



Angelman syndrome

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Angelman syndrome (AS) is an uncommon neurogenetic disorder characterized by mental retardation, abnormal gait, speech impairment, seizures, and an inappropriate happy demeanor that includes frequent laughing, smiling, and excitability. The uncoordinated gait and laughter have caused some people to refer to this disorder as the "happy puppet" syndrome.

The genetic basis of AS is very complex, but the majority of cases are due to a deletion of segment 15q11-q13 on the maternally derived chromosome 15. When this same region is missing from the paternally derived chromosome, an entirely different disorder, Prader-Willi syndrome, results. This phenomenon—when the expression of genetic material depends on whether it has been inherited from the mother or the father—is termed genomic imprinting.

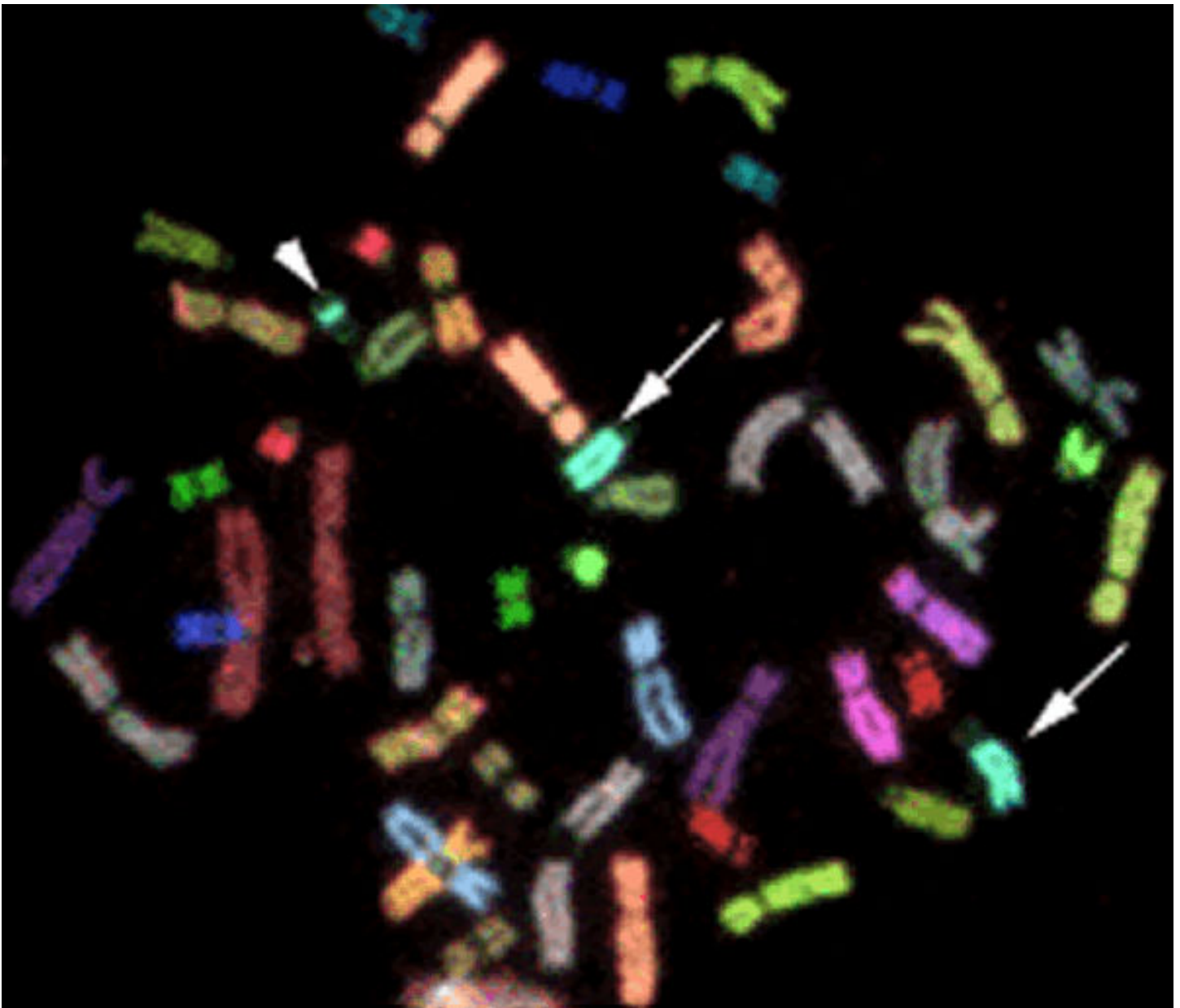
The ubiquitin ligase gene (UBE3A) is found in the AS chromosomal region. It codes for an enzyme that is a key part of a cellular protein degradation system. AS is thought to occur when mutations in UBE3A disrupt protein break down during brain development.

In a mouse model of AS, affected animals had much less maternally inherited UBE3A than their unaffected litter mates. However, this difference in UBE3A levels was only found in the hippocampus and the cerebellum, and not all of the brain. This animal model and other molecular techniques are helping us learn more about the disparate maternal and paternal expression of the UBE3A gene.

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Chromosome painting. Chromosome painting techniques such as M-FISH tint each pair of the 24 human chromosomes a different color. This allows the fragment (arrow head) to be identified as an extra piece of chromosome, since it is the same aqua color as the two normal copies of chromosome 15 (arrows). This technique may help in the diagnosis of genetic disorders that arise from chromosomal changes too subtle for conventional techniques.

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