Receptor-mediated ubiquitination signaling
as a novel therapeutic target for tumor immunity and autoimmunity

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Ubiquitination has been implicated in many dynamic cellular processes, including transcriptional regulation, regulation of protein-protein interactions and association with ubiquitin-binding scaffolds, and thus the defects within these pathways cause a wide range of diseases. Pellino1 (Peli1) is initially characterized as a family of ubiquitin E3 ligases that can catalyse the ubiquitination of several proteins involved in the regulation of innate and adaptive immune responses. Importantly, Peli1 is a receptor-mediated signal responsive ubiquitin ligase that promotes the lysine 11-, 48- or 63-linked ubiquitination of target substrates.

Ligand-independent activation of receptor-mediated signaling is one of critical mediators for triggering pathogenic processes. Interestingly, the expression of Peli1 protein is highly suppressed under normal and non-pathogenic conditions and is distinctly activated in response to the various receptor-mediated signaling. We have recently found that the constitutive expression of Peli1 resulted in ligand-independent responses of B and T cells and facilitated the development of diseases, such as B cell lymphoma and autoimmunity. To further examine the gain- or loss-of-functional role of Peli1 in autoimmunity and tumor immunity, we employed both inducible transgenic and T cell specific knockout mouse models. Thus, this study will include the immunologic basis of Peli1-mediated macrophage, B and T cell regulations, the related pathogenesis, and therapeutics.