

Interaction between 5'-nucleotidase cN-II and the inflammasome protein NLRC4/Ipaf suggests new roles of cN-II in cell biology

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The 5'-nucleotidase is involved in intracellular nucleotide metabolism through its action on nucleotide monophosphates. Due to the very strong conservation of its primary sequence through the vertebrata taxon, we hypothesized that this enzyme could interact with other proteins and thus play additional roles in cell biology.

A two-hybrid system screening was set up, and interaction between cN-II and the leucine-rich region (LRR) of the inflammasome protein Ipaf was detected. This interaction was confirmed both in vitro using recombinant proteins and the implication of LRR was confirmed in cell extracts by immunoprecipitation after transfection with various plasmids. Finally, interaction was detected in human cancer cells using proximity ligation assay in cells expressing cN-II but not cells without cN-II expression.

Recent data shows that Ipaf, in addition to its role in innate immunity, can mediate cellular answers to intracellular stress signals. Based on our results, we hypothesize that cN-II can interact with Ipaf in order to regulate its folding and conformation, thus acting as a sensor of global health state of the cell capable of regulating cell death. This clearly shows that cN-II has new roles in human cells which might be independent of its enzymatic activity and nucleotide metabolism.