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Unravelling the physiological and molecular function of the betaine-sensitive receptor in *Caenorhabditis elegans*: a new target for anthelmintic drugs.

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The free-living nematode *Caenorhabditis elegans* is a model of parasitic nematodes. This worm has the most extensive family of Cys-loop receptors, which are pentameric ligand-gated ion channels that include nicotinic receptors (nAChRs). *C. elegans* contains an extended family of nAChRs but the functional properties and roles of many of these nAChRs remain unknown. ACR-23 is a nAChR present in neuronal and muscle cells of nematodes and is not conserved in vertebrates. It is a cation-selective channel activated by betaine (BE) and sensitive to monepantel (MNP), a new anthelmintic drug. Given the limited information about its functional role in nematodes, we explored ACR-23 from a pharmacological, physiological, and molecular perspective. Locomotion assays of adult worm showed that BE significantly increased motility. This effect was not observed in *acr-23* mutants, indicating that BE acts through ACR-23. MNP decreased worm motility in the adult stage in a concentration-dependent manner with an EC₅₀ of about 30 µM. The *acr-23* mutant showed different MNP sensitivity compared to the wild-type strain, indicating that, in addition to ACR-23, other receptors may be targeted by MNP. By using a primary culture of *C. elegans* muscle cells, we described for the first time the properties of BE-elicited single-channel currents. Opening events showed a mean duration of 0.3 ms and amplitude of about 2.4 pA at a holding potential of 100 mV. The identification and functional characterization of receptors for BE and MNP provides insights into the molecular basis of anthelmintic action, which pave the way for anthelmintic drug design.

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