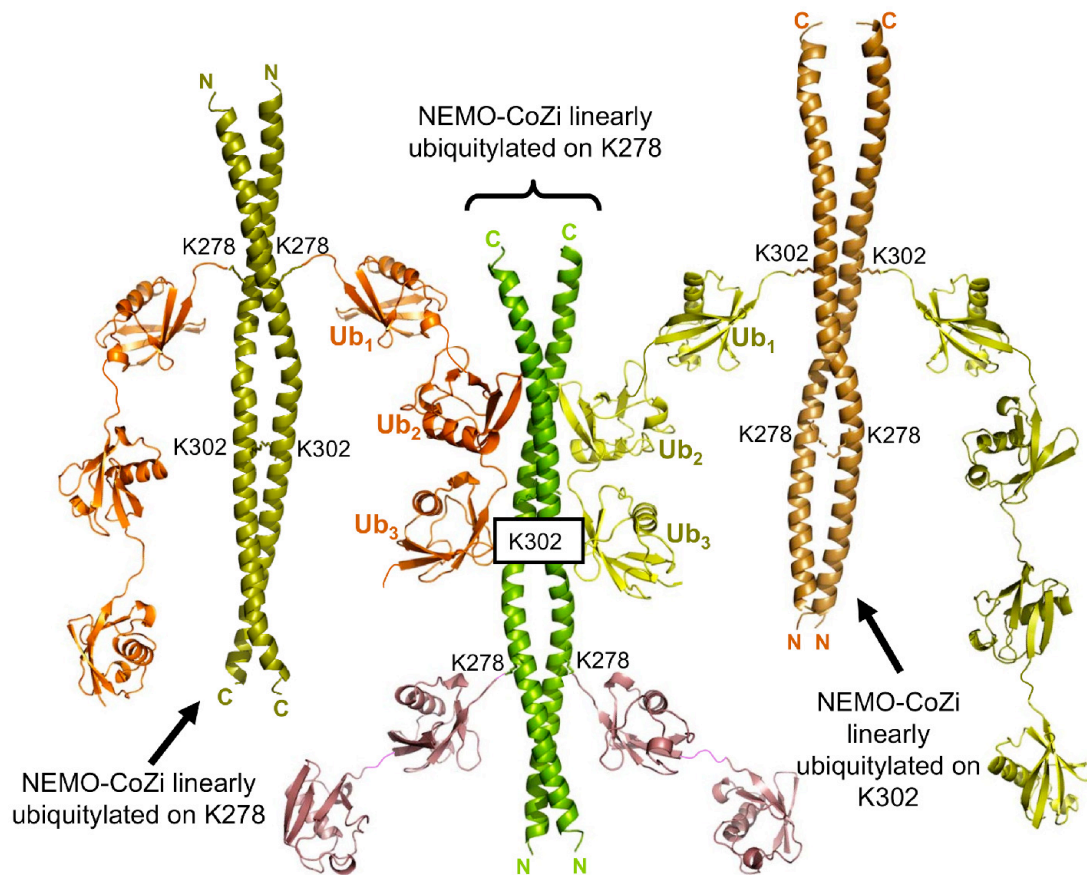




Supplementary information S3 (figure) | Linear ubiquitylation and ubiquitin-binding of NEMO. Ubiquitylation of an adaptor protein NEMO could affect its oligomerization, which may result in more efficient activation of IKK kinase complex. Lys285 and Lys309 of the human NEMO UBAN motif (corresponding to Lys278 and Lys302 in mouse sequence, respectively) were shown to be linearly ubiquitylated by the LUBAC ligase¹. The crystal structure of the complex between the mouse NEMO UBAN motif and linear diubiquitin² suggests a possibility of non-covalent *trans* interactions between non-ubiquitylated NEMO UBAN motif and linear ubiquitin chains of neighbouring NEMO molecules, which are ubiquitylated at either Lys278 (left) or Lys302 (right). The crystal structure also indicates that NEMO molecules ubiquitylated at Lys302 (human Lys309), which is at the core of the ubiquitin-binding interface, cannot recognize linear ubiquitin chains anymore while those linearly ubiquitylated on Lys278 can still have such interactions. Therefore, it is possible that these two linear-ubiquitylation events, one on Lys278 and another on Lys302, are differentially used to regulate oligomerization of ubiquitylated NEMO molecules, leading to different levels of IKK kinase activation.

Bibliography:

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