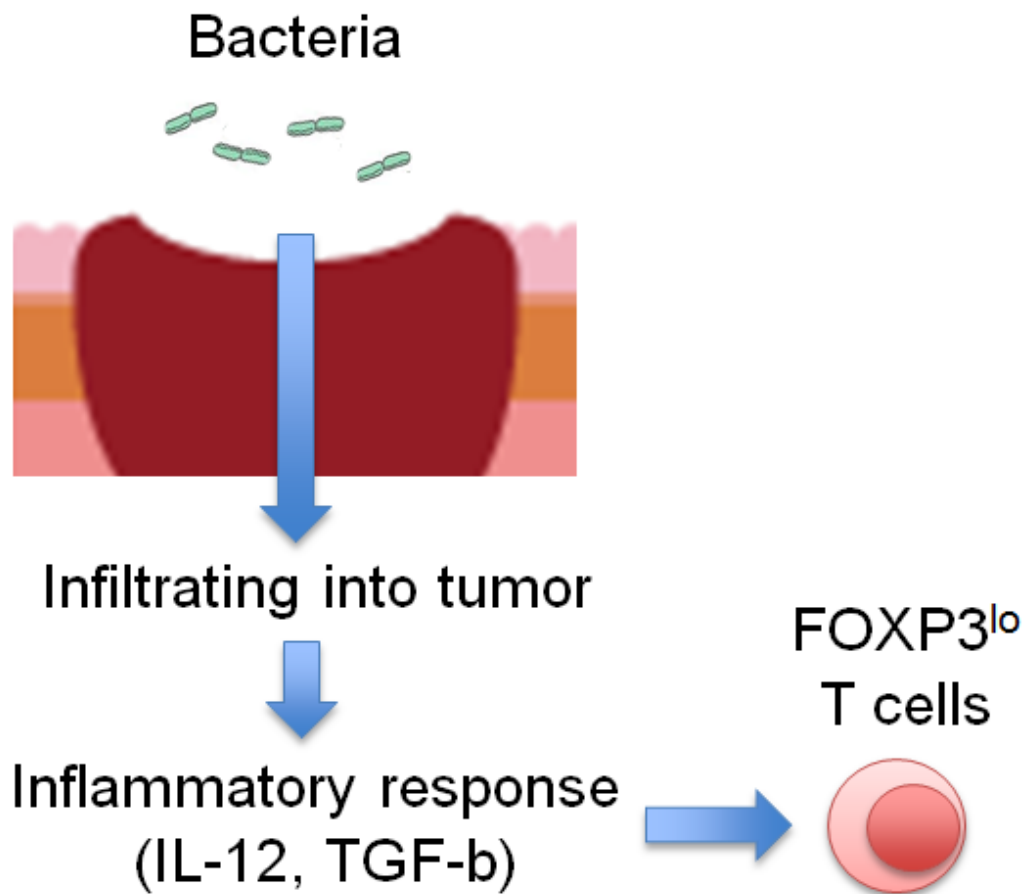


# Regulatory T cells' involvement in the progress of colon cancer

July 5 2016



Bacteria infiltration into colorectal tumors leads to inflammatory responses in tumor, which induces FOXP3<sup>lo</sup> T cells, then enhancing anti-tumor immunity.  
Credit: Osaka University

Researchers at Osaka University, clarified that T-lymphocytes expressing FOXP3 at a low level found in colorectal cancers (CRCs) facilitated cancer immunity. FOXP3 is a master gene of Regulatory T (Treg) cells that suppress various immune responses including cancer immunity. They found that a certain intestinal bacteria species was involved in the induction of such FOXP3-low T cells enhancing tumor immunity. These findings suggest new potentials in the treatment of CRCs via regulation of intestinal bacteria.

Treg [cells](#) have been drawing attention in cancer immunotherapy. Since Treg cells suppress the [immune cells](#) that attack tumors, they are thought to be disadvantageous for antitumor immunity. Indeed tumor-infiltrating Treg cells have been reported as a factor for poor prognosis in many cancers. However, results running counter to the notion have been found with CRCs, leaving the roles of Treg cells in CRCs unclear.

A research group led by Professor Shimon Sakaguchi at the Immunology Frontier Research Center, Osaka University now discovered that among the FOXP3+ cells that had infiltrated deeply into CRCs, a group of T-cells with low FOXP3 expression were facilitating cancer immunity. Although the majority of FOXP3+ T-cells are thought to be immunosuppressive Treg cells, this research showed that a group of FOXP3-low (FOXP3<sup>lo</sup>) cells did not possess immune-suppressing functions but rather augment immune responses and that they were induced by inflammatory cytokines such as IL-12, which was induced by intestinal bacteria attaching to CRCs. CRCs with abundant infiltration of such inflammatory FOXP3<sup>lo</sup> Treg cells showed good prognosis, while those with predominant FOXP3<sup>hi</sup> Treg cell infiltration like other cancers showed poor prognosis.

Detailed analysis of the lymphocytes invading CRCs allowed the researchers to clarify the roles of Treg cells and FOXP3+ cells as well as the influence of intestinal bacteria in inducing these cells. Intestinal

bacteria attaching to CRCs cause tumor-internal inflammation by invading the tumor, thereby inducing FOXP3<sup>lo</sup> Treg cells facilitating tumor immunity. In addition, the researchers found that FOXP3<sup>hi</sup> Treg cells, unlike FOXP3<sup>lo</sup> T-cells, suppressed antitumor immunity response as seen with other cancers.

In this research, the researchers were able to conduct an accurate assessment of FOXP3+ cells in CRCs. Precise identification of these cell groups will become a useful marker for assessing immune status in cancer tissues. Since cancer immunotherapy is effective for only some types of tumors, the research results suggest new potentials for [cancer immunotherapy](#) targeting Treg cells while also defining new patient groups. Furthermore, new preventive potentials for intestinal cancers can be expected by controlling [intestinal bacteria](#) as it was demonstrated that these bacteria can increase cancer immunity via inflammation in tumors.

**More information:** Takuro Saito et al. Two FOXP3+CD4+ T cell subpopulations distinctly control the prognosis of colorectal cancers, *Nature Medicine* (2016). [DOI: 10.1038/nm.4086](https://doi.org/10.1038/nm.4086)

Provided by Osaka University

Citation: Regulatory T cells' involvement in the progress of colon cancer (2016, July 5) retrieved 3 May 2024 from

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