Poster
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58 Roles of a novel splice variant of human IFI16 in innate immune response

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DNA from viral or bacterial pathogens activates innate immune response. The recognition of self-DNA would induce autoimmune diseases such as systemic lupus erythematosus (SLE). In human, AIM2 like receptors (ALRs) including AIM2, IFI16, IFIX and MNDA are DNA binding proteins implicated in DNA sensing. Most ALRs contain an N-terminal pyrin domain and C-terminal HIN200 domains. However, mouse SLE susceptibility locus p202 encodes only HIN200 domains. A human homolog of p202 was not found. Here, we identified and characterized a novel splice variant of human IFI16, which has a similar domain structure as mouse p202. We named it as IFI16β and the original version became IFI16α. We found that IFI16β has its own promoter and is regulated independently of IFI16α. IFI16β was more abundant in human THP-1 monocytic leukemia cells and it was induced substantially by interferon β in HEK293T and HepG2 cells. Expression of IFI16β was significantly higher in peripheral blood leukocytes of SLE patients. IFI16β was also found to interact with AIM2 and STING. Whereas IFI16α was predominantly found in the nucleus, IFN16β localized to the cytoplasm. Interestingly, IFI16β was a potent inhibitor of NLRP3 inflammasomes. Further investigations are required to determine whether IFI16β exerts its suppressive activity on NLRP3 inflammasomes by counteracting AIM2. Taken together, human IFI16β is a novel alternatively spliced variant that might have inhibitory activity on inflammasome activation in the cytoplasm.

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59 Transcriptional activation and biochemical activities of Small Alarmone Synthase (SAS) proteins from *Staphylococcus aureus*

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The stringent response is a key regulatory process exhibited by bacteria in response to amino acid deprivation or other challenging environmental conditions. It is mediated by the nucleotides guanosine 3',5'-bis(diphosphate) (ppGpp) and guanosine 3'-diphosphate, 5'-triphosphate (pppGpp), collectively known as (p)ppGpp. Rel-family proteins (RSH: RelA, SpoT) are responsible for the synthesis and hydrolysis of (p)ppGpp in most bacterial species. However, many bacteria also encode one or two smaller Rel-family proteins, known as small alarmone synthases (SAS), which are also capable of producing (p)ppGpp. In this study, we investigated the transcription and biochemical activities of the Rel-family proteins (SA-Rel, SA-RelP, SA-RelQ) from the notable bacterial pathogen *Staphylococcus aureus*. The respective abilities of the SA-Rel, SA-RelP and SA- RelQ proteins to catalyze the synthesis of alarmones were characterized by analyzing enzymatic reaction mixtures by anion exchange chromatography. Quantitative real-time PCR (qRT-PCR) was used to determine their transcription levels under various 'stress-inducing' conditions. The SA-RelP and SA-RelQ proteins could effectively synthesize (p)ppGpp alarmones, but had no hydrolytic activities. The transcription of SA-Rel, SA-RelP and SA-RelQ was induced by the presence of the antibiotic mupirocin, which is known to induce the stringent response. Transcription patterns for SA-Rel, SA-RelP and SA-RelQ were more variable in response to other stressful environmental conditions. In brief conclusion, our data indicates that all three Rel-family proteins play important roles in helping *S. aureus* alter its cellular physiology to respond to challenging nutritional and environmental conditions.