Tuning Vaccine Physical Properties to Improve Anti-tumor Response Using Polyplexes

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I identified physical features in a candidate cancer vaccine that lead to improved anti-tumor response. Though cancer vaccines present an attractive strategy to coax the immune system to target tumor cells specifically, they have exhibited limited clinical success. One contributing factor is that cancer vaccines lack defined physical criteria for effective delivery, which my project strives to address. I electrostatically assembled an anionic immunostimulatory signal (CpG) and a melanoma antigen (Trp2), modified with arginine groups (R) to be cationic, into nanoparticles known as polyplexes. The CpG signal induces dendritic cells (DCs) to expand and activate tumor-specific cytotoxic T cells (CTLs) that can specifically seek out and attack melanoma. Polyplexes eliminate the presence of extraneous materials usually required to deliver vaccine, simplifying design to just two spontaneously assembling components delivered at high density. This project takes advantage of polyplex tunability to control physical properties and immune outcomes in cancer. I discovered that increasing the number of Trp2 arginine groups produced smaller, more cationic particles, while decreasing the number of arginine groups produced particles with higher levels of antigen. I linked these properties to delivery efficacy, with smaller cationic particles increasing DC uptake, while higher antigen levels correlated with greater CTL activation. Trp2R3 formulations improved mean survival time by over 60% in a mouse model of cancer. This project demonstrated how polyplex physical properties can be tuned to improve anti-tumor response, and suggested that small size, cationic charge, and high antigen composition are favorable features to incorporate in future cancer vaccine design.

Awards Won:
Third Award of $1,000