

Sestrin 3

SESN3 sestrin 3

This gene encodes a member of the sestrin family of stress-induced proteins. The encoded protein reduces the levels of intracellular reactive oxygen species induced by activated Ras downstream of RAC-alpha serine/threonine-protein kinase (Akt) and FoxO transcription factor. The protein is required for normal regulation of blood glucose, insulin resistance and plays a role in lipid storage in obesity. Alternative splicing results in multiple transcript variants. [provided by RefSeq, Oct 2012]

In the TLE patients, Johnson et al. map the trans-acting genetic control of this proconvulsive module to Sestrin 3 (SESN3), and demonstrate that SESN3 positively regulates the module in macrophages, microglia and neurons. Morpholino-mediated Sesn3 knockdown in zebrafish confirms the regulation of the transcriptional module, and attenuates chemically induced behavioural seizures in vivo ¹⁾.

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Johnson MR, Behmoaras J, Bottolo L, Krishnan ML, Pernhorst K, Santoscoy PL, Rossetti T, Speed D, Srivastava PK, Chadeau-Hyam M, Hajji N, Dabrowska A, Rotival M, Razzaghi B, Kovac S, Wanisch K, Grillo FW, Slaviero A, Langley SR, Shkura K, Roncon P, De T, Mattheisen M, Niehusmann P, O'Brien TJ, Petrovski S, von Lehe M, Hoffmann P, Eriksson J, Coffey AJ, Cichon S, Walker M, Simonato M, Danis B, Mazzuferi M, Foerch P, Schoch S, De Paola V, Kaminski RM, Cunliffe VT, Becker AJ, Petretto E. Systems genetics identifies Sestrin 3 as a regulator of a proconvulsant gene network in human epileptic hippocampus. Nat Commun. 2015 Jan 23;6:6031. doi: 10.1038/ncomms7031. PubMed PMID: 25615886.

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