High BMI doesn't always spell obesity, Jackson Laboratory researchers show

For years doctors have used the body mass index (BMI), a ratio of height and weight, to characterize the clinical weight status of their patients. The lower the number, the presumption goes, the leaner the person, and anyone with a BMI above 30 is characterized as obese and at high risk for the associated complications.

But the BMI has come under scrutiny lately, and other techniques that measure how the weight is distributed on the body are thought to provide a better way to assess risk. Now a study in mice by scientists at The Jackson Laboratory indicates that the usefulness of the BMI is suspect even at the genetic level.

In research published in PLoS Genetics, the investigators from Jackson and the J.L. Pettis VA Medical Center and led by Dr. Gary Churchill of Jackson used a combination of computational, molecular and genetic tools to identify locations on the mouse genome that influence adiposity (amount of body fat), overall body size and bone structure. Applying an analytical technique called "structural equation modeling" to the genetic and physical characteristics of mouse inbred crosses, the scientists went beyond the one-gene, one-trait approach to reveal the networks of effects created by the influence of multiple genes.

"We found that the genetic network affecting adiposity is separate from that affecting overall body size," Churchill says, "providing strong evidence that a high weight is not necessarily directly associated with a high percentage of fat."

At the clinical level, the research suggests that more refined measurements are needed to distinguish individuals with a large body mass from those who are truly obese and consequently at high risk for diabetes, heart disease and other disorders.

Churchill and colleagues at Jackson recently received a 5-year, $15.1 million National Institute of General Medical Sciences grant to form an interdisciplinary Center for Genome Dynamics to study complex biomedical problems. "The most common diseases

and health disorders, including obesity as well as heart disease, diabetes and cancer, result from an interaction of multiple genes and environmental factors that add up to a dauntingly complex mix of variables," Churchill says. "We're working to unravel those factors to lay the groundwork for improved treatments."

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The Jackson Laboratory is an independent, nonprofit research institution based in Bar Harbor, Maine, with facilities in West Sacramento, Calif. Its research staff of more than 450 investigates the genetic basis of cancers, heart disease, osteoporosis, Alzheimer's disease, glaucoma, diabetes, and many other human diseases and disorders, as well as normal mammalian development and bioinformatics. The Laboratory is also the world's source for nearly 3,000 strains of genetically defined mice, home of the Mouse Genome Database and many other publicly available information resources, and an international hub for scientific courses, conferences, training and education.