Washington University in St. Louis
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ENGINEERED ADENOVIRUS VECTOR FOR EFFICIENT DENDRITIC CELL ANTIGEN LOADING IN CANCER IMMUNOTHERAPY

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Disease indication - Cancer

Drug format – Adenoviral vector for immunotherapy/dendritic cell therapy

Drug class – Improvement

Research stage and Preliminary data:

- *In vitro* – dendritic cell infectivity and gene transfer assays demonstrated improvement of engineered vector (Ad5-PK) compared to wild-type adenovirus (HAdV5)
- *In vivo* – mice vaccinated with Ad5-PK had enhanced T-cell-mediated release of interferon gamma in response to both a mesothelin peptide and a tumor line expressing mesothelin

Target – Carbohydrate biomarkers of cancer

Background:

Dendritic cells (DCs) are potent antigen presenting cells (APCs) with a unique ability to prime an immune response. This activity has been harnessed as an immunotherapy intervention against cancer. The ability of DCs to induce an anti-tumor T-cell-mediated immune response depends on both the properties of the antigen and the method of antigen delivery to the DC.

Adenoviral vectors (e.g., HAdV5) are commonly used for delivering genetic material to non-dividing cells such as DCs. However, in the past it has been difficult to utilize HAdV5 for loading tumor-specific antigens into DCs because DCs lack CAR (coxsackie-and-adenovirus receptor - the native receptor for HAdV5). In order to achieve meaningful therapeutic efficacy of adenovirus-based therapies, new approaches for infection of human DCs are required.

Keywords – adenovirus; dendritic cells; cancer vaccine; cancer immunotherapy

Mode of action:

This engineered adenoviral vector enhances DC infection/antigen loading by replacing the CAR binding domain with a fiber knob derived from porcine adenovirus type 4 (PK). The resulting chimeric vector, Ad5-PK, can then enter the DCs through glycosylated cell surface proteins, independent of CAR. This increases DC antigen loading, which is necessary to avoid tolerance and drive T-cell activation for effective cancer immunotherapy.

Competitive edge:

- **Enhanced immune response –** by using the porcine knob, Ad5-PK:
  - improves infectivity, gene transfer, targeted antigen expression and subsequent T-cell activation in dendritic cells compared to wild-type HAdV5
  - enables highly efficient tumor antigen loading
- **CAR-independent –** PK mediates infection through glycosylated cell surface proteins expressed by dendritic cells instead of relying on the conventional coxsackie-and-adenovirus receptor (CAR)

Publications

- Wilkinson-Ryan, I., Kim, J., Kim, S., Ak, F., Dodson, L., Colonna, M., ... & Goedegebuure, S. P. (2015). Incorporation of porcine adenovirus 4 fiber protein enhances infectivity of adenovirus vector on dendritic cells: Implications for immune-mediated cancer therapy. *PloS one*, 10(5), e0125851.

Patents

- Porcine knob xenotype chimeric adenoviral vector for dendritic cell infection (U.S. Patent No. 9267153)
- Additional foreign patents

Website

- Curiel Lab