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Selected Publication

Chen, J., Feng, W., Jiang, J., Deng, Y. and Huen, MS. (2012) Ring finger protein RNF169 antagnonizes the ubiquitin-dependent signaling cascade at sites of DNA damage. *J Bio Chem*, 287, 27715-22.

Research Aims and Interests

Our research encompasses the study of cell responses to DNA damage, including those that arise from DNA double-strand breaks (DSBs) and stressed replication forks. Specifically, we are keen in identifying the components that sense and propagate DNA damage signals, and in elucidating the determining factors that contribute to the tempospatial regulation of the many DNA damage responses.

In the past few years we have worked with a number of human ubiquitin enzymes that modify DSBs to productively assemble DNA damage mediator and signaling factors for effective checkpoint control and DNA repair processes. Aside studying the many positive regulators of DSB signal transduction pathways, we have more recently become very interested in the self-limiting mechanisms that restrain excessive spreading of DSB-associated chromatin responses. How are chromatin ubiquitylating activities limited to the vicinity of DSBs? What happens if cell responses to DSBs become hyperactive?

We have recently identified RNF169 as a negative regulator of DSB responses. By competing for ubiquitin adducts at DSBs, RNF169 limits 53BP1-dependent processes, including non-homologous end joining (NHEJ) and checkpoint control. Despite its clear role as a limiting mechanism that balances DSB signal amplification, its functionality and physiological relevance remain unexplored. To this end, we have affinity purified RNF169 protein complexes and are currently characterizing these networks.