S59-3 A Novel regulatory mechanism of the MAPK signaling mediated by RNA

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Mitogen-activated protein kinases (MAPKs) are evolutionary conserved enzymes that convert extracellular signals into various outputs such as cell growth, differentiation and cell death. The MAPK signalling pathway has long been known as a transcriptional regulator of cellular signalling by phosphorylating various transcription factors. Our genetic screen has efficiently isolated negative regulators of the Pmk1 MAPK pathway. These include *rnc1*$^{+}$ encoding a novel KH-type RNA-binding protein. We demonstrated that Rnc1 binds and stabilizes the mRNA of a MAPK phosphatase at the post-transcriptional level. Notably, the Pmk1-mediated phosphorylation enhances the RNA-binding activity of Rnc1 to bind and stabilize Pmp1 mRNA, thus identifying Rnc1 as a component of a novel negative-feedback loop that regulates the Pmk1 pathway (Sugiura *et al*., *Nature* 2003). We also identified Nrd1, an RRM-type RNA-binding protein as a target for the Pmk1 MAPK. Nrd1 binds and stabilizes the mRNA of the essential myosin II light chain Cdc4, thereby suppressing the cytokinesis defects of the *cdc4* mutants. Pmk1 phosphorylates Nrd1, thereby negatively regulating the binding activity of Nrd1 to Cdc4 mRNA (Satoh *et al*., *Mol. Biol. Cell* 2009). One important aspect of our findings is that the increase in mRNA levels involves not only the transcriptional upregulation, but also the post-transcriptional gene regulation. Our discovery also highlights a potential role and an emerging view of RNA-binding protein as a regulator of MAPK signaling and as a future target of drug discovery.