Directed Mesenchymal Stem Cell Platform

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BACKGROUND

Mesenchymal stem cells (MSC) have been the subject of an expanding number of studies for decades with over 75,000 publications as of November 2022. The FDA currently lists over 1400 interventional clinical trials of which over 350 early trials (phase 1 or phase 2) have been completed and over 80 have been enrolled in phase 3 despite many conflicting and unclear clinical results that report diversely varied hypotheses on the mechanisms of action and therapeutic effects.

MSC represent a safe and attractive cellular therapeutic option for a diverse group of degenerative neurological and immunological disorders and can be harvested from a broad range of tissues such as skin, peripheral blood, synovium, endometrium, muscle, bone marrow, adipose tissue, placenta and other neonatal sources.

TECHNOLOGY

Directed priming mesenchymal stem cells utilizing a robotics cell media, selection and expansion platform induces discrete uniform cell phenotypes effective in suppressing inflammatory abnormalities, GVHD, multiple sclerosis, carcinogenesis, virogenesis and host of systemic autoimmune diseases and fibrotic disorders.

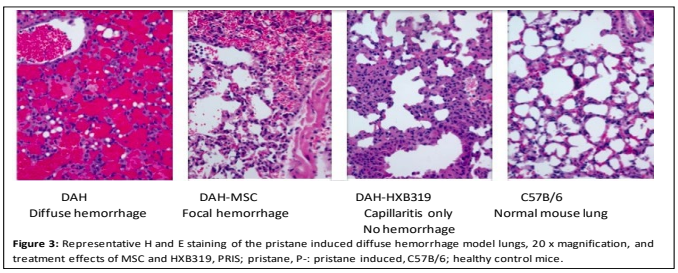

Figure 3: Representative H and E staining of the pristane induced diffuse hemorrhage model lungs, 20 x magnification, and treatment effects of MSC and HXB319, PRIS; pristane, P-: pristane induced, C57B/6; healthy control mice.

Directed MSC priming platform provides discrete, uniform and predictable *ex vivo* expanded and induced, or activated populations of stem cells useful in a wide range of cell-based therapies. MSC priming technology immunomodulation includes downregulation of specific cytokines, cytoxic activity and associated antibody production and their effects on immune cells and immune related cell populations.

Disease specific MSC priming media contains novel and specific cytokine components that synergistically induce stem cell phenotypes that activates the adapative immune system promoting the development of high-affinity antigen-specific T and B cell responses and immunological memory.

DATA

Directed MSCs were evaluated for the differentiation of immunologic pathways, gene expression of anti-inflammatory factors indoleamine 2, 3-Dioxygenase (IDO) and secreted proteins/factors and their pathways (using method-mass spectrophotometry), proteomics.

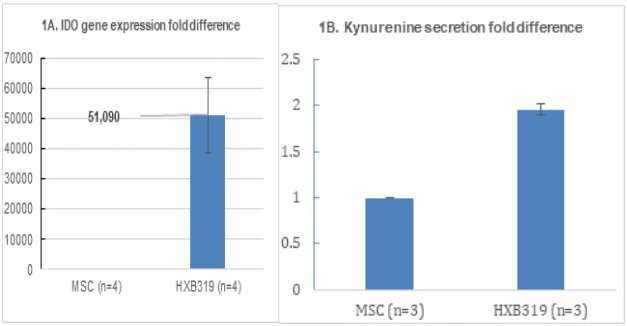

Figure 1A: A shows the median gene expression fold difference between the plain MSCs and HXB-319, using RT-PCR. **Figure1B** shows the IDO activity assays as measured by increased Kynurenine secretion in the tissue culture media at 24 hours' time point, demonstrated as fold difference as compared to the naked MSCs.

Directed MSCs secretome was shown to differ significantly from naïve MSCs from the same donor confirmed using 3 sets of GMP-grade directed MSC cells and 3 sets of naïve (un-directed) MSCs from different donor sets.

ADVANTAGES

Directed MSC Platform Technology

- Allogenic off-the-shelf
- Functionalized cell therapy specific to disease
- Uniform safe and efficacious cell populations
- Lower costs compared to autologous cell therapy
- Large markets with unmet medical needs

INTELLECTUAL PROPERTY

Patents:

- PCT/US20/40931
  Priming Media and Methods For Stem Cell Culture
- EPC 20746807.5, US 17/624,347, AU 2020311877, JP 2022-500052

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