Heat shock response

Heat shock response (HSR) is a highly conserved transcriptional program that protects organisms against various stressful conditions. However, the molecular mechanisms modulating HSR, especially the suppression of HSR, is poorly understood.

Lin et al. found that RIP140, a wide-spectrum cofactor of nuclear hormone receptors, acts as a co-repressor of heat shock factor 1 (HSF1) to suppress HSR in healthy neurons. When neurons are stressed such as by heat shock or sodium arsenite (As), cells engage specific proteosome-mediated degradation to reduce RIP140 level, thereby relieving the suppression and activating HSR. RIP140 degradation requires specific Tyr-phosphorylation by Syk that is activated in stressful conditions. Lowering RIP140 level protects hippocampal neurons from As stress, significantly it increases neuron survival and improves spine density. Reducing hippocampal RIP140 in the mouse rescues chronic As-induced spatial learning deficits. This is the first study elucidating RIP140-mediated suppression of HSF1-activated HSR in neurons and brain. Importantly, degradation of RIP140 in stressed neurons relieves this suppression, allowing neurons to efficiently and timely engage HSR programs and recover. Therefore, stimulating RIP140 degradation to activate anti-stress program provides a potential preventive or therapeutic strategy for neurodegeneration diseases [1)].

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Lin YL, Tsai HC, Liu PY, Benneyworth M, Wei LN. Receptor-interacting protein 140 as a co-repressor of Heat Shock Factor 1 regulates neuronal stress response. Cell Death Dis. 2017 Dec 12;8(12):3203. doi: 10.1038/s41419-017-0008-5. PubMed PMID: 29233969.