

Manipulating the Inhibitory Arm of the Immune System, a Needed Strategy for Cancer Therapy

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The scientific community has been working for more than 3 decades in developing effective targeted immune therapy and cancer vaccines with no notable major success. It has been shown clearly that the development process lacked the knowledge of a delicate interaction between the immune system and the tumor and of the ability of cancer cells to manipulate the immune system by promoting its inhibitory arm and suppressing its effector arm. This led to an apparent deficiency in the strategies addressing the development of effective immunotherapy and cancer vaccines. The inhibitory mechanism of the immune system play a major role in suppressing an infected immune response against tumors. The mechanisms by which the immune system is inhibited, now we know, are many. These include: inhibitory cells include both T and myeloid cells (T. regulatory cells and myelosuppressive cells); Co-inhibitory molecules that can be expressed on tumors sending suppressive and refill signals to T cells such as PDL1; and the secreted inhibitory cytokines and factors such as interleukin-10 and TGF-beta. Accordingly, developing strategies to inhibit these suppressive mechanisms would be crucial for the development of an effective immune response against cancer. Our laboratory has been working on addressing some of these mechanisms including the selective inhibition of T. regulatory cells and strategies combining blockade of co-inhibitory signaling with targeted vaccines to enhance their therapeutic effect. Some of immune suppressive mechanisms and strategies designed to inhibit those mechanisms will be addressed in the talk.