Inflammasome-independent role of NLRC4 in suppressing melanoma progression

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The immune system has evolved to fight off numerous different types of pathogens including bacteria, viruses, and parasites. The first line of defense against these pathogens are innate immune cells including macrophages. Macrophages ingest pathogens and a family of cytosolic proteins, known as NOD-like receptors (NLR), recognize conserved sequences on the pathogens. Recognition of pathogens by NLRs alerts the immune system to the presence of an invader and subsequent control of infection. In addition to pathogen recognition NLRs recognized endogenous cell danger signals that are released during cell stress.

Melanoma is one of the most deadly forms of skin cancer due to limited therapeutic options and a weak immune response to cancer cells. Due to the suboptimal immune response the tumor is able to grow and eventually metastasize. Whether NLRs can recognize healthy or dying tumors cells remains unclear. Subsequently, the role NLR proteins play during tumor progression and metastasis is also unknown.

We investigated the role of a specific NLR protein, NLRC4, in a mouse model of melanoma. Interestingly, we found that mice that lack the NLRC4 protein developed significantly larger tumors than mice that express NLRC4. Mice deficient in NLRC4 had a diminished immune response to melanoma leading to enhanced tumor growth. We also observed decreased expression of NLRC4 in metastatic melanoma tissue in humans. We conclude from these observations that expression of NLRC4 is important for recognizing melanoma and initiating an immune response to melanoma.

Ann Janowski Biographical Sketch

Ann is the daughter of Wayne and Colleen Janowski and she was born and raised in the city of Chicago, Illinois. Growing up Ann was enthusiastic about academics and sports. That enthusiasm carried over to college where her love for science grew. Ann got her start doing research at St. Louis University (Go Billikens!) in Dr. Laurie Shornick’s laboratory. Under Dr. Shornick’s guidance Ann learned a variety of scientific techniques and got her first experience presenting at the Autumn Immunology Conference.

Ann’s interest in research continued to blossom after college at Loyola University medical center in Dr. Edward Campbell’s laboratory. It was at this time she decided that she wanted to pursue a PhD in Immunology and that the University of Iowa was the best possible fit. What particularly fascinated Ann about the immune system is that the immune response must be carefully regulated. An overly robust immune response may control infection, but also result in pathology of host tissue. Ann was excited to learn more about this delicate balance.

During her first year of graduate school Ann joined the Sutterwala/Cassel laboratory. She developed an interest in tumor biology, specifically the innate immune response to melanoma. When Ann is not in the lab she enjoys spending time with friends, trying new restaurants in the Iowa City area, and doing CrossFit.

Ann is grateful for your attendance of this seminar and hopes you enjoy the talk!