Mouse PML protein isoforms and their role in innate antiviral immunity

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Promyelocytic leukaemia nuclear bodies (PML NBs) are dynamic, multiprotein, membrane-less structures composed of the main scaffold PML protein and various stable or transient partner proteins. Beyond their diverse endogenous functions, PML NBs present important factors of antiviral defence, involved in both direct restriction *of viruses* and regulation of interferon (IFN) responses. The PML protein exists in several isoforms that affect the composition and functions of PML NBs, with only some isoforms demonstrated to exhibit specific antiviral functions in humans. To study the potential antiviral role of PML isoforms in a mouse system, we use murine polyomavirus (MPyV), a model of the human Polyomaviruses – viruses causing severe diseases in immunocompromised hosts. The mouse PML (mPML) protein occurs in three experimentally confirmed (mPML1-3) and six computationally predicted (mPMLX1-X6) isoforms, although information on them is very limited. Here, we provide the first experimental evidence confirming the expression of all predicted mPMLX1-X6 isoforms in various mouse cell lines and tissues, and we identify a novel isoform named mPMLXK. All mPML isoforms were characterised based on their formation of mPML NBs, partner proteins and exchange dynamics, presenting a more accessible tool for studying PML-associated processes. Our preliminary findings show that PML NBs localize in close proximity to viral replication centres during MPyV infection, implying a potential antiviral function of PML NBs and/or the PML protein itself. The proposed antiviral roles of individual mPML isoforms, particularly regarding the regulation of IFN I response during MPyV infection, are currently under investigation.