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Why is Apert's syndrome so common when mutation rate is so low?

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Aperts syndrome is a condition caused by a mutation that produces fused fingers and toes, and alters cranial development in affected children. It arises spontaneously, but why the mutation that causes this syndrome appears so frequently has been a mystery.

In a new study published this week in the open-access journal *PLoS Biology*, Jian Qin, Norman Arnheim, and colleagues from University of Southern California provide compelling evidence that suggests the syndrome is perpetuated because the cells carrying the mutation in the testes, and that give rise to sperm, out-replicate normal cells.

The researchers have shown that the single base-pair mutation responsible for over 60% of Aperts cases occurs with such high frequency not because the relevant gene sits at a “mutation hotspot,” but because mutant cells reproduce more frequently then normal cells.

The Aperts mutation occurs in cells with a frequency between 100 and a 1000 times higher than would be predicted given a standard mutation rate. The researchers have developed a new experimental approach that measures the anatomical distribution of the mutant cells in order to investigate the mutation’s origin. They dissected healthy testes to map where the mutations had arisen, and found that mutant cells were clustered together. This distribution cannot be explained by the “hotspot” model, which would place the mutant cells randomly throughout the organ.

Instead, this paper shows that clustered mutations arise because cells carrying the genetic change out-compete normal testes cells and tend to accumulate, producing more sperm that carry the mutation and a higher frequency of transmission.

Source: Public Library of Science