

P015 The paralytic action of the anthelmintic emodepside requires latrophilin and presynaptic neurotransmitter release
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Emodepside is a novel cyclodepsipeptide anthelmintic that paralyzes parasitic nematodes. In vitro studies have shown that this paralysis is dependent on external calcium and potassium ions and furthermore requires an intact nerve cord. To further define the mode of action of this novel paralytic agent we have exploited the fact that emodepside also potently paralyzes the pharyngeal and body-wall muscle of the model genetic animal *Caenorhabditis elegans*. Animals with reduction of function or null mutations in genes encoding proteins required for neurotransmitter release confer resistance to emodepside. Concurrently, a receptor for cyclodepsipeptides has been expression cloned from the parasitic nematode *Haemonchus contortus* (Saeger et al., 2001 FASEB J. 15, 1332-4.). This receptor has homology to mammalian receptors for latrotoxin, the latrophilins. *C. elegans* is predicted to have two genes encoding latrophilins, *lat-1* and *lat-2*. Further support for an involvement of latrophilin in the mechanism of action of emodepside is provided by the observation that RNAi for *C. elegans* latrophilins confers resistance to the drug. Gene deletion mutants for both *lat-1* and *lat-2* have recently been obtained and are currently being analysed for their sensitivity to emodepside. Supported by BBSRC CASE and Bayer. We are grateful to the *C. elegans* knockout consortium (USA and Japan) for the provision of strains.