive neural cells, definitive endoderm and fibroblasts as demonstrated by morphology, immunohistochemical staining and RT-PCR.

Recent progress has been stimulated by the discovery that induced pluripotent stem cells (iPCs), can be created from fully differentiated cells using retrovirus vectors (Cell 126: 663,2006). Such iPCs are widely studied as possible sources of cells for the treatment of human disease. This work has almost entirely been focused on a search for cures and treatments for specific diseases, and has been hampered by issues of malignant transformation of iPCs, and by immune rejection of "non-self" cells. We are aware that previous claims to successful identification of cells with universal differentiation from non-gonadal adult tissue have resulted in some well publicized scandals, involving fabricated data. These scandals have understandably created a skeptical audience for us. Such pluripotent stem cells are thought not to exist in adult animals (SciON 311: 814 2006), and until our recent discovery, we believed the same. Confidence in our admittedly unprecedented ideas is provided by information from other species. It is known that a salamander can re-grow an entire arm after amputation, but that ablation of the nerve stump will block the regeneration. Similarly, a starfish will regenerate an entire arm as well, but similarly, will not do so if the nerve supply is ablated (Kumar and Brokes Trend. Neurosci 2012 p691).

We propose that this new knowledge will also explain the puzzling and vexing clinical problem of impaired wound healing experienced by severely diabetic patients and victims of leprosy. We suggest that the associated clinical neuropathies explain this. The other implication of this discovery is that we may now have a new opportunity for individual specific "self-to-self" stem cell treatments, based on patient specific peripheral nerve harvest.

Biography

Michael H Heggeness has completed his PhD at UC San Diego in Membrane Biology and a Post-doctorate at Rockefeller University in Virology. He has received his MD from the University of Miami. After his Residency in Orthopedic Surgery, he has completed a Fellowship in Spine Surgery at the University of Toronto. He has then joined the Faculty at Baylor College of Medicine where he became Chairman of Orthopedic Surgery in 2004. He then moved to take the chair at University of Kansas in Wichita in 2013. He has 84 publications and 4 issued patents to his credit. His interest has centered on intraosseous nerves and nerve derived stem cells.

mheggeness@kumc.edu