SL02 **Negative Feedback Regulation of Inflammation & Novel Anti-Inflammatory Strategy**

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Inducible Negative Feedback Regulation of Inflammation

Inflammation is a hallmark of many important human diseases including infectious diseases, chronic obstructive pulmonary diseases, otitis media, asthma, arthritis, inflammatory bowel disease, atherosclerosis and cancer. Although an appropriate inflammation is beneficial, if excessive, it is clearly detrimental to health. Thus, inflammation must be tightly regulated. However, how inflammation is tightly controlled remains largely unknown. Inducible negative feedback regulators play an essential role in controlling overactive inflammation. Our ***objective*** is to understand the molecular mechanisms by which inflammation is tightly regulated in human inflammatory diseases and identify novel therapeutic targets. We and others have shown that CYLD, a novel deubiquitinase, acts as a key inducible negative feedback regulator for inflammation, cancer and fibrosis *(Nat Commun 2012)*.

Novel Anti-inflammatory Strategy by Up-regulating Negative Regulators Through Drug Repositioning

Over the past decades, most anti-inflammatory strategies have focused on directly targeting the positive pathways to suppress inflammation. While these agents often showed reasonable efficacy, they exhibited significant adverse effects, e.g., increased susceptibility to infection, which prevented their further clinical use. Thus, there is an urgent need for developing novel therapeutic strategies without serious side effects by up-regulating the negative regulators of inflammation. We recently found that Roflumilast, an existing drug for asthma, suppressed inflammation by up-regulating CYLD, the negative regulator of inflammation *(Nat Commun 2013)*. In addition to treating inflammatory diseases, up-regulating CYLD may also lead to promising therapeutic strategies for tumors and fibrosis.