

A common mitochondrial DNA variant is associated with thinness in mothers and their 20-yr-old offspring.

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A common mitochondrial (mt)DNA variant that is maternally inherited, the 16189 variant, is associated with type 2 diabetes and thinness at birth. To elucidate the association of the variant with thinness, we studied the 16189 variant in a well-characterized Australian cohort (n = 161) who were followed up from birth to age 20 yr. PCR analysis and mtDNA haplotyping was carried out on DNA from 161 offspring from consecutive, normal, singleton pregnancies followed from birth to age 20 yr. The 16189 mtDNA variant was present in 14 of the 161 20 yr olds (8.7%). Both the mothers with the 16189 variant and their 20-yr-old offspring were thinner than those without. Median (interquartile range) BMI was 21.9 kg/m² (20.4 to 22.9) in mothers with the variant compared with 23.5 (21.4 to 26.6) in those without (P = 0.013) and 22.2 (21.1 to 23.8) in 20 yr olds with the variant compared with 22.7 (20.8 to 25.6) in those without (P = 0.019). The 16189 variant was also associated with a high placental weight and high placental-to-birth weight ratio (P = 0.051 and P = 0.0024, respectively). Insulin sensitivity was normal in 20 yr olds with the 16189 variant. This contrasts with 20 yr olds who did not have the variant but who had been thin or small at birth and who had normal BMI and normal placental-to-birth weight ratio, but were insulin resistant. This study suggests that the 16189 mtDNA variant is associated with maternally inherited thinness in young adults. This may be mediated by effects on mtDNA replication and, thence, placental function. Further research is required to confirm these hypotheses.