Orphan Inflammasome Sensors and Inherited Skin Cancer

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Abstract
The inflammasome is a major innate immune effector complex that is involved in multiple aspects of pathogen defense and auto-immunity. The human genome encodes more than a dozen inflammasome sensor proteins. While a few of these sensor proteins are known to recognize conserved pathogen derived molecules, the function and ligand specificity of most inflammasome sensors remain obscure. In this seminar, I will describe our recent discovery of an inherited Mendelian skin cancer syndrome caused by mutations in an orphan inflammasome sensor, NLRP1. Patients harboring NLRP1 mutations suffer from pediatric-onset recurrent hyperplastic lesions on their palms and soles, with a high risk of malignant transformation to aggressive squamous cell carcinoma. I will describe recent biochemical and ex vivo skin culture experiments that uncover the unique properties of NLRP1 that differ from known inflammasome sensors and highlight an unprecedented mechanism of inflammasome activation in the skin. I will also touch upon some ongoing work and future research directions that aim to define the repertoire of additional orphan inflammasome sensors in epidermal/mucosal surfaces and characterize their functions in immune defense and carcinogenesis.

About our Speaker
Dr Franklin Zhong graduated from Stanford University with a PhD in Cancer Biology in 2014. During his doctoral research, he made seminal discoveries on how human telomerase accesses the telomeric chromatin to confer cell immortality. This work led to the identification of the genetic basis for a telomere-related premature aging disease, as well as a novel therapeutic strategy to target telomerase in cancer. Presently, Dr Zhong’s research interest is in the intersection between cancer, inflammation and innate immunity, especially in relation to inflammatory skin diseases and skin cancer.

Selected Publications:

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