

Diabetes in bay area Chinese population linked to fat fibrosis

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A new UC San Francisco study has discovered a key biological difference in how people of European and Chinese descent put on weight—a finding that could help explain why Asians often develop type 2 diabetes at a much lower body weight than Caucasians.

The research, published online May 28, 2018 in the *Journal of Clinical Endocrinology & Metabolism*, could be used to develop new biomarkers for [diabetes risk](#) in Asian populations and could even lead to new classes of drugs to slow the progression of the disease across all ethnicities, the authors say.

The worldwide epidemic of type 2 diabetes has long been associated with rising levels of obesity. But while obesity is certainly a major risk factor for the disease, particularly in Caucasians, only a minority of people with obesity actually develop the disease, says UCSF Health endocrinologist Suneil Koliwad, MD, Ph.D., an assistant professor of medicine and member of the Diabetes Center at UCSF.

On the other hand, some ethnic groups, such as people of Asian and South Asian descent, often develop type 2 diabetes long before they would be considered obese. As a result, people in Asian communities get type 2 diabetes more frequently and at a younger age than Caucasians, and are often diagnosed late because clinicians don't expect to see the disease in young people who appear otherwise healthy.

"Right now as clinicians the best we can do to reduce the risk of diabetes

is tell people to exercise, eat right, and try to lose a little weight, but we're fighting against an environment and culture that really encourages people to gain weight," said Koliwad, a physician-scientist who holds the Gerold Grodsky, Ph.D./JAB Chair in Diabetes Research at UCSF. "But I've always wondered if there is something protective in the majority of people who are clinically obese but don't get diabetes, or some other risk factor in groups like Asians who develop diabetes without being obese, that could help us develop better treatments."

Previous research has pointed to the fact that people of Asian and European descent put on fat in different ways: Europeans tend to first accumulate fat under the skin of the arms, hips, buttocks and thighs as so-called subcutaneous fat, which is generally considered "healthy fat" and not a major risk factor for type 2 diabetes. In obesity, an individual's subcutaneous "fat depots" fill up, and their bodies begin storing [excess fat](#) as "belly fat" in secondary sites around internal organs.

It is this obesity-associated "belly fat" that has been linked to heightened inflammation, insulin resistance, and the onset of diabetes in people of European descent. In contrast, people of Asian descent tend to start putting on belly fat almost immediately, putting them at risk for type 2 diabetes at a relatively low BMI (body mass index, an estimate of overall body fat composition based on an individual's height and weight that is widely used to track obesity and diabetes risk).

The American Medical Association recently advised doctors to screen people of Asian descent for early signs of type 2 diabetes at a lower BMI than is recommended for European Americans, but scientists still don't fully understand why Asians put on unhealthy belly fat so much earlier than other ethnic groups or what to do about it.

In 2015, with funds from UCSF and the National Institute of Diabetes and Digestive and Kidney Diseases, Koliwad's team launched a study to

examine ethnic differences in diabetes risk in a group of Asian, Hispanic, and Caucasian men recruited from around the San Francisco Bay Area, which they dubbed the Inflammation, Diabetes, Ethnicity and Obesity (IDEO) Cohort.

"We felt it was important to ask these questions in a group of participants who all live in the same region, where we control for important variables like climate, environmental exposures, diet, and so on to really focus on how ethnicity itself impacts fat metabolism," Koliwad said.

In the new study, led by Diana Alba, MD, a researcher in Koliwad's lab, researchers have identified a key difference in the biology of [fat tissue](#) in IDEO participants of Chinese and European descent that could help explain the ethnic disparity in type 2 diabetes rates.

The researchers studied the body composition and glucose metabolism of 32 Chinese-American participants and 30 Caucasian participants, and found that in Chinese-Americans belly fat, not overall body fat, predicted insulin resistance, a symptom of prediabetes. In contrast, both belly fat and overall body fat were correlated with insulin resistance in Caucasian participants.

In addition, X-ray-based DEXA scans of [body fat distribution](#) revealed that BMI correlated with actual fat mass only in Caucasian subjects, and did not mark true obesity in Chinese individuals. This lack of correlation prompted the investigators to search for molecular markers in the fat tissue itself that might be more predictive of diabetes risk.

Koliwad's team took fat biopsies from under the skin of the "love handle" area in 48 study participants, and performed genetic and biochemical analysis of this tissue. The results revealed that a condition called fibrosis—a form of tissue stiffening that also occurs in scar

tissue—in subcutaneous fat was highly predictive of a build-up of unhealthy belly fat in Chinese participants as well as the onset of insulin resistance. No such connection was seen in Caucasian participants.

The results suggest a novel hypothesis for why Chinese Americans put on belly fat and develop diabetic symptoms earlier and at a lower BMI than Caucasians, Koliwad said: as the Chinese-American participants in this study put on weight, the healthy fat stores under their skin quickly stiffened with fibrosis, which prevented these fat depots from expanding further. But as a consequence, these participants started accumulating [belly fat](#), followed by inflammation and [insulin resistance](#), at a much lower BMI than Caucasian participants—in whom fibrosis typically didn't begin occurring until the participants were clinically obese.

"We have identified fibrosis as a previously unrecognized indicator of [diabetes](#) risk in Chinese-Americans, a population in which our results suggest standard BMI measurements may be of relatively little value," Koliwad said.

More information: *Journal of Clinical Endocrinology & Metabolism* (2018). [academic.oup.com/jcem/advance- ... 05941?searchresult=1](https://academic.oup.com/jcem/advance-article-abstract/doi/10.1210/clinem.aa05941)

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