# β-damascone: Using the aroma component of rose fragrance as a novel immunomodulator

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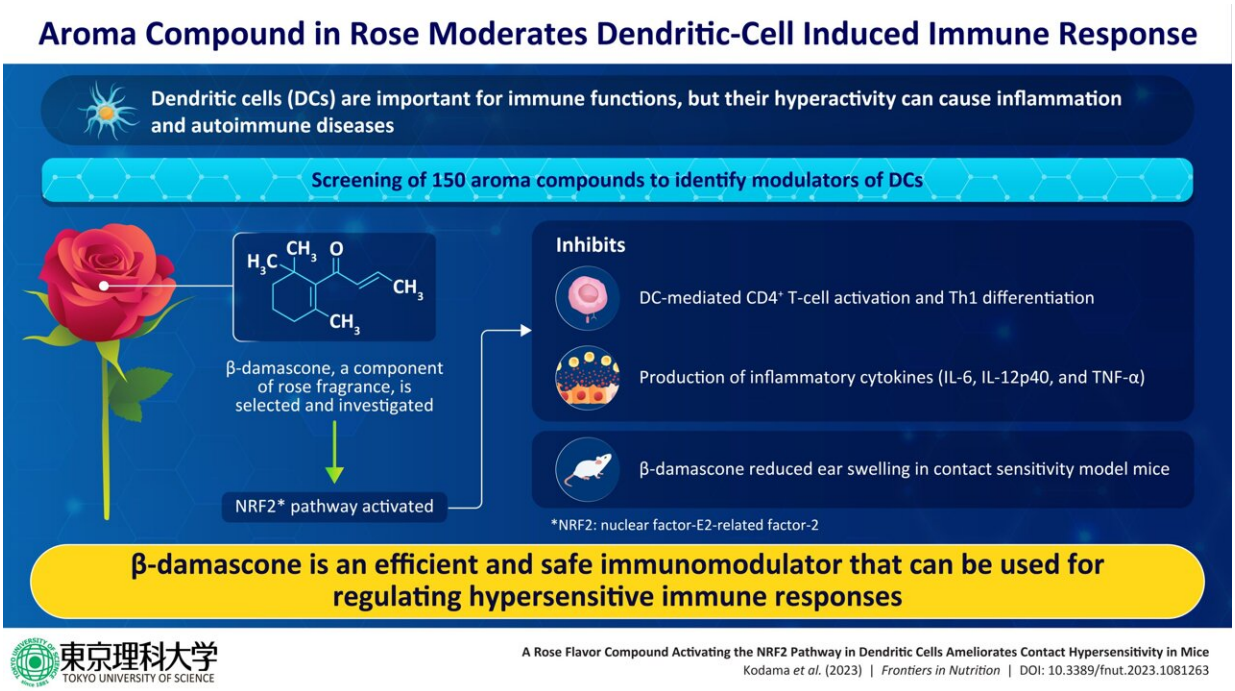


Overactivation of dendritic cells (DCs), components of the immune system, can cause immune diseases. β-damascone, a constituent of rose fragrance was identified as a natural, potent immunomodulator of DC cell functions. Credit: Chiharu Nishiyama from Tokyo University of Science

Dendritic cells (DCs) are important players of the immune system with important functions such as the identification of infectious pathogens, production of cytokines (chemical signalers of the immune system),

presentation of antigens to activate T-cells, and more. Despite performing such key functions, DCs may lead to inflammatory and autoimmune diseases when hyperactive. Therefore, to prevent DC-mediated diseases, it is necessary to identify molecules that can modulate the functions of DCs.

Previous studies have indicated that natural compounds can serve as potent immunomodulators. To explore the role of such compounds in modulating the functions of DCs, a team of researchers from Japan, led by Prof. Chiharu Nishiyama from Tokyo University of Science, including Dr. Hikaru Okada, Dr. Masakazu Hachisu, and Dr. Naoki Kodama screened 150 types of natural aroma compounds.

"Natural fragrant compounds are found in plants and microorganisms and are also commonly used in foods and daily necessities. However, not much research has been conducted on the physiological activities of individual flavor compounds, particularly on immune responses," remarks Prof. Nishiyama while discussing their motivation behind this study, which was published in *Frontiers in Nutrition*.

First, the team conducted a two-step screening process of aroma compounds, which led to the identification of a novel and effective modulator of DCs known as β-damascone—a primary component that constitutes rose fragrance.

Next, through a series of molecular and immunological assays, the team found out that β-damascone inhibited several functions of DCs including antigen-dependent activation of CD4+ T-cells and the development of Th1 cells (Type-1 helper cells). In addition, β-damascone reduced the production of inflammatory cytokines such as, interleukin (IL)-6, IL-12p40, and tumor necrosis factor (TNF)-a.

Discussing these findings, Prof. Nishiyama further adds, "We wanted

not only to observe the effective active ingredients, but also to thoroughly examine their mechanisms of action at the molecular level, up to the point of verifying whether they exert physiologically meaningful effects."

True to their word, on exploring the mechanisms underlying the inhibitory functions of β-damascone, the team noted that these functions were mediated by NRF2—a master transcription factor with crucial antioxidative roles. NRF2 was found to exert these effects via its target genes, Hmox1 and Nqo1.

The function of β-damascone was further confirmed by in vivo experiments in contact hypersensitivity mice models. The oral administration of β-damascone reduced ear inflammation in these mice models. Notably, these experiments also corroborated the role of NRF2 in β-damascone-mediated immunomodulation. Indeed, ear swelling was not suppressed in NRF2 knockout mice models, i.e., mice that lacked NRF2.

Taken together, this comprehensive study showed that β-damascone can function as an efficient modulator of DC-mediated functions and can effectively reduce the inflammatory effects of DC-hyperactivation.

**More information:** Naoki Kodama et al, A rose flavor compound activating the NRF2 pathway in dendritic cells ameliorates contact hypersensitivity in mice, *Frontiers in Nutrition* (2023). DOI: 10.3389/fnut.2023.1081263

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