Abstract

DNA sensors are molecules with the ability to sense DNA constituting an important tool of innate immunity. They are initiators of various signalling pathways, one of them being the production of interferons, which induce not only an anti-viral cell state but also protect cells of treats not related to pathogens. At least, fourteen DNA sensors have been described so far, among them – IFI16 and cGAS. Both sensors signal via an adaptor protein STING resulting in the production of type I IFN. All three of these molecules (cGAS, IFI16, STING) are strictly regulated either by host-cells in order to prevent immune over-activation or by viruses for the immune evasion. This work focuses on the mechanisms of negative regulation of the three molecules: post-translational modifications such as phosphorylation, ubiquitination, SUMOylation, acetylation and methylation; protein-protein interactions; degradation by the proteasomal system or by autophagy. Not surprisingly, viruses encode proteins able to down-regulate IFN responses for example, some proteins of herpes viruses interact with cGAS, IFI16 or STING preventing their activation or leading to their degradation. Other proteins of herpes viruses cause the degradation of the mRNA of the sensors or the adaptor. Dengue protease factor NS2B degrades cGAS or the viral polymerase of hepatitis B virus, E7 protein of human papilloma virus and E1A of adenoviruses bind STING and cause its inactivation.

Key words: cGAS, IFI16, STING, IFN, negative regulation, innate immunity, interferons, DNA sensors