定量生命科学研究所セミナー

Linear ubiquitination: Unexpected regulation and involvement in immunological disorders



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Linear (M1-linked) ubiquitin chains, which are exclusively generated by the LUBAC ubiquitin ligase complex, played crucial roles in inflammatory signaling by inducing NF-kB activation and suppressing programmed cell death including apoptosis and necroptosis. LUBAC is composed of three subunits and the HOIP subunit has the catalytic center for linear ubiquitination. The HOIL-1L subunit also has the E3 ligase center, however, precise function of HOIL-1L E3 has not been elucidated. We unexpectedly found that HOIL-1L E3 attenuates LUBAC function by conjugating mono-ubiquitin to all three LUBAC subunits. Introduction of E3-defective HOIL-1L mutants augments NF-kB activation and suppresses programmed cell death. We are now dissecting roles of linear ubiquitination in immunological disorders and found that augmented LUBAC activity appears causative to some human autoimmune diseases. Our current progress will be presented in this lecture.

幹事:クロマチン構造機能研究分野

主催:東京大学定量生命科学研究所

共催:ERATO 胡桃坂クロマチンアトラスプロジェクト

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