

## **Understanding how RIPK2 inhibitors affect ubiquitin-mediated inflammatory signalling**

**July 23, 2018** – Activation of the bacteria-sensing NOD receptors triggers inflammatory signalling via Receptor-interacting protein kinase 2 (RIPK2). Since RIPK2 inhibitors targeting the ATP-binding pocket have been shown to block this signalling pathway, it was assumed that RIPK2 kinase activity was important for signal transmission. In this work published recently in [EMBO Journal](#), Hrdinka, Schlicher and colleagues from [Mads Gyrd-Hansen's lab](#) demonstrate that kinase activity is in fact dispensable for NOD signalling and that these RIPK2 inhibitors are instead preventing the binding of the ubiquitin ligase, XIAP, and the subsequent XIAP-mediated ubiquitination of RIPK2 necessary for downstream signalling. This work could have therapeutic implications since NOD signalling is associated with several chronic inflammatory conditions such as Crohn's disease.