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IN BRIEF

TASTE RECEPTORS

Salt leaves a bitter taste

Although low concentrations of salt in food are appetitive, salt becomes aversive with increasing concentration, thus helping to avoid excessive consumption that would disrupt electrolyte homeostasis. The mechanism underlying this aversive response is unknown, but Oka *et al*. show that a high concentration of salt recruits bitter- and sour-sensing aversive pathways. Inhibition of activity in these pathways by gene silencing had no effect on the appetitive effect of salt; indeed, salt remained appetitive even at very high concentrations. The co-opting of aversive pathways could protect against harmful ingestion of large amounts of salt.

ORIGINAL RESEARCH PAPER Oka, Y. *et al.* High salt recruits aversive taste pathways. *Nature* 13 Feb 2013 (doi:10.1038/nature11905)

GENE EXPRESSION

RAC1 overexpression beats depression

Major depressive disorder (MDD) is notoriously difficult to treat in the long term. In mice subjected to chronic social defeat stress (a preclinical model of depression-like behaviours), the authors found both reduced *Rac1* transcription in the nucleus accumbens (NAc) and depression-like behaviour, which were rescued by pharmacological inhibition of class I histone deacetylases. Similar molecular changes were observed in the NAc of depressive subjects. Furthermore, RAC1 overexpression prevented the stubby spines observed in the NAc of mice subjected to social defeat stress and the depression-related behaviours. These findings suggest that epigenetic regulation of RAC1 in the NAc could be involved in MDD.

ORIGINAL RESEARCH PAPER Golden, S. A. *et al.* Epigenetic regulation of RAC1 induces synaptic remodeling in stress disorders and depression. *Nature Med.* 17 Feb 2013 (doi:10.1038/nm.3090)

NEURODEGENERATIVE DISORDERS

It's translation, Jim, but not as we know it

Hexanucleotide (GGGGCC) repeat expansions in *C9ORF72* (chromosome 9 open reading frame 72) are the most common cause of frontotemporal dementia and amyotrophic lateral sclerosis (c9FTD/ALS). These disorders are characterized by intracellular inclusions, but the mechanism underlying their formation is unknown. GGGGCC repeats lack AGT start codons, and Mori *et al*. found that a rare form of repeat-associated non-AGT (RAN) translation of the *C9ORF72* hexanucleotide expansion resulted in various dipeptide repeat (DPR) proteins that formed insoluble aggregates. DPR proteins (mostly poly-(Gly-Ala)) were found in inclusions in the hippocampus and cerebellum from patients with ALS carrying the *C9ORF72* mutation but not in those who did not. Ash *et al*. used immunohistochemical analysis to determine the presence of RAN translation products in neuronal inclusions from patients with c9FTD/ALS. Highly selective antibodies were used to detect RAN translation products including poly-(Gly-Ala) in nuclear inclusions in the hippocampus and cerebellum from subjects with c9FTD/ALS but not in those with other disorders. Such antibodies could serve as important biomarkers for FTD/ALS and suggest possible therapeutic targeting of production and aggregation of RAN-translated peptides.

ORIGINAL RESEARCH PAPERS Mori, K. *et al.* The *C9orf72* GGGGCC repeat is translated into aggregating dipeptide-repeat proteins in FTLD/ALS. *Science* 7 Feb 2013 (doi:10.1126/science.1232927) | Ash, P. E. *et al.* Unconventional translation of *C9ORF72* GGGGCC expansion generates insoluble polypeptides specific to c9FTD/ALS. *Neuron* **77**, 639–646 (2013)