Methods for Dynamic Modeling and Closed-Loop Control of Inflammation

An engineering methodology to model and control the temporal dynamics of immune response

Georgia Tech inventors have developed an engineering methodology to model and control the temporal dynamics of immune response. Current strategies for intervening in chronic inflammatory diseases include local or systemic delivery of mesenchymal stem cells, systemic delivery of antibodies targeting inflammatory cytokines, corticosteroids, and allograft application of placental membranes. Systemic methods, in particular, can lose efficacy and exhibit numerous side effects, such as development of pneumonia. Current approaches are limited to giving, e.g., a single drug for an extended duration, and in many cases do not work or do not have sustained efficacy. Proper temporal evolution of immune activity is essential for restoring or promoting tissue function in a large number of chronic inflammatory diseases and will have application to a number of tissue engineering applications, such as tissue vascularization. Their method, for the first time, conceptualizes immune cell response to external stimuli as a temporal dynamic response taking on the same types of simple black-box model structures (transfer functions) that can be used for modeling and predicting engineered systems. Their approach identifies temporal profiles to deliver one or more drugs that can optimally promote normal immune function.

Summary Bullets

- **Dynamic Adjustments:** can make dynamic adjustments to obtain control over the response
- **Predict Stimuli:** will predict when pro- and anti-inflammatory stimuli should be applied to generate the appropriate temporal profile of cellular response

Solution Advantages

- **Dynamic Adjustments:** can make dynamic adjustments to obtain control over the response
- **Predict Stimuli:** will predict when pro- and anti-inflammatory stimuli should be applied to generate the appropriate temporal profile of cellular response

Potential Commercial Applications

- This approach will provide new therapeutic strategies for a variety of chronic inflammatory diseases, ranging from diabetic ulcers to Alzheimer’s disease, and to a number of tissue engineering applications, such as tissue vascularization on a chip.

- Useful for regulated blood vessel growth and other tissue engineering applications

Background and More Information

Properly regulated inflammation is a critical feature of wound healing, tissue regeneration, and pathogen clearance. However, dysregulated chronic inflammation can contribute to progression of numerous diseases and conditions, including Alzheimer's disease, chronic obstructive pulmonary disorder, inflammatory bowel disease, and diabetic foot ulcers, among others. Balanced, dynamically regulated immune response is essential for restoration and maintenance of tissue homeostasis. Moreover, current strategies aimed at broad immune suppression, e.g., via delivery of corticosteroids, can equally limit successful regeneration and recovery of tissue homeostasis. Furthermore, while MSC therapies are state of the art and hypothesized to function by acting as dynamic controllers of immune cell function, their mechanism(s) of action remains poorly understood and are subject to high variability in efficacy. There remains an unmet critical need to intervene in chronic inflammatory diseases. To address this need, we have developed a highly novel exogenous control methodology for regulating immune cell function by using a combination of data driven modeling and system dynamics and control theory.

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