Docket #: S16-253

Inducible production of IL-4 for precise control of immunomodulation in situ

Researchers at Stanford have developed methods and compositions to provide inducible production of anti-inflammatory cytokines in mesenchymal stem cells (MSCs). MSCs have great potential in therapeutic applications, including treatment of tissue injury and immune disorders, because of their immunomodulation and multi-lineage differentiation abilities. The inventors sought to further enhance the therapeutic effects of MSCs. This technology provides compositions and methods for inducible production of anti-inflammatory cytokines, including IL-4. This inducible model can sense the inflammatory environment and secrete a physiological level of immunomodulatory cytokines. The secretion will be turned off when the inflammation has resolved and can be turned back on in response to additional inflammatory signals. These methods and compositions can be used to improve MSC-based therapy.

Stage of research
The method has been demonstrated in MSCs *in vitro*. Additional *in vivo* studies using mouse models are ongoing.

Applications

- Mesenchymal stem cell-based therapy for inflammatory-associated diseases, including:
    - Bone healing
    - Osteoarthritis
    - Myocardial infarction
    - Diabetes

- Spinal cord injury

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Advantages

- Simple design with great sensitivity and specificity
- Enhances the immunomodulation and tissue repair capabilities of MSCs
- Real-time response to the inflammation status in the tissue environment
- Expandable to other cell-based immunomodulation therapy

Publications

- Lin et al. Transplanted interleukin-4–secreting mesenchymal stromal cells show extended survival and increased bone mineral density in the murine femur *Cytotherapy*, 2018, 20: 1028-1036.
- Lin et al. NF?B sensing IL-4 secreting mesenchymal stem cells mitigate the proinflammatory response of macrophages exposed to polyethylene wear particles *J Biomater Res Part A* 2018: 106A:2744.
- PCT Patent Application Serial No. PCT/US2017/055502.

Patents

- Published Application: WO2018071295
- Published Application: 20190255151
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