Review of: "Classical swine fever virus NS5A inhibits NF-κB signaling by targeting NEMO"

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Li et al has demonstrated that NS5A inhibits the activity of NF-κB signaling pathway by targeting NEMO. Mechanistic analysis revealed that NS5A mediated proteasomal degradation of NEMO through K27-linked polyubiquitination. Although they have present many ubiquitination assays, there are still some concerns about the regulation mechanism in details.

1、 As we know, NEMO is mainly localized in the cytoplasm and formed a complex with IKKα/IKKβ and it was also reported that genotoxic stress causes nuclear localization of IKK-unbound NEMO. So we wonder the exactly subcellular localization of NEMO where it interacts with NS5A after CSFV infection.

2、 The authors have proved that NS5A could induce K27-linked polyubiquitination of NEMO and meanwhile, NS5A could block K63-linked polyubiquitination of NEMO. It seems like that NS5A functions as both an ubiquitin E3 ligase and a deubiqitinase. So we wonder that which domain(s) is responsible for these modification.