



A hybrid peptide in nematodes that promotes larval survival

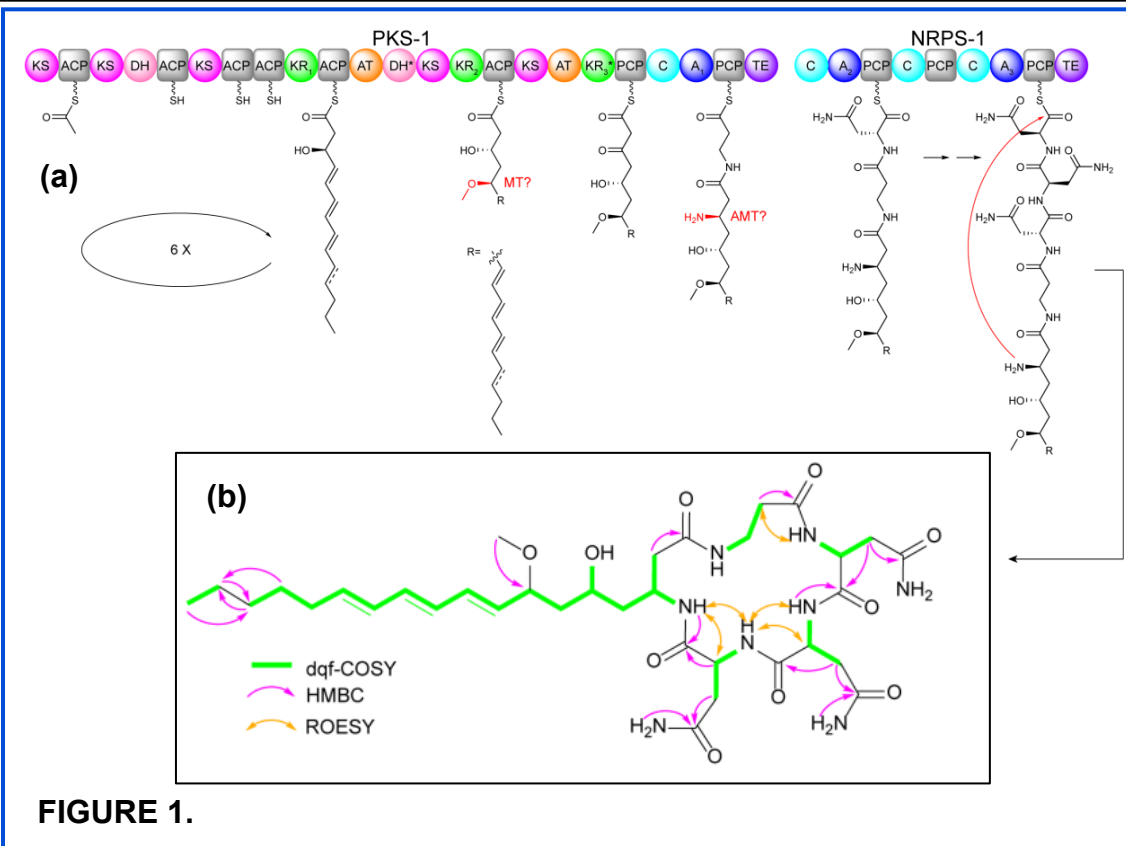
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Funding Grants: R.A. Butcher (NSF, Career 1555050; NIH, GM118775; Ellison Medical Foundation, AG-NS-0963-12; Alfred P. Sloan Foundation, BR2014-071) ; G.S. Boebinger (NSF DMR-1157490)

Polyketides and nonribosomal peptides are structurally complex natural products that have been developed into many important therapeutics. Hybrid polyketide-nonribosomal peptides (that were named “nemamides”) were purified from the nematode *Caenorhabditis elegans* and structurally characterized. As microorganisms and plants are usually responsible for producing structurally complex natural products, it is quite remarkable to discover these types of natural products in an animal species.

The nemamides were identified by comparing the metabolomes of wild-type worms and *pkcs-1* and *nrps-1* mutant worms that lack the biosynthetic genes required for nemamide biosynthesis. Only very minute quantities of the nemamides could be purified from *C. elegans* (70 µg of nemamides from 50L of worms). Thus, the ultra-sensitive high-temperature superconducting NMR probe at the MagLab was required to structurally characterize the nemamides (see Fig. 1b).



Identification of the chemical structures of the nemamides will enable their biosynthesis in the worm to be studied (Fig. 1a). The nemamides promote larval survival during starvation by influencing insulin signaling in *C. elegans*. Future work will investigate the exact mechanism of action of the nemamides. Other nematode species, including parasitic ones, likely produce nemamide-like molecules, and these molecules may play an important role in larval survival in these other species as well.

Facilities: AMRIS, Agilent 600 MHz spectrometer with high-resolution 1.5mm high temperature superconducting probe

Citation: Shou, Q., Feng, L., Long, Y., Han, J., Nunnery, J.K., Powell, D.H., Butcher, R.A., A hybrid polyketide-nonribosomal peptide that promotes larval survival. *Nat. Chem. Biol.* (2016) e-publication ahead of print, <http://dx.doi.org/10.1038/nchembio.2144>