Crystal structure of the autoinhibited form of NOD2

Authors
Umeharu Ohto, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan
Sakiko Maekawa, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan
Toshiyuki Shimizu, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan

Nucleotide-binding and oligomerization domain (NOD)-like receptors (NLRs) are pattern recognition receptors that recognize pathogen-associated molecular patterns or damage-associated molecular patterns in the innate immune system. NOD2, a member of the NLRs family, is activated by muramyl dipeptide (MDP), a bacterial cell wall fragment. Mutations of NOD2 have been associated with chronic inflammatory disorders such as Crohn's disease (CD), Blau Syndrome (BS), and early-onset sarcoidosis (EOS), but little is known about its signaling mechanism and the role it plays in these diseases. Here, we report the crystal structure of rabbit NOD2 in an ADP-bound state (Maekawa et al., Nature Commun., 2016). Based on the structure, we discuss the autoinhibition mechanism of NOD2 and the possible effect of disease-related mutations.