Docket #: S19-434

Combinatorial Antibody Blockade of IL6 and PD-1/CD47 as Lung Fibrosis Treatment and Adjunct Cancer Immunotherapy

Technology summary

JUN has a critical role in regulating fibrosis through immune checkpoints such as PD-1/CD47. Immune checkpoints are upregulated by activated JUN in fibrotic tissue, leading to an immunosuppressive environment and further pathogenesis. The suppression of immune cells by activated JUN is further amplified by IL6, a pro-inflammatory cytokine often produced by pathologic fibroblasts. Thus, dual inhibition of IL6 and PD-1/CD47 relieves the subdued innate immunity of the host and can even reverse damage in fibrotic tissue. This has significant potential as a synergistic treatment for fibrotic diseases like idiopathic pulmonary fibrosis (IPF) and Covid-19 as well.

Stage of Development

In vivo, preclinical models of fibrotic diseases and graft-versus-host disease.

Applications

- Treatment of fibrotic diseases (e.g. pulmonary fibrosis, radiation fibrosis, liver fibrosis, kidney fibrosis, skin fibrosis), graft-versus-host disease and Covid-19
- Adjuvant cancer therapy with dual blockade of IL6 and immune checkpoint

Advantages

- Synergism of checkpoint blockade, PD-1/CD47, and IL6 blockade
- JUN could be used as a prognostic biomarker

Publications

- Cui, L., Chen, SY., Lerbs, T. et al. "Activation of JUN in fibroblasts promotes pro-fibrotic programme and modulates protective immunity." Nat Commun 11, 2795 (2020).
- G. Wernig, S.-Y. Chen, L. Cui, C. Van Neste, J.M. Tsai, N. Kambham, H. Vogel, Y. Natkunam, D.G. Gilliland, G. Nolan, I.L. Weissman Unifying mechanism for different fibrotic diseases *PNAS* May, 2, 2017.

Patents

- Published Application: WO2021101966
- Published Application: 20220411500
- Issued: 12,655,214 (USA)

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