Docket #: S18-395

Reversal of Tumor-Induced CAR-T cell and CD8+ T-cell Exhaustion with Annexin V

Researchers at Stanford University have discovered an invention to reverse tumor-induced CAR-T cell and CD8+ T cell exhaustion with administration of annexin V. The application of CAR-T cell anti-cancer therapy for treatment of hematologic cancers have been successful, however the tumor microenvironment (TME) surrounding solid tumors exhibit an immunosuppressive effect that directly inhibits CAR-T cell function. An important component of the immunosuppressive TME is phospholipid phosphatidylserine (PS) externalization causing anti-tumor immunity including arrest of T-cell signaling within cytotoxic CD4+ and CD8+ T lymphocytes. This essentially blocks immune signaling and inactivates CAR-T CD8+ lymphocytes. Stanford researchers have found that exogenous administration of annexin V, which binds to PS with high affinity, masks the highly immunosuppressive effects of externalized PS found in the TME. Furthermore, the combination of tumor specific CAR-T cell therapy with continuous administration of annexin V over several weeks' reverses tumor induced CAR-T cell exhaustion, a novel invention that has the potential to make CAR-T therapy a viable treatment for solid tumors.

Applications

- Administration of combination CAR-T cell therapy with annexin V for the treatment of solid tumors
- Continuous systemic or local infusion of annexin V at doses of 2 to 2.5 mg/kg/day for 2 to 4 weeks based on animal model work is well tolerated

Advantages

- Annexin V is a human protein with nanomolar affinity for PS
- CAR-T cell therapy has been ineffective in treating solid tumors, combination therapy with annexin V could make it a viable treatment option

Patents

- Published Application: WO2022212352

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