Hunter College of the City University of New York Department of Biological Sciences Fall 2023 Inga Richter Seminar Series

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How B cell tumors use embryonic "superpowers" to outcompete healthy immune cells

A small fitness gain during the Darwinian selection of B cells can reproduce supercompetition, a process that normally only occurs during embryonic development and may help explain the nature of difficult-to-treat B cell tumors.

Most cancers of the immune system (i.e. lymphomas) arise from B cells undergoing an intense natural selection process required for specialized immune protection (e.g. against new viruses). These B cells repetitively and vigorously compete against each other for a chance to receive selection signals to survive and grow. Changes in a gene called BTG1 are uniquely found in patients with B cell lymphoma and associate with poor response to currently available treatments. We find that these BTG1 changes confer a slight edge in the competition against healthy cells, allowing them to grow and expand more quickly. This effect is repeated many times over the course of the immune response, resulting in "supercompetitors" that entirely outcompete healthy B cells. This behavior is reminiscent of the embryonic "supercompetition" process and recalls "survival of the fittest" features, pointing to BTG1 as an important gate-keeper of natural selection during the immune response. These findings suggest a delicate trade-off between defending multicellular organisms from infection and the risk of facilitating certain features in B cells promoting the growth of cancer. Despite ongoing research, there are no effective treatments for about 40% of patients with B cell lymphoma. Therefore, understanding the processes involved in the formation of the worst and most lethal forms of these tumors represents a first step toward intervention.

> Monday, Nov. 27, 2023 @12:30pm Hunter North Room 926 Host: Hualin Zhong