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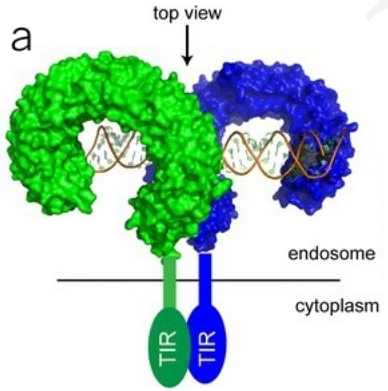
Toll-like receptor 3 (TLR3) regulation mechanisms and roles in antiviral innate immune responses

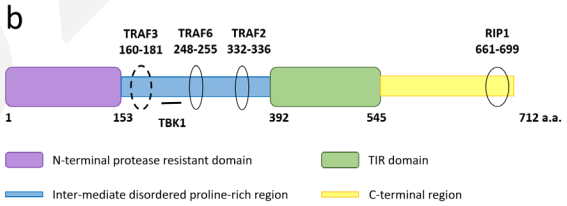
Key words: **Toll-like receptor 3, TRIF, innate immune, antiviral response**

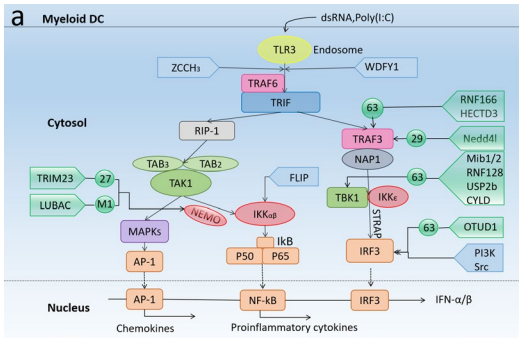
Summary

This review mainly focused on the regulation mechanism and antiviral effects of TLR3, and discussed TLR3-mediated antiviral response in the following aspects:

- **Characteristics and recognition of TLR3**
- **TLR3-TRIF-signaling pathway**
- **Negative regulation of TLR3 signaling**
- **Antiviral effects of TLR3**







Innovation points

- **Introduction of TLR3-TRIF-signaling pathway from primary signal transduction factors to auxiliary proteins.**

- **Emphasis of five categories of negative regulators, which inhibit TLR3 signaling.**

- **Summary of the most updated research progress about antiviral effects of TLR3 during viral infections.**

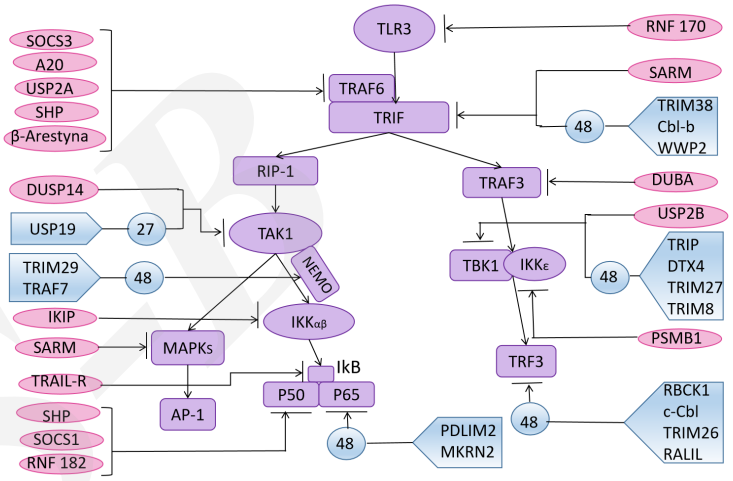


Table 1 The role of TLR3 in antiviral responses

Effects	Virus	Target organ	Disease	Role of TLR3
Protection	Herpes simplex virus type 1 (HSV-1)	Central nervous system (CNS)	Encephalitis, other	TLR3 recruits the metabolic checkpoint kinase complex mTORC2, thus enabling the activation of molecules (including mTORC1) required for type I IFN induction (Mielcarska et al., 2018).
	…	…	…	…
Deterioration	Phlebovirus	Liver	Hepatopathy	Compared with TLR3-deficient mice, wild-type mice demonstrate decreased resistance to lethal infection (Gowen et al., 2006).
	…	…	…	…
Bi-direction	Hepatitis C virus (HCV)	Liver	Hepatitis C	Protection: TLR3 inhibits HCV replication in Huh7 cells (Zhou et al., 2016). Deterioration: TLR3 possibly contributes to the intrahepatic and unbalanced proinflammatory response (Li et al., 2012).
	…	…	…	…
Unclear	Influenza A (H1N1)	Lung	Pneumonia	TLR3 does not worsen the pathogenesis of pH1N1 infection (Leung et al., 2014).
	…	…	…	…

Innovation points

A series of comprehensive figures and tables were generated to summarize the latest knowledge about TLR3.

Figs. 1a&1b | The structure of the TLR3-dsRNA signaling complex.

Fig. 2a | Mechanism of the TLR3-TRIF-signaling pathway.

Fig. 2b | Schematic structure of human TRIF.

Fig. 3 | Negative regulation of TLR3 signaling.

Table 1 | The role of TLR3 in antiviral responses.

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