SRGAP2

SLIT-ROBO Rho GTPase-activating protein 2 (srGAP2) also known as formin-binding protein 2 (FNBP2) is a protein that in humans is encoded by the SRGAP2 gene.

SRGAP2 is involved in neuronal migration and neuronal differentiation. SRGAP2 also plays a critical role in synaptic development.

SRGAP2C slows maturation of some neurons and increases neuronal spine density.

Downregulation of srGAP2 inhibits cell-cell repulsion and enhances cell-cell contact duration.

This gene is one of the 23 genes that are duplicated in humans but not in other primates.

This protein in humans has been duplicated three times in the human genome in the past 3.4 million years: one duplication 3.4 million years ago (mya) called SRGAP2B, a second duplication 2.4 mya (called SRGAP2C), and one final duplication ~1 mya (SRGAP2D). The ancestral gene SRGAP2 is found in all mammals and the human copy has been renamed SRGAP2A. The 2.4 million year-old duplication (SRGAP2C) expresses a shortened version that 100% of humans possess.

This shortened version SRGAP2C inhibits the function of the ancestral copy SRGAP2A and allows faster migration of neurons by interfering with filopodia production and slows the rate of synaptic maturation and increases the density of synapses in the cerebral cortex.

One of the most fascinating questions in evolutionary biology is how traits unique to humans, such as their high cognitive abilities, erect bipedalism, and hairless skin, are encoded in the genome. Recent advances in genomics have begun to reveal differences between the genomes of the great apes. It has become evident that one of the many mutation types, segmental duplication, has drastically increased in the primate genomes, and most remarkably in the human genome. Genes contained in these segmental duplications have a tremendous potential to cause genetic innovation, probably accounting for the acquisition of human-specific traits. In this review, I begin with an overview of the genes, which have increased their copy number specifically in the human lineage, following its separation from the common ancestor with our closest living relative, the chimpanzee. Then, I introduce the recent experimental approaches, focusing on SRGAP2, which has been partially duplicated, to elucidate the role of SRGAP2 protein and its human-specific paralogs in human brain development and evolution [1)].

1)

Sassa T. The role of human-specific gene duplications during brain development and evolution. J Neurogenet. 2013 Sep;27(3):86-96. doi: 10.3109/01677063.2013.789512. Epub 2013 Jun 20. PubMed PMID: 23782070.