ReScribe: Transcription factors for reprogramming of diseased musculoskeletal related cells

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Technology description

The Need

Musculoskeletal diseases including osteoarthritis and chronic low back pain, are debilitating, painful, and often difficult to treat. Intervertebral disc (IVD) degeneration, as an example, is strongly associated with low back pain, a leading cause of disability worldwide. According to the American Chiropractic Association, the total economic burden of lower back pain in the United States can exceed $100 billion when lost wages and decreased productivity are taken into account. Current treatments for these diseases have many problems. For example, PEEK cages for lumbar infusion and lumbar disc replacement are highly invasive surgical procedures. Other non-invasive treatments, such as physical therapy or administration of NSAIDS, don’ t incur the burden of surgery, but are also less effective for serious injuries. Additionally, use of opioids for pain control, while somewhat efficacious, have resulted in a medical crisis and have long-term effects on health and economic burden. Therefore, a curative, rather than palliative, treatment for musculoskeletal diseases is needed in order to reduce the pain of patients diagnosed with musculoskeletal diseases and improve outcomes for patient satisfaction and reduce socio-economic burden.

On-going investigations in the field of musculoskeletal therapies for better treatment options include engineered intervertebral discs, cell therapies, drug delivery, growth factors, viral reprogramming, and gene editing. However, each of these strategies have their own issues and associated risks. For example, engineered constructs for replacement of musculoskeletal components are often disadvantageous in their biocompatibility and mechanical integrity in the body. Cell therapies are also problematic because of their poor efficacy in terms of long-term cell viability due to the harsh avascular environment of tissues such as the intervertebral disc. Injection of anti-inflammatory drugs provides short term relief of symptoms but cannot cure the underlying disease. None of the current studies have demonstrated a treatment that is both efficacious and unhindered by side effects, complications, or viability issues. Furthermore, there are no strategies that address both the structural changes of tissue regeneration and pain.

The Technology

The technology, developed here at The Ohio State University by Dr. Devina (Purmessur) Walter and colleagues, is a group of transcription factors (TFs) that can be used to reprogram diseased musculoskeletal cells to promote healthy cell growth, extracellular matrix synthesis and reverse disease progression. The TFs, such as those from the FOX and SOX families of transcription factors, can be administered via minimally invasive methods such as tissue nanotechnology, engineered vesicles, and liposomal delivery. These TFs have the potential to be delivered during outpatient or inpatient procedures depending on the disease state and type of surgery being performed. After administration, these factors would upregulate the target genes within the diseased cells, thus promoting healthy cell growth and matrix accumulation.In vitrocellular results are promising, as described in a recent published peer-reviewed manuscript andin vivomurine studies are in progress.
The advantages to this technology are numerous. First, only autologous patient tissue would be used which alleviates the risk of rejection by the host, a major issue when using foreign tissues. The TFs are also unlikely to integrate into the host genome, reducing the changes of unplanned mutation and adverse effects. Second, the delivery of the TFs is accomplished via minimally invasive techniques, as described previously, reducing the burden of therapy and the post-operative need for powerful pain management solutions, such as opioids. Finally, these TFs are tissue specific, which reduces the risk of undesired, non-specific gene regulation in non-diseased tissues. This technology offers a curative solution to musculoskeletal diseases, such as intervertebral disc degeneration, and associated low back pain.

Research Interests

The Ohio State University laboratory that developed this technology has expertise in 3D hydrogel models, development of bioreactor systems, immune cell modulation, and whole joint tissue cross-talk with focuses applications in spine related diseases. They specialize in developing disease models and treatments for intervertebral disc degeneration across both humanin vitroandin vivoanimal models; specifically, dynamic mechanical characterizations, cell and tissue interactions, immunology and inflammation, gene expression, imaging, and histological characterization. The lab focuses on the development of knowledge and treatments for cell/tissue regeneration and inhibiting musculoskeletal disease progression and is open for collaboration for future products and investigational routes.
Transcription factors that can upregulate desired genes in diseased tissue to reprogram diseased cells, thereby reversing the disease and creating healthy non-diseased phenotype genes. These transcription factors would be especially useful in musculoskeletal diseases such as back pain and osteoarthritis.

Application area

Musculoskeletal disease therapy
Genetic-based disease therapy and research
Intervertebral Disc Regeneration

Advantages

Minimally invasive
Derived from autologous tissue
Target tissue specific
Reduced risk of rejection and adverse effects in host
Possible decrease in low back pain complaints and associated costs

Institution

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