# Tolerating foreign materials in food

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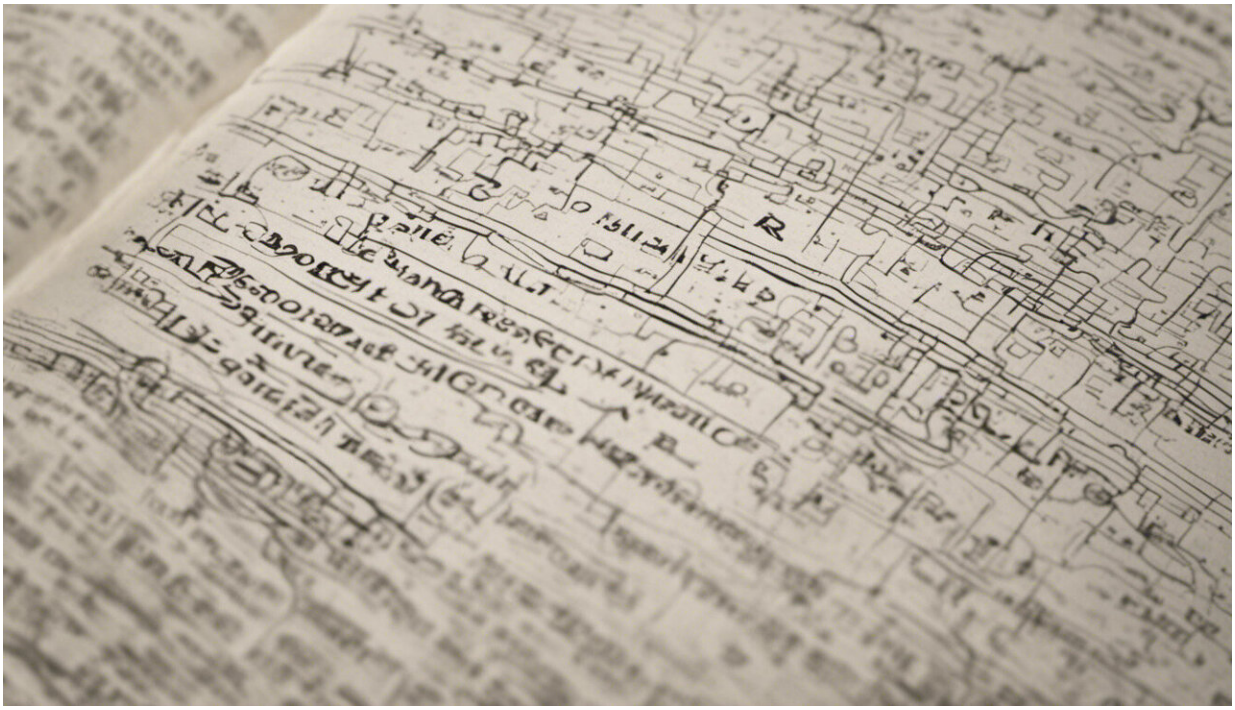

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An international team of molecular biologists led by RIKEN researchers (Japan) has unraveled key details of the molecular mechanism whereby the body's immune system determines what to attack among the organisms and food taken into the mouth, and what to leave alone or tolerate. The researchers have shown the pivotal role of two proteins found on the surface of cells that stimulate the immune system into action, the dendritic antigen-presenting cells (APCs). The work may lead

to new therapies for immune disorders, and to ways of boosting the effectiveness of oral vaccines.

Animals could not survive without the nutrients and beneficial micro-organisms they ingest when feeding. But the foreign material taken in through the mouth and passing through the gut also contains harmful substances and organisms. So the immune system must balance active protection against pathogens and toxins with a non-responsiveness to food and commensal bacteria known as oral tolerance. In the past, researchers have proposed two mechanisms for oral tolerance—reducing the numbers of effector T cells, the immune-system foot soldiers that move against foreign material and suppress their action by means of specialized regulatory T cells.

The triggering of effector T cells depends on interaction with two distinct types of proteins on the surface of the APCs, antigens that are markers of foreign material and co-stimulatory proteins of the B7 family, which regulate the response. Both must be present, however, to initiate any action.

Using mice deficient in B7 co-stimulatory proteins Katsuaki Sato and colleagues from the RIKEN Research Center for Allergy and Immunology in Yokohama, together with researchers from other laboratories in Japan, and in the US and France, found that oral tolerance demanded the presence of B7-H1 and B7-DC proteins1. In fact, without these proteins the immune response was enhanced. Of the APCs, the dendritic cells of the mesenteric lymph nodes, in the membranes surrounding the digestive system, display higher levels of these proteins.

When the researchers investigated the role of the two B7 proteins, again using B7-deficient mice, they discovered the proteins induced the generation of regulatory T cells rather than normal effector cells. These regulatory T cells then damp down the immune response promoting

tolerance. During inflammation, however, their action is swamped.

The research group wants to continue analyzing the role of different groups of dendritic cells in live mice, Sato says. “In particular, we wish to identify the molecular basis of the regulation of the function of these cells.”

**More information:** Fukaya, T., et al. Crucial roles of B7-H1 and B7-DC expressed on mesenteric lymph node dendritic cells in the generation of antigen-specific CD4+Foxp3+ regulatory T cells in the establishment of oral tolerance. *Blood* 116, 2266–2276 (2010). Article

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