Unexpected role for the IKK complex in protecting cells from death

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The team of Prof. Bertrand in the group of Prof. Vandenabeele, demonstrates that the IKK complex protects cells from death by inactivating RIPK1, thereby revealing an unexpected NF-kB-independent new role of the IKK complex.

TNF is a master pro-inflammatory cytokine and inappropriate TNF signaling has been demonstrated to drive many inflammatory diseases. Ligation of TNF to its receptor TNFR1 promotes inflammation either directly by the NF-kB-dependent induction of pro-inflammatory mediators, or indirectly by promoting cell death.

This cellular suicide exacerbates inflammation by releasing danger signals in the cellular environment as well as by affecting the permeability of the bodily barriers to microbes. The molecular mechanism controlling death induced by TNF is still far from clear. In the group of Prof. Vandenabeele, the team of Prof. Bertrand demonstrates that the IKK complex protects cells from death by inactivating RIPK1, thereby revealing an unexpected NF-kB-independent new role of the IKK complex.

Mathieu Bertrand (VIB/UGent): "Our results indicate that RIPK1-dependent death contributes to inflammatory conditions resulting from inactive IKK complex. Knowing that RIPK1 inhibitors exist, I hope these insights will help to develop future therapeutic protocols for inflammatory conditions."

More information: "NF-κB-Independent Role of IKKα/IKKβ in Preventing RIPK1 Kinase-Dependent Apoptotic and Necroptotic Cell Death during TNF Signaling." *Mol Cell*. 2015 Sep 2. pii: S1097-2765(15)00616-4. DOI: 10.1016/j.molcel.2015.07.032

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