

Polymerase III transcription is necessary for T cell priming by dendritic cells

Exposure to Microbe Associated Molecular Patterns (MAMPs) causes dendritic cells (DCs) to undergo a remarkable maturation characterized by changes in specific biochemical mechanisms. These lead to an increase in antigen processing and presentation as well as strengthening their capacity to stimulate naïve T cells proliferation. Here, we show that in response to the MAMPS lipopolysaccharide (LPS) and polyribinosinic:polyribocytidylic acid (poly(I:C)), RNA polymerase III (Pol III)-dependent transcription and consequently tRNAs genes expression is strongly induced in DCs. This enhancement is caused by the phosphorylation and nuclear export of the Pol III repressor Maf1. It occurs via a synergistic Casein Kinase 2- (CK2) and mTOR-dependent signaling cascade, downstream of Toll-like Receptors (TLRs). The resulting enhanced tRNA expression is necessary to augment globally protein synthesis and favors translation of DC-specific mRNA; activated DCs exhibit higher rates of tRNA degradation upon MAMPs sensing and type-I Interferon exposure. TLR-dependent CK2 and RNA Pol III activation is therefore key to coordinate several metabolic pathways required to maintain tRNA expression and elevated protein synthesis levels. This is crucial for the acquisition of T cell immune-stimulatory functions by DCs.

Keywords : dendritic cells, TLR, T cell priming, tRNA, Interferon

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