pH-dependent regulation of p62/SQSTM1 autophagy adaptor

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In macroautophagy, p62/SQSTM1 has dual roles as a key adaptor for cargo selection and an autophagic degradation substrate itself. p62 connects N-degrons and/or ubiquitylated cargoes to autophagosome by forming homo- or hetero-oligomer. However, little is known about how p62 recognizes N-degron and how its oligomerization is regulated. We have recently shown that p62 is a new type of N-recognin. The ZZ-domain of p62 provides a negative charged binding pocket to Arg charged N-degron (Nt-Arg), a prototype type-1 substrate. Although differences in binding affinity exist for each N-degron, p62 also interacts with the type-2 N-degrons such as Nt-Tyr and Nt-Trp. Intriguingly, the interaction between ZZ-domain and various N-degrons is greatly influenced with pH-dependent p62 oligomerization *via* PB1 domain. It has been known that the cellular pH conditions in the autophagic process vary from neutral to acidic depending on the stage. Therefore, it is likely that the pH-dependent regulation of oligomeric state of p62 is tightly coupled with the autophagic process.