

A mechanism for immune regulation by the nervous system

Control of lymphocyte trafficking by adrenergic nerves

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Adrenergic nerve, Adrenergic receptor, Chemokine receptor, Lymphocyte dynamics

A group of researchers led by **Kazuhiro Suzuki** (Associate Professor, Immunology Frontier Research Center [IFReC], Osaka University) revealed that β_2 -adrenergic receptors (β_2 ARs) expressed on lymphocytes regulate their egress from lymph nodes by altering the responsiveness of chemokine receptors CCR7 and CXCR4. In mouse models of inflammation, signals through β_2 ARs were shown to inhibit trafficking of pathogenic lymphocytes and reduce their numbers recruited into inflamed tissues.

As the proverb "Illness starts in mind." says, it has long been proposed that some aspects of immune responses are affected by activities of the nervous system. Indeed, lymphoid organs are innervated by various types of neurons and immune cells express corresponding neurotransmitter receptors. However, the cellular and molecular basis for neural regulation of immunity has been largely unknown. Adrenergic nerves transmit activities of the sympathetic nervous system to every organ system and play a major role in mediating stress responses. The group looked into how adrenergic nerves control the immune system, focusing on lymphocyte dynamics in the body.

This study demonstrated:

1. Adrenergic nerves contribute to the homeostasis of lymphocyte dynamics by regulating lymphocyte egress from lymph nodes through β_2 ARs expressed on lymphocytes.
2. There is a functional crosstalk between β_2 ARs and chemokine receptors CCR7 and CXCR4, by which inputs through β_2 ARs enhance responsiveness of these chemokine receptors to inhibit lymphocyte egress from lymph nodes.

3. In mouse models of inflammatory diseases, signals through β_2 ARs inhibit lymph node egress of pathogenic lymphocytes and prevent their migration to inflammatory sites, suggesting a mechanism for β_2 AR-mediated suppression of inflammation.

Collectively, the group revealed a molecular mechanism by which adrenergic nerves control lymphocyte dynamics in homeostatic and pathological conditions. This study implies how stress or emotional changes are reflected on immune functions through adrenergic nerves and provides a rationale for developing therapeutic strategies for immune disorders that control stress responses.

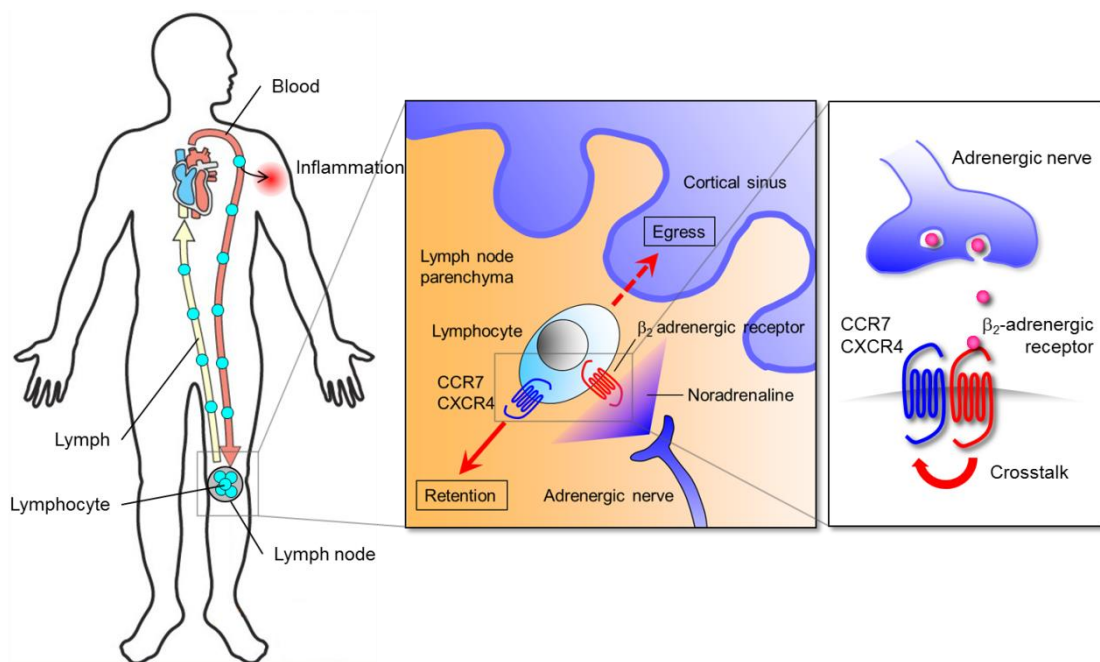


Figure. A model for adrenergic control of lymphocyte dynamics.