# A unique patient case inspires research in lipodystrophy syndromes

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Mallory and Oral at a recent visit. Photo courtesy of Oral. Credit: Oral

Mallory Mattison is a film student at Western Michigan University, studying in hopes of someday becoming a producer of medical documentaries.

She loves creating and editing videos, assembling puzzles and belting it out during a good round of karaoke with friends.

Mattison is also the inspiration behind critical medical research that's supporting other patients like her.

## Mattison's case

Mattison's story began when she was 11, when her arms and legs became very thin.

Her family didn't know what was wrong, theorizing that perhaps Mattison, now 22, was dehydrated or wasn't getting enough protein.

Her primary care providers referred her to an endocrinologist with Michigan Medicine, Michael Wood, M.D., who suspected the diagnosis of lipodystrophy and referred her to Elif A. Oral, M.D. at Metabolism, Endocrinology & Diabetes Clinic.

Oral has devoted her entire career to the study of lipodystrophy syndromes and is credited for bringing the first therapy approved for this condition (metreleptin—a recombinant form of the hormone leptin) to patients with lipodystrophy.

Oral describes lipodystrophy syndromes as diseases where people don't have normal fat.

They may lose fat or have a genetic reason not to develop it.

Because the hormone leptin comes from fat, people who have lipodystrophy have very low levels of leptin.

In part because of their low leptin, patients who have the condition develop diabetes with severe insulin resistance (making it very difficult to treat), and high levels of fats in their liver and blood.

Because of the high levels of fats in the blood, they may develop lots of abdominal pain or recurrent pancreatitis episodes.

In Mattison's case, she was having pancreatic episodes that kept her in the hospital for two to three weeks at a time.

Mattison participated in a study to receive metreleptin.

Initially, this drug worked well, but then Mattison developed an antibody to metreleptin that made the drug ineffective.

At that point, the real havoc started.

Oral estimates that during her junior and senior years of high school, Mattison was spending more time in the hospital than in school.

Oral began collaborations with Regeneron to develop novel therapies for lipodystrophy and knew that a drug they were developing could assist in treating Mattison's lipodystrophy by directly stimulating her leptin receptor to mimic the effects of leptin or metreleptin.

They took a "leap of faith," about trying the drug with Mattison—at the time they brought the drug to her, only very early trials had been done and no humans had been treated with it for more than 12-weeks.

"We didn't really know what to expect. But we knew that we needed to do something because I couldn't spend that much time in the hospital anymore," Mattison said.

Once the team got their approvals, Mattison began her treatment with Regeneron's drug, which originally called REGN4461 before being given the name Mibavademab.

Thankfully, this "leap of faith" yielded desired results.

Mattison said the drug was immediately life changing.

She felt much better, her liver lost fat, her triglycerides improved, and her pancreatic episodes subsided.

"I didn't feel sick or in pain at all, and it was so nice," Mattison said.

"I could sleep again. I felt normal. I could go back to school full time, and I felt like I didn't have this debilitating disease anymore."

## The 'dream team'

Mattison's team, who she refers to as her "dream team" (led by Oral and including researchers like Maria Foss-Freitas) found her case beneficial not just for her, but for finding answers and more treatment options for others with lipodystrophy.

Oral's team, together with scientists at Regeneron, have since authored detailed patient centered research about the drug and about Mattison's case, which was published in *Science Translational Medicine*.

"I do believe that she really helped us understand her condition and this drug better by allowing us to treat her with it. Seeing what was happening with Mattison allowed us to gain experience for effective and safe dosing in this disease," Oral said.

"This was a win-win. Our patient got access to a drug that she really needed, and a new drug development program for lipodystrophy came to life."

Oral also mentions that this research could only be done in a place like

Michigan, where investment enables targeted approaches to understand rare diseases and where expanded access programs help researchers like her bring very early investigational drugs to patients.

"The team is wonderful and represents a hallmark of the Michigan difference," said Oral.

Oral also added, "This is not a cure, but an effective treatment. Our team will not stop until we reach a cure for every patient with lipodystrophy."

In addition, the team hopes that as they learn why patients with lipodystrophy lose their fat cells, so they can gain insights about how to tackle obesity (the opposite problem) and other forms of diabetes.

"There are similarities between lipodystrophy and obesity," Oral said.

## Continuing research

In today's environment, when there is constant access to nutrition, the capacity of the fat cells can be exceeded, causing all of the excess lipids and nutrients that would normally be stored in fat to spill over to places where they should not go—like the liver or the muscle.

This spillover represents a root cause of metabolic diseases, including common lipid disorders and forms of diabetes. In lipodystrophy, there is not fat and this spillover and these problems happen very quickly.

By participating in research, Mattison enables studies that investigate the mechanisms of fat loss in her body.

She also credits her mother for supporting her through each appointment, and even donating blood and tissue to help understand the basis of Mattison's disease and to develop a treatment for her.

She's grateful for her ability to take part in the research that will support treatments for other patients.

"I feel really special and honored. I feel lucky that they picked my case specifically because this not only is a rare disease, but also a rare case," Mattison said.

"The fact that they want to help me so they can help others is so cool. I'm just so happy that I get to be that first patient."

Oral's team is grateful to her and others like her for their trust and partnership.

**More information:** Judith Y. Altarejos et al, Preclinical, randomized phase 1, and compassionate use evaluation of REGN4461, a leptin receptor agonist antibody for leptin deficiency, *Science Translational Medicine* (2023). DOI: 10.1126/scitranslmed.add4897

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