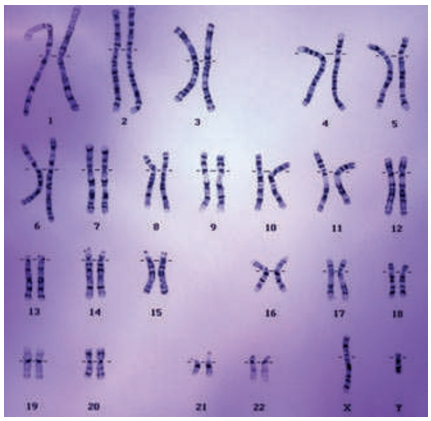
OBESITY

Rare copy number variants are associated with severe early-onset obesity

A deletion in the chromosomal region 16p11.2 is associated with familial severe early-onset obesity and severe insulin resistance, according to a new study published in *Nature*.

UK researchers analyzed copy number variants in 300 white patients with severe early-onset obesity, 143 of whom also showed a developmental delay. Large (>500 kb) and rare (<1%) deletions were significantly enriched in patients compared with 7,366 healthy individuals (P <0.001).



The investigators found 15,407 copy number variants in 284 patients and 403,098 in control individuals.

The most frequent copy number variant detected in patients with severe obesity was identified in five unrelated patients with deletions in the chromosomal region 16p11.2. A 220 kb deletion (28.73–28.95 Mb) was detected in three patients and cosegregated with severe early-onset obesity alone. A longer deletion of ~1.7 Mb that was detected in two patients encompassed the 220 kb deletion and extended through a 593 kb region (29.5–30.1 Mb)—a region in which deletions have previously been associated with autism and mental retardation. Both patients had mild developmental delay in addition to their severe obesity.

The minimal deleted region contained several genes associated with neurological diseases, immunity and some genes of unknown function, as well as *SH2B1*, which encodes an adaptor protein involved in leptin and insulin signaling.

Although the contribution of other genes has not been excluded, the findings of the UK study were consistent with a role for the *SH2B1*-containing 28.73–28.95 Mb region in severe obesity and for a role of the 29.5–30.1 Mb region in brain development.

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Original article Bochukova, E. G. *et al.* Large, rare chromosomal deletions associated with severe early-onset obesity. *Nature* **4**, 666–670 (2010)