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Abstract of the proposed project for 2024-2025 PhD Fellowship

Enhancing anti-tumor immunity by promoting IL-17-induced signaling and Tregs conversion

The adaptive immune system can recognize and target tumor cells. However, anti-tumor immunity is potently suppressed by regulatory T cells (Tregs), which are physiologically required to avoid the destruction of the host's own tissues. Therefore, the goal of tumor immunotherapy is to release immunosuppression to permit an immune attack against cancer cells. This project aims to enhance anti-tumor immunity by supercharging the signaling triggered by the proinflammatory cytokine Interleukin-17 (IL-17).

IL-17 is produced by a specialized set of T helper 17 (Th17) cells that are infiltrating tumors. The receptor for IL-17 is widely expressed. However, IL-17 itself is a very weak activator of signaling response due to a potent negative feedback loop that operates at the level of IL-17 receptor signaling complex assembly. Our work showed that targeting this inhibitory loop massively enhances IL-17 responses, which strongly potentiates the production of various proinflammatory cytokines, including IL-1, IL-6, and IL-23. Apart from promoting inflammation, these cytokines trigger the conversion of Tregs into Th17 cells, thus potentiating immune system activation. The core hypothesis of this project is that removing the inhibition of IL-17 signaling within the tumor microenvironment would strongly enhance Tregs conversion and unleash the immune system to destroy cancer cells.

The research has two aims. The first goal is to characterize the inhibitory feedback loop operating at the level of IL-17 receptor complex assembly to identify the best strategy to target it. The second goal is to assess whether promoting IL-17 signaling can trigger potent anti-tumor immunity in vivo. The prospective PhD students will gain a deep understanding of the immune system and tumor immunology and gain expertise in a broad range of methods, including molecular biology, biochemistry, flow cytometry, and analysis of tumor models.