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Characterization of protein-protein interactions relevant for TRPA1 mediated nociception

Transient Receptor Potential Ankyrin1 (TRPA1) is a transduction ion channel expressed in nociceptive sensory neurons of dorsal root ganglia (DRG) and trigeminal ganglia (TG). In these tissues TRPA1 is critically involved in acute and inflammatory pain elicited by harmful chemicals, noxious cold and tissue damage. The activity of TRPA1 undergoes varying degrees of modulation, but exact molecular details remain vague. Current evidence indicates the importance of TRPA1-associated protein complexes in the regulation and modulation of TRPA1-dependent nociceptive signaling. In order to get insights into pain-specific TRPA1-protein interactions we established a comparative and quantitative mass spectrometry-based proteomics approach. These efforts have led to the discovery of 4-Nitrophenylphosphatase domain and non-neuronal SNAP25-like protein homolog 1 (NIPSNAP1).

We performed several experiments to characterize the functional interaction between NIPSNAP1 and TRPA1 in the context of nociceptive signaling in vitro. In addition, we have investigated if nocistatin, a neuropeptide that is on its part identified to interact with NIPSNAP1 to result in altered pain transmission, is involved in the modulation of TRPA1-mediated nociception.

Our results suggest the involvement of NIPSNAP1 in limiting the activity and/or surface expression of TRPA1. On the other hand nocistatin appears to enhance TRPA1-specific neuronal response. If and how these two proteins co-ordinate in their modulation of TRPA1 function is still under investigation.