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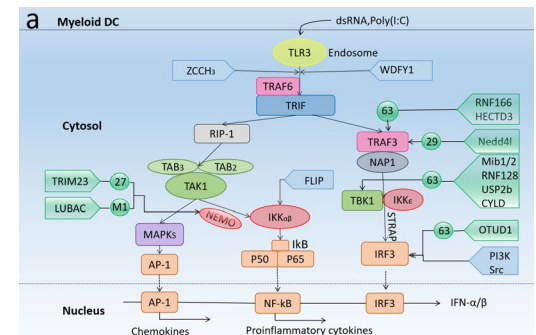
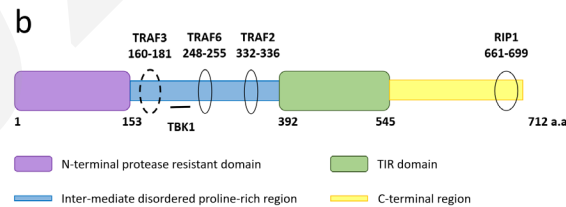
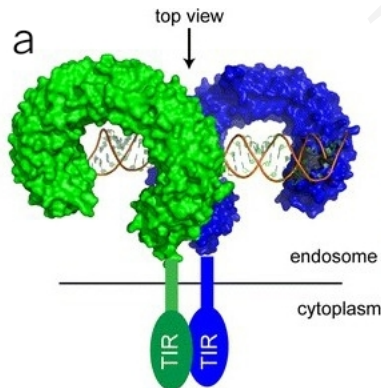
# **Toll-like receptor 3 (TLR3) regulation mechanisms and roles in antiviral innate immune responses**

**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.**

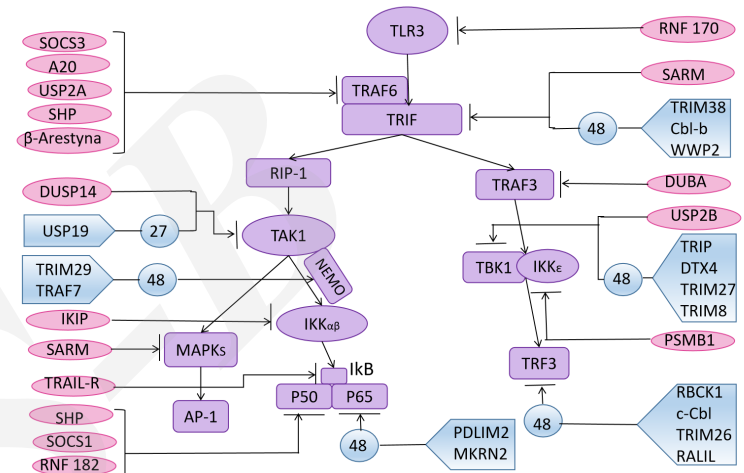


Table 1 The role of TLR3 in antiviral responses

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.**