

# Towards structural characterization of a polymodal ion channel

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Neurotransmitter receptors mediate and regulate the excitation state and firing rate of neurons resulting in a plethora of cognitive and motoric functions. The most prominent superfamily of the neurotransmitter gated ion channels are the Cys-loop receptors whose activation rely on a diverse range of ligands (biogenic amines, amino acids and acetylcholine). Upon activation of the ion channel, it will induce either excitation or the inhibition of the postsynaptic neuron. Recently, new members of this class of proteins were deorphanized in the free-living nematode *C. elegans*<sup>1</sup>. Among them, the ligand gated ion channel 39 (LGC-39) was electrophysiologically characterised and classified to be a receptor for both aminergic and cholinergic ligands, thus making it the first true polymodal receptor that has been reported up to date. We aim to determine the cryo-EM structure of LGC-39 both in ground state and upon binding with the two types of neurotransmitters. This information combined with *in vivo* behavioural assays in *C. elegans* will aim at deciphering how a single receptor can integrate signals from both cholinergic and aminergic neurons and how this integration results in diverse behavioural outputs.

1. Hardege, I. *et al.* (2023) A novel and functionally diverse class of acetylcholine-gated ion channels, *The Journal of neuroscience : the official journal of the Society for Neuroscience*. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9962794/> (Accessed: 07 May 2024).