OPTIMIZING ANTI-CANCER VACCINES TO PREFERENTIALLY STIMULATE HIGH-AVIDITY T CELLS

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ABSTRACT

Despite stimulating large numbers of anti-cancer T cells, anti-cancer peptide vaccines often do not result in a strong anti-tumor T cell response. To resolve this paradox, an experimental study has shown that the majority of vaccine-elicited T cells may be of low avidity to cancer antigen [1]. Furthermore, these low avidity T cells not only fail to kill tumor cells, but also inhibit cancer killing by high-avidity T cells, which might explain the poor performance of certain peptide vaccines.

By using a system of ordinary differential equations, we develop a mathematical model of the stimulation of high and low-avidity T cells by peptide vaccines and the inhibition of the T cell response by low-avidity T cells. We propose vaccination strategies to optimize the preferential stimulation of high-avidity T cells by controlling peptide vaccine delivery and dosage. Our simulations predict that daily, low-dose injections of vaccine may result in a greater than 2000-fold reduction in cancer cells. By contrast, an unoptimized vaccine protocol such as a high-dose injection given every 3 weeks induces only a 30-fold reduction. A sensitivity analysis of our model reveals that our results are robust, thereby offering a simple technique to potentially improve existing therapies.

REFERENCES

1. Chung, B., Stuge, T. B., Murad, J. P., Beilhack, G., Andersen, E., Armstrong, B. D., Weber, J. S. 5. and Lee, P. P., “Antigen-specific inhibition of high-avidity T cell target lysis by low-avidity T cells via trogocytosis”, *Cell Reports*, 8(3): 2014, pp. 871-882.