# Mono-ADP-ribosylation in the control of intracellular membrane traffic

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ADP-ribosylation, a pivotal post-translational modification catalyzed by mono- and poly-ADP-ribosyltransferases (ARTs), modifies key protein residues, impacting various cellular functions. Originating from an ancient enzyme superfamily, ARTs have evolved within bacterial defense and offense systems and have been integrated through lateral gene transfer during eukaryotic evolution. As a result, ARTs target proteins essential for numerous cellular processes, revealing their potential role in physiological and pathological conditions.
The mechanism of mono-ADP-ribosylation was first revealed through the action of diphtheria toxin, a mono-ART that hinders protein synthesis by modifying the GTPase elongation factor 2. Similar ART activities have been identified in other toxins that target proteins essential for cellular functions, like the small GTPases of the Rab family.
Our studies show that PARP12, a mono-ART localized at the Golgi complex, is key in controlling some intracellular membrane traffic pathways. In response to oxidative stress, PARP12 relocates to stress granules, thereby disrupting traffic from the Golgi to the plasma membrane. Importantly, PARP12 modifies Golgin-97 and Rab14, proteins that are central to exocytic and endocytic pathways, respectively. This action on the Golgin and Rab families underlines the significance of mono-ADP-ribosylation in membrane traffic regulation. Furthermore, the modification of Rab5 and Rab1A by mono-ARTs points to the broader impact of this post-translational modification in cellular functions. PARPs are also active in other contexts like cytosol-to-nucleus transport and in the development of cancer invasiveness.
In summary, the role of mono-ARTs underlines that mono-ADP-ribosylation is a significant modifier of intracellular trafficking and numerous other cellular mechanisms, with profound implications for both health and disease.