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Cytokine Optimization of Anti-tumor Vaccines

[An anti-tumor vaccine will be developed and optimized to overcome tumor immune evasion.]

Vaccines have been fundamental in protecting the public against epidemics of viruses such as smallpox, polio, and the measles. With a well-grounded history of effectiveness in treating viral disease, vaccine therapy of cancer is a possible treatment. The advantages of tumor vaccination include the potential to treat both a primary tumor recurrence and metastasis. However, the role of vaccine treatment in cancer therapy would differ from the preventative role in traditional immunizations because cancer vaccine therapy is used to treat afflicted individuals versus prevent occurrence in healthy individuals. In addition, tumors have evolved a variety of ways of evading the immune system. This project will a)explain possible ways that tumors escape immune detection and b)result in the design of effective anti-tumor vaccines to overcome this immune escape. In the development of a tumor immune response, three things are essential, a tumor protein (so that the immune system has a specific target), a special cell that instructs the immune system to respond against that tumor protein target, and finally the proper helper factors to drive the whole system. A tumor may release inhibitory factors that influence the immune response. Specifically, these inhibitory factors may prevent the cells involved in presenting the tumor protein from working, thus breaking down an essential part of the immune response. We will assess the specific actions of these inhibitory factors such that a more effective anti-tumor vaccine can be designed. To overcome the actions of tumor inhibitory factors, DNA and virus vaccines will be generated as anti-tumor therapy. These vaccines activate the immune system by acting as a substitute for the tumor protein target needed in stimulating an immune response. But because of the inhibitory factors produced by the tumor, the vaccines may not be sufficient to mount an immune response. Therefore, additional helper factors will be added to overcome the effects of the inhibitory factors. These helper factors are normally present in immune responses, but may be lower in cancer patients. By supplementing with the helper factors, the balance may be shifted from a tumor-controlled environment to a tumor-killing environment. Thus, by determining how the tumor disrupts the components of an effective immune response, vaccines and helper factors can be made to supplement these disrupted components to generate a more effective cancer treatment.