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Nanoparticles Containing Toll-Like Receptor Agonist for Enhanced Efficacy of Immune Checkpoint Blockade

Stanford inventors have developed a nanoparticle containing the toll-like receptor agonist (TLR7-NP) that elicits a potent anti-tumor immune response in multiple cancer types without inducing undesired systemic inflammation and toxicity. The nanoparticles precisely incorporate the TLR agonist, yielding a tightly controlled composition that is then released at a consistent manner under physiological conditions, therefore reducing toxicity. Researchers in the Davis lab treated mice with these engineered TLR7-NPs and observed inhibition of tumor growth, prolonged survival, and effective immunological memory in colon, pancreatic, and glioma cancer models. Mice treated with TLR7-NPs and anti-PD-1 checkpoint blockade therapy in combination exhibited even more robust antitumor efficacy, eliminating all tumors in a colon cancer model, and rejecting the second tumor challenge. This combination therapy also induces tumor regression and improves survival in a pancreatic cancer model. These results were recapitulated in a human skin tumor organoid where TLR7-NP and anti-PD-1 combination therapy induced a robust T cell response. Mechanistically, the TLR7-NPs are hypothesized to increase conventional dendritic cells in the tumor draining lymph nodes, expanding functional CD8+ T cell memory and activation for antitumor responses. The TLR7-NPs represent a robust and broadly applicable cancer immunotherapy that can be used in conjunction with checkpoint blockade therapies.

Stage of Development

In vivo

Applications

- Novel cancer immunotherapy modality

Advantages

- Potent yet safe method to deliver toll-like receptor agonists to elicit anti-tumor immune response
- Sustained release of TLR7 agonist allows for continuous immune stimulation using low drug doses in the local microenvironment
- Broadly applicable cancer immunotherapeutic strategy that is effective against multiple tumor types (colon, pancreatic, glioblastoma)
- Nanoparticles allow surface modification for precise spatial control
- Nanoparticles have well-controlled physiochemical properties with precise composition, drug loading, and tunable drug release kinetics
- Versatile delivery routes: both intratumoral and intravenous delivery
- Facile scale-up manufacturing suitable for widespread use

Patents

- Published Application: WO2022226032
- Published Application: 20240197910
- Issued: 12,678,516 (USA)

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