

Gut bacteria linked to weight gain following chemotherapy treatment for breast cancer

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Approximately 30% of breast cancer patients who receive chemotherapy treatment gain weight, though it is unclear why this phenomenon occurs in some women but not in others. Beyond weight gain, chemotherapy is also known to increase the risk of high blood pressure and glucose intolerance, a prediabetes condition. Although this is a familiar phenomenon, the mechanisms underlying these processes have not yet been identified. A new study, just published in the journal *BMC Medicine*, suggests that gut bacteria are partially responsible for metabolic changes that lead to weight gain following chemotherapy treatment.

The research was initiated by Dr. Ayelet Shai, Director of Oncology at the Galilee Medical Center, who led the study with Prof. Omry Koren, an expert in gastrointestinal bacteria at the Azrieli Faculty of Medicine of Bar-Ilan University.

Dr. Shai says that symptoms she has witnessed as an oncologist led her to initiate the study: "In my clinical work with <u>women</u> recovering from breast and gynecological tumors, I have seen many of them gain <u>weight</u> following treatment and experience difficulty returning to their original weight. When I read in medical literature about the link between the microbiome and obesity in people without cancer, I thought it would be interesting to see if the microbiome of patients is one of the causes of obesity and other metabolic changes," she says.

The study conducted by Dr. Shai and Prof. Koren involved 33 women who were about to begin <u>chemotherapy</u> for breast cancer and gynecological cancer. The women were weighed once before the



treatment, and once again approximately five weeks after treatment began. Prior to treatment, a stool sample was used to genetically characterize the microbiome of each of the women. Nine of the women were found to have gained weight to a degree that was defined as significant (3% or more). The microbiome of these women exhibited a smaller diversity of gut bacteria and different bacterial strains compared to that of the women who did not experience weight gain.

The study showed that the composition of intestinal bacteria may predict which women will gain weight as a result of chemotherapy. In addition when the gut microbiota of women who gained weight were transferred to germ-free mice, they developed glucose intolerance and signs of chronic inflammatory condition were detected in their blood. These findings suggest that bacteria are partially responsible for metabolic changes that lead to weight gain following chemotherapy treatment.

"We have shown for the first time that the pre-treatment microbiome of patients that gained weight following chemotherapy is different than the microbiome of patients that did not gain weight, and that fecal transplantation from patients that gained weight results in glucose intolerance, adverse lipid changes and inflammatory changes in germfree mice," says Prof. Koren. These results suggest that the intestinal microbiome is mediating metabolic changes in women treated by chemotherapy. Moreover, the pre-chemotherapy composition of the intestinal microbiome can predict which patients will gain weight following treatment.

Dr. Shai and Prof. Koren are currently in the midst of a follow-up study which aims to examine the results in a larger patient population and to examine the <u>microbiome</u> of women at the end of chemotherapy in order to understand the effect of the treatment on bacterial composition. The researchers also plan to study the effect of chemotherapy on obesity in germ-free mice following fecal transplantation.



If the results obtained in the initial study are repeated, it will be possible to consider a stool test for women before starting treatment, so that the patient knows if she is at risk of gaining weight. As October marks Breast Cancer Awareness Month, Dr. Shai says, "We hope that in the future we will be able to identify those women who are at risk for weight gain through a simple examination and perhaps even suggest ways to prevent this phenomenon."

More information: Atara Uzan-Yulzari et al, The intestinal microbiome, weight, and metabolic changes in women treated by adjuvant chemotherapy for breast and gynecological malignancies, *BMC Medicine* (2020). DOI: 10.1186/s12916-020-01751-2

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