

# Neuroimmunology of rabies: new insights into an ancient disease

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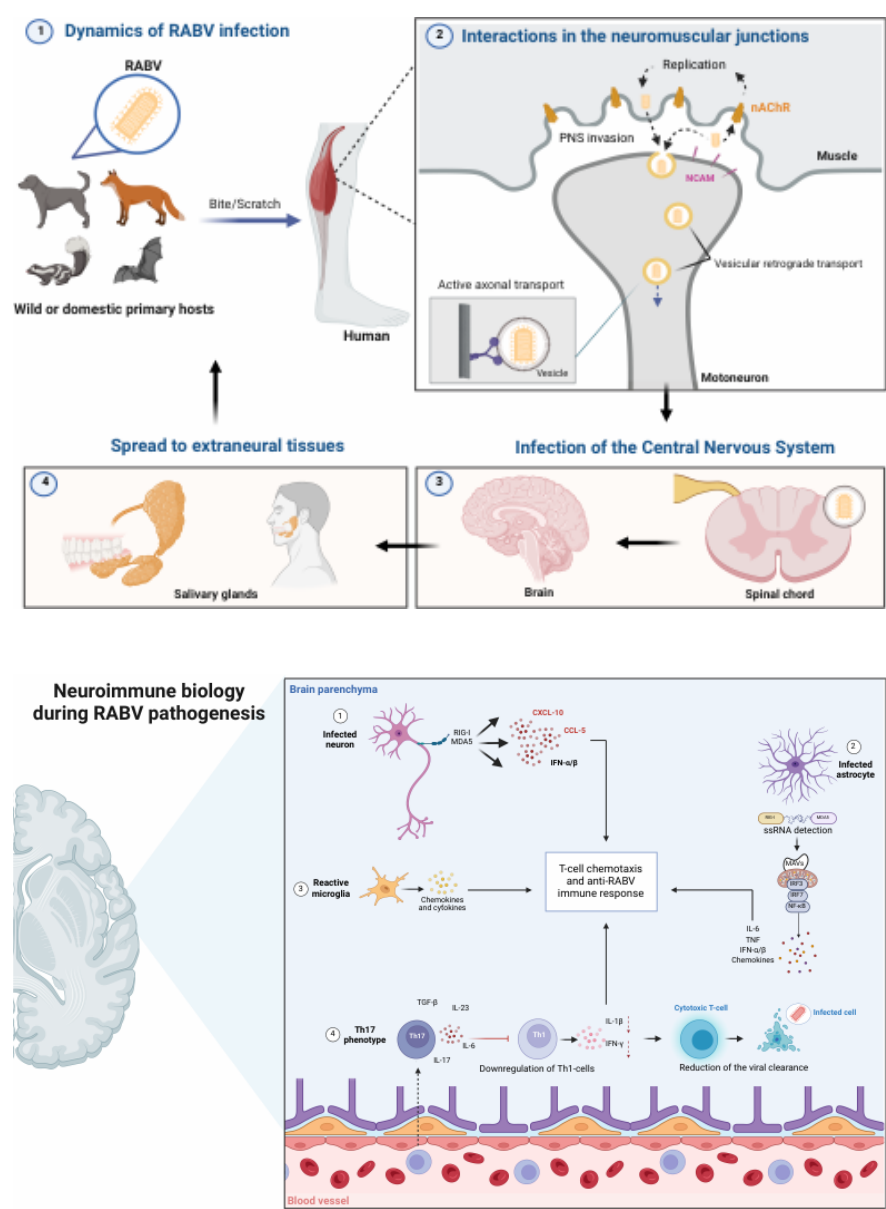
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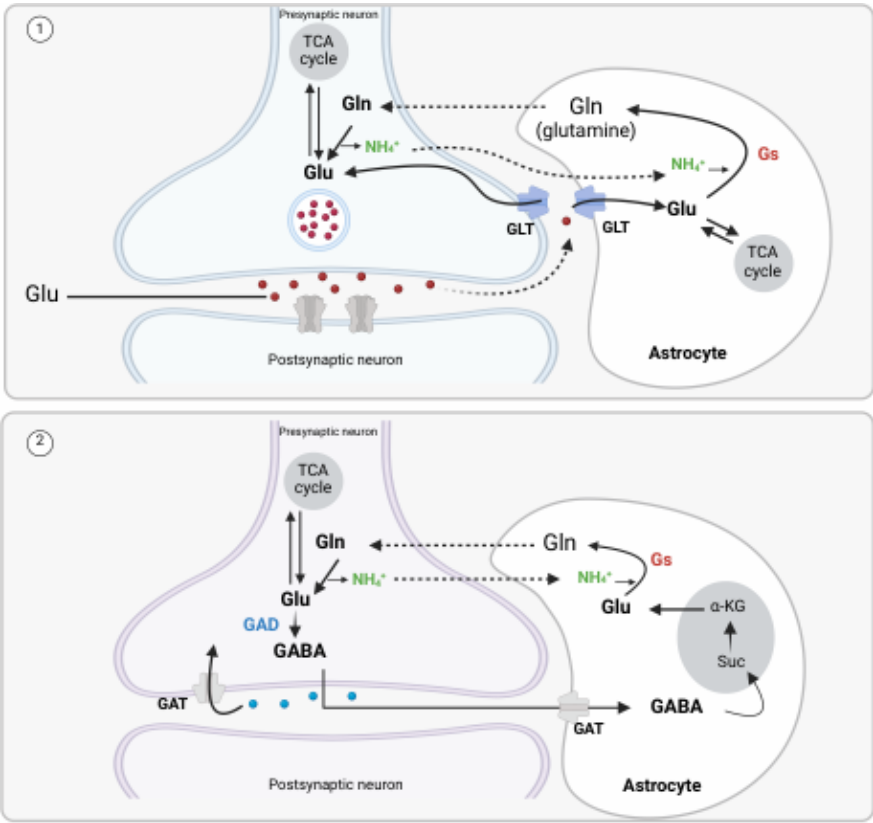
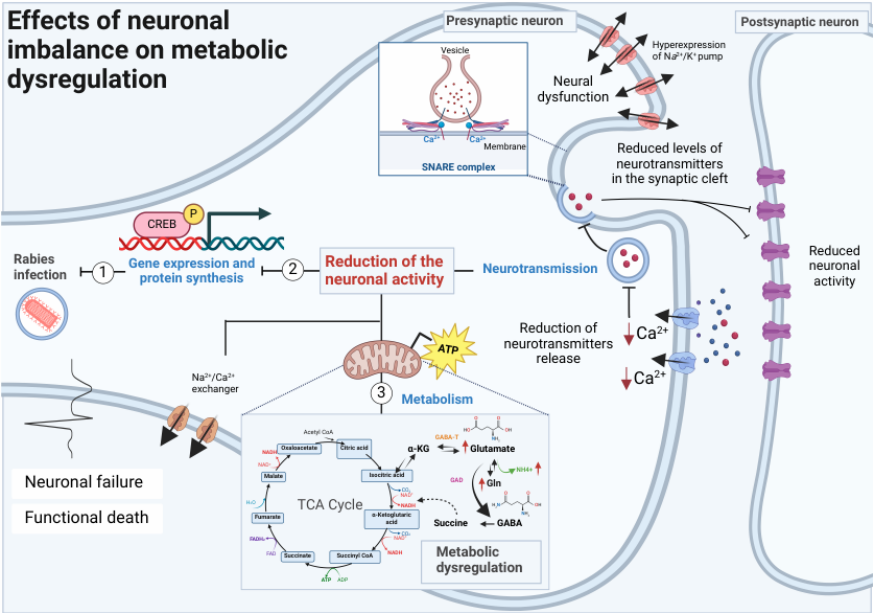
## Abstract

