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The innate immune response is a universal mechanism against invading pathogens. Pathogen–associated RNA is recognized by highly specialized endosomal-coupled and cytoplasmic receptors. Toll–like Receptors (TLRs) are a group of endosomal receptors that bind RNA: TLR3 recognizes dsRNA, TLR7 and TLR8 ssRNA. A sequence of 10 bases: CGGAAAGACC of the bacterial ribosomal 23sRNA is recognized by TLR13.

The other group represent a cytoplasmic receptors, including Protein Kinase RNA Dependent (PKR) and a group of three proteins called RIG-I Like Receptors (RLRs): RIG-I (Retinoic acid-Inducible Gene I), MDA5 (Melanoma Differentiation Associated protein 5) and LGP2 (Laboratory of Genetics and Physiology 2), all of which bind exogenous RNA. RLR are mainly engaged in the sensing of viral genetic material and some products of its replication.

Recognition of such factor, and activation of the receptor induces an antiviral response aimed at limiting the infected cell metabolism and elimination of the pathogen from the body. So far only a few of the essential proteins involved in signal transduction from the receptor to the effector of activated transcription factors was characterized.

Our preliminary results indicate that Pellino3 ubiquitin ligase plays an important role in the Sendai virus induced production of type I interferons, and its enzymatic activity is crucial in this process. In the context of the obtained preliminary results which identified the new enzyme in RLR pathway the goal of this project is to understand the role of Pellino3 in response to RIG-I and MDA5 activation by viral infection.

This project aims to provide new information about the mechanism of the signal transduction from the RLR receptor and is crucial for understanding of the immune response. Furthermore, in the future perspective the identification of the Pellino3 ligase function will help to identify potential therapeutic targets that enable the control of antiviral response and production of IFNβ modulated by Pellino3.