A method for induction of immune-regulatory properties on mesenchymal stem cells to be used for cell therapy (Hadasit)

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Need:

Many pathological conditions arise from dysregulation of the immune system. In autoimmune diseases, Graft-versus-Host Disease (GVHD) and transplanted organ rejection, the increased pathological activity of immune system cells damages bodily / transplanted tissues with outcomes that can be life-threatening. Conventional immune-suppressive therapies have significant adverse safety profiles. There is growing interest in using mesenchymal stem cells (MSCs) as immune-regulatory agents for modulating pathological immune cells as treatment of such immune disorders, but inconsistent results from clinical trials using MSCs for such disorders emphasizes the need for MSCs to be activated ex vivo to a more desirable immuno-regulatory phenotype before administration to patients.

The market for immunosuppressive drugs for autoimmune and inflammatory diseases consists of biologics that inhibit TNF-α, T-cell-suppressors including steroids, and anti-metabolites. The market for TNF-α biologics alone is >$40B. However, this is an unsatisfied market given the significant adverse safety profiles of these drugs. The >$1B market for treatment of GVHD and transplantation also is in need of improved therapies, Thus, a new treatment, such as ex-vivo enhanced MSCs, that would have a superior safety profile should be targeting a market of >$10B.

Innovation:

A method for enhancing the immune-regulatory properties of MSCs to be used for cell therapy as treatment to ameliorate immune dysregulation. The invention uses IFN-γ, TGF-β and kyneurenine as an ex-vivo triple combination treatment (TCT) of MSCs, resulting in the enhancement of an immuno-regulatory MSC phenotype.

Findings:

In vitro:

Characterization of upregulated molecular pathways and MSC cellular phenotype following TCT, which shows an immune-regulatory phenotype that should provide for enhanced immune-regulatory activity in vivo.

In vivo:

The immune-regulatory function of TCT MSCs was shown to be significantly enhanced compared to untreated MSC therapy as manifest by increased efficacy in three animal models of immune system dysregulation:

1. GVHD stage IV
2. Skin transplantation
3. Autoimmune disease

Indications/applications:

Improved efficacy of treatment for autoimmune diseases, GVHD and organ transplantations.

Competitive advantages:

Improving safety and tolerability profile in a wide range of immune-based diseases.

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