Rabies is an ancient neuroinvasive viral (genus *Lyssavirus*, family *Rhabdoviridae*) disease affecting approximately 59,000 people worldwide. The central nervous system (CNS) is targeted, and rabies has a case fatality rate of almost 100% in humans and animals. Rabies is entirely preventable through proper vaccination, and thus, the highest incidence is typically observed in developing countries, mainly in Africa and Asia. However, there are still cases in European countries and the US. Recently, demographic, increasing income levels, and the coronavirus disease 2019 (COVID-19) pandemic have caused a massive raising in the animal population, enhancing the need for preventive measures (e.g., vaccination, surveillance, animal control programs), post-exposure prophylaxis, and a better understanding of rabies pathophysiology to identify therapeutic targets, since there is no effective treatment after the onset of clinical manifestations. Here we review the neuroimmune biology and mechanisms of rabies. Its pathogenesis involves a complex and poorly understood modulation of immune and brain functions associated with metabolic, synaptic, and neuronal impairments, resulting in fatal outcomes without significant histopathological lesions in the CNS. In this context, the neuroimmunological and neurochemical aspects of excitatory/inhibitory signaling (e.g., GABA/glutamate crosstalk) are likely related to the clinical manifestations of rabies infection. Uncovering new links between immunopathological mechanisms and neurochemical imbalance will be essential to identify novel potential therapeutic targets to reduce rabies morbidity and mortality.

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