Intestinal bacteria metabolite found to promote capture of antigens by dendritic cells

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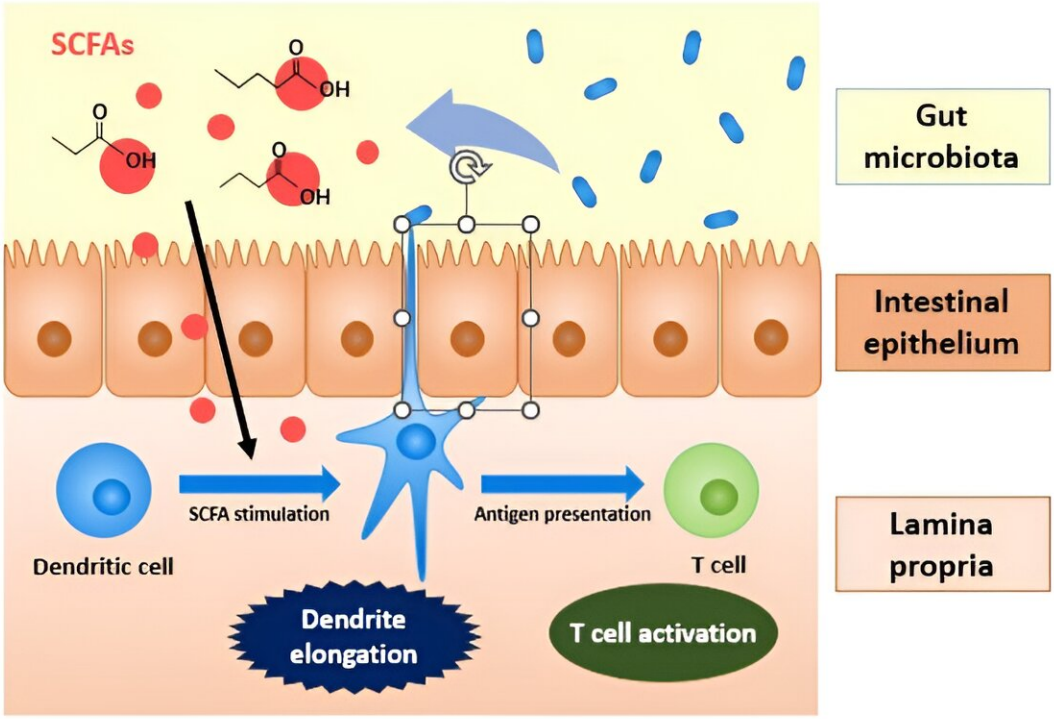

A recent study by Okayama University researchers found that short-chain fatty acids produced by intestinal bacteria trigger the extension of the dendrites of dendritic cells by inhibiting an enzyme known as histone deacetylase. This results in a stonger immune response. Credit: Dr. Kazuyuki Furuta from Okayama University, Japan

Dendritic cells play a key role in the mammalian immune system. These

cells are present throughout the human body and are known to capture foreign bodies, or antigens, using extendable "arms" called dendrites. Once captured, dendritic cells present these substances to immune T cells, thereby initiating an immune response.

Dendritic cells are responsive to their environment and capable of changing their morphology and other attributes dynamically. For instance, dendritic cells in the intestine's mucosa (inner layer) capture harmful bacteria by extending their dendrites through the epithelium (outermost layer) and into the intestinal lumen (inner space). However, the exact mechanism through which they do is not clear.

In a study that was published in The FEBS Journal, a team of researchers led by Associate Professor Kazuyuki Furuta, Mr. Takuho Inamoto, Dr. Kazuya Ishikawa, and Dr. Chikara Kaito from the Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences at Okayama University, Japan found that short-chain fatty acids (SCFAs) produced by intestinal bacteria are responsible for initiating the extension of dendrites into the intestinal lumen by dendritic cells.

SCFAs are a group of fatty acids with six or fewer carbon atoms, found in high concentrations in the intestine. The research team found that SCFAs such as acetic, propionic, butyric and valeric acids induce dendrite elongation by inhibiting an enzyme called histone deacetylase.

Inhibition of histone deacetylase leads to the reorganization of the actin cytoskeleton of dendritic cells, inducing morphological changes. To arrive at these findings, the team examined the effects of SCFAs on a dendritic cell line (DC2.4 cells) and mouse bone marrow-derived dendritic cells (BMDCs) in a laboratory setting.

"Ours is the first study to demonstrate that SCFAs induce dendrite elongation by inhibiting histone deacetylase. Moreover, dendritic cells

activated by SCFAs exhibited more stronger immune responses, due to increased pathogen uptake," explains Dr. Furuta.

Upon conducting further analyses, the team found that treating dendritic cells with valeric acid led to an increase in the uptake of soluble proteins, insoluble beads, and Staphylococcus aureus bacteria. In contrast, the treatment of BMDCs with valeric acid enhanced their antigen presentation ability.

It was also observed that SCAFs activated dendrite elongation by stimulating a signaling pathway involved in reorganization of the actin cytoskeleton—forces responsible for cell movement and cell morphology.

"Our findings may be leveraged to identify beneficial intestinal bacteria producing SCFAs to activate immune responses and aid in the prevention of diseases. In addition, the dendritic elongation mechanism we discovered can be used as a target to develop drugs regulate immune responses artificially," says Dr. Furuta.

More information: Takuho Inamoto et al, Short-chain fatty acids stimulate dendrite elongation in dendritic cells by inhibiting histone deacetylase, *The FEBS Journal* (2023). DOI: 10.1111/febs.16945

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