

What You Can Control: Your Microbiome, Diet, Stress & Melanoma

People with melanoma can modify lifestyle factors such as diet, stress and the gut microbiome to improve treatment outcomes.

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Every day, we hear from patients who want to know what, if anything, they can do to have the best health outcomes possible. For people facing melanoma, it's common to feel overwhelmed and out of control with everything that a melanoma diagnosis and treatment entail. Yet, how one faces those challenges can make a big difference. Melanoma Research Alliance-funded investigator Lorenzo Cohen, PhD, is working hard to help patients understand the pivotal role of the microbiome, diet, stress—and their melanoma—on treatment outcomes.

Cohen, distinguished professor in clinical cancer prevention and director of the Integrative Medicine Program at the University of Texas MD Anderson Cancer Center, is interested in lifestyle factors that may be able to help improve treatment outcomes and the lives of patients.

“We are looking at different lifestyle habits,” says Cohen. “In addition to assessing diet, we're also assessing stress, social support, physical activity, and with our colleague Takis Benos, PhD at the University of Pittsburgh, we are doing some complex modeling to see what are the factors that are the most predictive of treatment response.”

In his 2018 MRA Team Science Award, Cohen, alongside collaborators Drs. Jennifer Wargo and Jennifer McQuade, aims to build upon existing research to further explore how lifestyle factors, including diet, exercise, and stress and anxiety, as well as the trillions of microorganisms living within the gut microbiome, can be modified to improve outcomes for patients with melanoma.

Over the last few years, it has become well understood that the microbiome plays a critical role in our lives. Thanks to research breakthroughs, including those by MRA-funded investigator Drs. Jennifer Wargo (MD Anderson), Thomas Gajewski (University of Chicago), and Yardena Samuels (Weizmann Institute), we know more than ever about the correlation between the microbiome and the immune system—including the body's response to immunotherapy.

Cohen and the research team have been able to show that melanoma patients with diets rich in fiber had an almost fivefold greater chance of responding to immunotherapy compared to patients with diets low in fiber.

“If the microbiome truly is the determiner of who responds to immunotherapy and who doesn’t, we potentially have it in our control to turn a non-responder into a responder and that could be through something as simple as modifying lifestyle factors,” explains Cohen. “Currently we know that [microbiome] biodiversity is key.”

Biodiversity refers to the variety of microbiomes found in the gut rather than the total number of microbiome organisms. In this way, Cohen recommends plant-based foods rather than pill-based probiotics that can sometimes push out diverse organisms in the name of quantity rather than quality and have the reverse intended effect. In fact, the research team found that probiotic use by melanoma patients was associated with worse outcomes to immunotherapy.

The microbiome also plays an important role on stress and mental health, and vice versa. “It’s called the gut-brain axis,” says Cohen. “It’s this reciprocal loop that’s going on. The health of the microbiome influences stress, and stress influences the microbiome.” Stress has long been found to have an impact on health, and as Cohen describes, “Stress makes your body more hospitable to cancer.”

The team is also looking at the role of stress and anxiety management on treatment response. That’s because while stress and anxiety are normal parts of life—and can be helpful in many situations—but left unchecked, they can also be detrimental to your health and wellbeing. Stress activates a host of nerve and hormonal signals that release a rush of hormones throughout the body, including adrenaline and cortisol.

We all know what a flood of adrenaline feels like, while boosting short-term energy levels it also elevates blood pressure and heart rate. Meanwhile, cortisol helps us better focus by upregulating the brain’s use of glucose and increasing the body’s ability to repair tissues. Unfortunately, these stress hormones also alter or down-regulate many body functions deemed unessential in a fight-or-flight situation, including our immune responses. It’s easy to see how this could become problematic for melanoma patients undergoing immunotherapy. There is also evidence that stress can alter the tumor microenvironment, making it more hospitable to cancer growth.

Fortunately, it’s possible to manage stress and anxiety through regular meditation, yoga or other exercise, prayer, other spiritual practices or hobbies.

Stress and stress management, along with food, sleep, exercise, and other lifestyle and behavior factors inform much of Cohen’s integrative medicine work. Integrative medicine incorporates elements of complementary and alternative medicine—such as yoga, acupuncture, or herbs—into a comprehensive treatment plan alongside conventional treatment. Through the Team Science Award, Cohen says that they are looking not only at the microbiome and the immune system but, indeed, the whole complex system which is the human being and the person’s interaction with the world.

“The type of funding that we receive from MRA allows us to push the envelope in answering these types of questions and to do so in very multidisciplinary ways,” says Cohen. “This is important because in medicine and science sometimes we can be reductionist in nature and miss the forest

from the trees.”

Cohen and his colleagues are optimistic about their findings to date and in unlocking further clues to the microbiome and how that can inform science, advance research and enhance patient lives.

For Cohen, this isn't just an academic interest. That's because he knows firsthand what it's like to experience the challenge patients face as they sit at the other side of the exam table. In 2018, after finishing his book *Anticancer Living: Transform Your Life and Health With the Mix of Six*, Cohen was diagnosed with stage III melanoma. “It's never too late in your life or cancer journey to start making changes to improve your life. You can't always guarantee an individual's length of life, but you can definitely improve quality by modifying key lifestyle factors and improving your microbiome.”

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