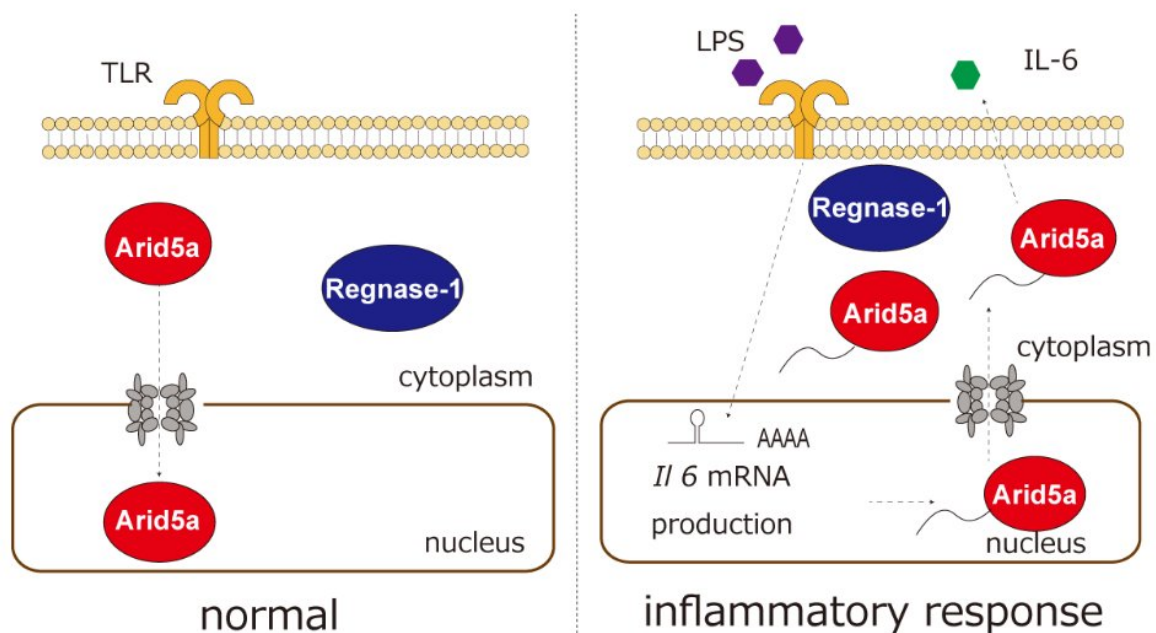


The subcellular dynamics of RNA stabilizing molecule in response to inflammation

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Model of inflammatory response by Arid5a/Regnase-1. Regnase-1 localizes to the cytoplasm. Arid5a is imported to the nucleus via an importin- α/β 1 pathway. In response to inflammation, the Toll-like receptor (TLR) is activated by LPS, and Il6 mRNA is induced by NF- κ B. After that, Arid5a interacts with Il6 mRNA and is exported to the cytoplasm. Credit: M. Higa, Osaka University

A research group at Osaka University revealed the regulatory mechanism

of subcellular localization of Arid5a in response to inflammation. It has been known that an inflammatory accelerator is localized in the nucleus, and an inflammatory brake is localized in the cytoplasm.

Tadamitsu Kishimoto (Professor, Immunology Frontier Research Center (IFReC), Osaka University) and his research group revealed the [regulatory mechanism](#) of subcellular localization of Arid5a in response to [inflammation](#). It has been known that an inflammatory accelerator, Arid5a, is localized in the [nucleus](#), and an inflammatory brake, regnase), is localized in the [cytoplasm](#). In this study, they showed that 1) Arid5a translocates to the cytoplasm from the nucleus in response to inflammation, 2) bimax, which inhibits cNLS-dependent nuclear import via high-affinity interactions with NLS-binding sites of importin- α , inhibits the nuclear import of Arid5a, and 3) a CRM1 inhibitor, Leptomycin B, inhibits the nuclear export of Arid5a after LPS stimulation.

Macrophages produce inflammatory cytokines to activate other immune cells and to exclude pathogens. However, over- or chronic inflammation causes diseases including a [septic shock](#) or autoimmunity. Therefore, the group has been studying the control mechanism of inflammation, especially focusing on the posttranscriptional regulation of the Il6 mRNA by Arid5a and Regnase-1. Their previous study showed that Arid5a binds to Il6 mRNA 3'UTR to inhibit Regnase-1-mediated

RNA decay. Additionally, Arid5a deficient mice showed down-regulated inflammatory cytokine production, resistance to septic shock, and bleomycin-induced lung injury. Although Arid5a is known to play an important role in immune regulation, whether and how Arid5a subcellular localization impacts immune regulation has remained unclear.

The group showed that Arid5a translocates from the nucleus to the

cytoplasm after LPS stimulation. Since the inhibition of Arid5a nuclear export causes the significant suppression of IL-6 production, further understanding of Arid5a dynamics may lead to novel therapeutic strategies of for septic shock or autoimmune diseases.

More information: Mitsuru Higa et al. Regulation of inflammatory responses by dynamic subcellular localization of RNA-binding protein Arid5a, *Proceedings of the National Academy of Sciences* (2018). [DOI: 10.1073/pnas.1719921115](https://doi.org/10.1073/pnas.1719921115)

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