Study finds fat and bone mass are genetically linked

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When it comes to body shape, diet and exercise can only take us so far. Our body shape and geometry are largely determined by genetic factors. Genetics also have an impact on our body composition – including soft fat tissue and hard bone tissue – and can lead to excess fat or osteoporosis.

Now Prof. Gregory Livshits of Tel Aviv University's Department of Anatomy and Anthropology at the Sackler Faculty of Medicine, working alongside Dr. Michael Korostishevsky, has uncovered a clear genetic link between fat and bone mass. These factors, which contribute to bone metabolism, also affect Body Mass Index (BMI), which often serves as an indicator of overall health.

Reported in the journal *Bone*, this finding is a step towards understanding how these tissues are inter-related on a biological level, and will help doctors develop better treatment plans for patients dealing with fat or bone related pathologies. "When a patient is prescribed a medication, it is always important to know the potential side effects," says Prof. Livshits. As a result of this genetic connection, "a medication that is prescribed to treat obesity might have a negative impact on skeletal health," he says.

Connections forged in fat and bone

Previous studies revealed that osteocalcin, a protein produced by bone

cells, has an impact not only on bone but also on fat tissue metabolism. The protein's function is associated with bone formation and bone mineralization. But recent data suggest that osteocalcin is also involved in the regulation of glucose and fat metabolism and that osteocalcin levels are lower in obese and overweight individuals. Prof. Livshits and Dr. Korostishevsky set out to determine the underlying mechanism of this osteocalcin link – whether it was purely environmental or had a genetic basis.

The researchers conducted their study on a European population called the Chuvasha – descendants of Bulgarian tribes that have lived along the Volga River for more than a thousand years. As a relatively isolated and ethnically homogeneous population, they are highly appropriate for the study of genetic effects. 1,112 participants over the age of 20 hailing from a total of 230 families were tested for variants in the osteocalcin gene. Genetic information was analyzed in connection with measurements that reflect body mass, including BMI, thickness of skin folds, reflecting the amount of fat beneath the skin and others.

"We discovered a statistically significant association between osteocalcin gene variants and measures of body mass, suggesting the involvement of this gene in body mass regulation," says Prof. Livshits. To check the reliability of their findings, they asked researchers at Tulane University in Louisiana to test the same association between genetic variants of the osteocalcin gene and body mass measurements in an extensive sample of 2,244 Americans of European background. The results revealed a very similar pattern.

Balancing treatment

Because the connection between fat and bone mass has been shown to be genetic rather than environmental, related issues can't be addressed separately, Prof. Livshits says. Bisphosphonates, for example, are

effective agents for the treatment of bone mineral density loss and are therefore commonly used to treat osteoporosis. However, it is also important to know how this therapy impacts fat tissue. "After a few years of treatment that improves the bones, we don't want to discover that we have harmed the fat tissue in the process," he adds.

In parallel studies, the researchers are also investigating the FTO (fat mass and obesity-associated) gene, which has been shown to impact fat and lean body mass and is suspected to impact bone mineral density too. Their future research will explore the extent to which osteocalcin, FTO, and several other genes impact muscle mass in addition to fat and bone mass. It is important to understand the extent to which these genes contribute to interdependence of all major body composition components, says Prof. Livshits.

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