MedicalXpress

How gut microbes help chemotherapy drugs

October 4 2016

Two bacterial species that inhabit the human gut activate immune cells to boost the effectiveness of a commonly prescribed anticancer drug, researchers report October 4 in *Immunity*. The study identifies a new role for *Enterococcus hirae* and *Barnesiella intestinihominis* in activating cancer-fighting T cell immune responses, thereby enhancing the effects of the chemotherapy drug cyclophosphamide. Moreover, this microbe-driven immune response predicted longer progression-free survival in advanced lung and ovarian cancer patients treated with chemo-immunotherapy.

"The anti-cancer drug's efficacy relies on a complex interplay between the microbiome of cancer patients and their ability to mount an efficient immune memory response against some bacteria of the gut microbiota," says co-senior study author Mathias Chamaillard, Inserm research director of the Center for Infection and Immunity of Lille (Inserm/CNRS/Lille University/Institut Pasteur de Lille). "This paradigm opens the way to improve treatment design by either optimizing the use of antibiotics, or implementing supplementation with so-called oncomicrobiotics or their bioactive metabolites, to promote the efficacy of anti-cancer drugs."

Recent studies have shown that some gut microbes can promote the growth of tumors, while others can protect against cancer. In a few cases, the antitumor effects of intestinal bacteria can also contribute to the effectiveness of chemotherapy drugs. However, it has not been clear which specific bacterial species activate antitumor immune responses in response to chemotherapy, and exactly how they do so.

In the new study, Chamaillard and senior study author Laurence Zitvogel of the Institut de Cancérologie Gustave Roussy Cancer Campus showed that two intestinal bacteria, *E. hirae* and *B. intestinihominis*, both act to orchestrate the anticancer therapeutic effects of cyclophosphamide—an immunosuppressive chemotherapy drug used to treat a wide range of cancers. Using mouse models, the researchers showed that oral treatment with *E. hirae* activated antitumor T cell responses in the spleen in parallel with the direct toxic effects of cisplatin on the tumor, thereby curbing tumor growth. On the other hand, oral treatment with *B. intestinihominis* achieved a similar effect by promoting the infiltration of T cells in various mouse tumors.

The researchers next analyzed blood T cell responses from 38 patients with advanced lung and ovarian cancer treated with chemo-immunotherapy. They found that memory T cell immune responses specific to *E. hirae* and *B. intestinihominis* predicted progression-free survival, that is, the length of time during and after treatment that a patient lives with the disease but it does not get worse.

In future studies, the researchers plan to identify which specific bacterial metabolites or immune-modulating molecules are responsible for enhancing the effects of cyclophosphamide. "Answering this question may provide a way to improve the survival of cyclophosphamide-treated cancer patients by supplementing them with bacterial-derived drugs instead of live microorganisms," Chamaillard says.

More information: *Immunity*, Daillère et al.: "Enterococcus hirae and Barnesiella intestinihominis Facilitate Cyclophosphamide-Induced Therapeutic Immunomodulatory Effects" www.cell.com/immunity/fulltext … 1074-7613(16)30378-8 , DOI: 10.1016/j.immuni.2016.09.009

Provided by Cell Press