microPublication BIOLOGY

8/27/2019 - *Open Access*

Low density lipoprotein receptors LRP-1 and LRP-2 in C. elegans

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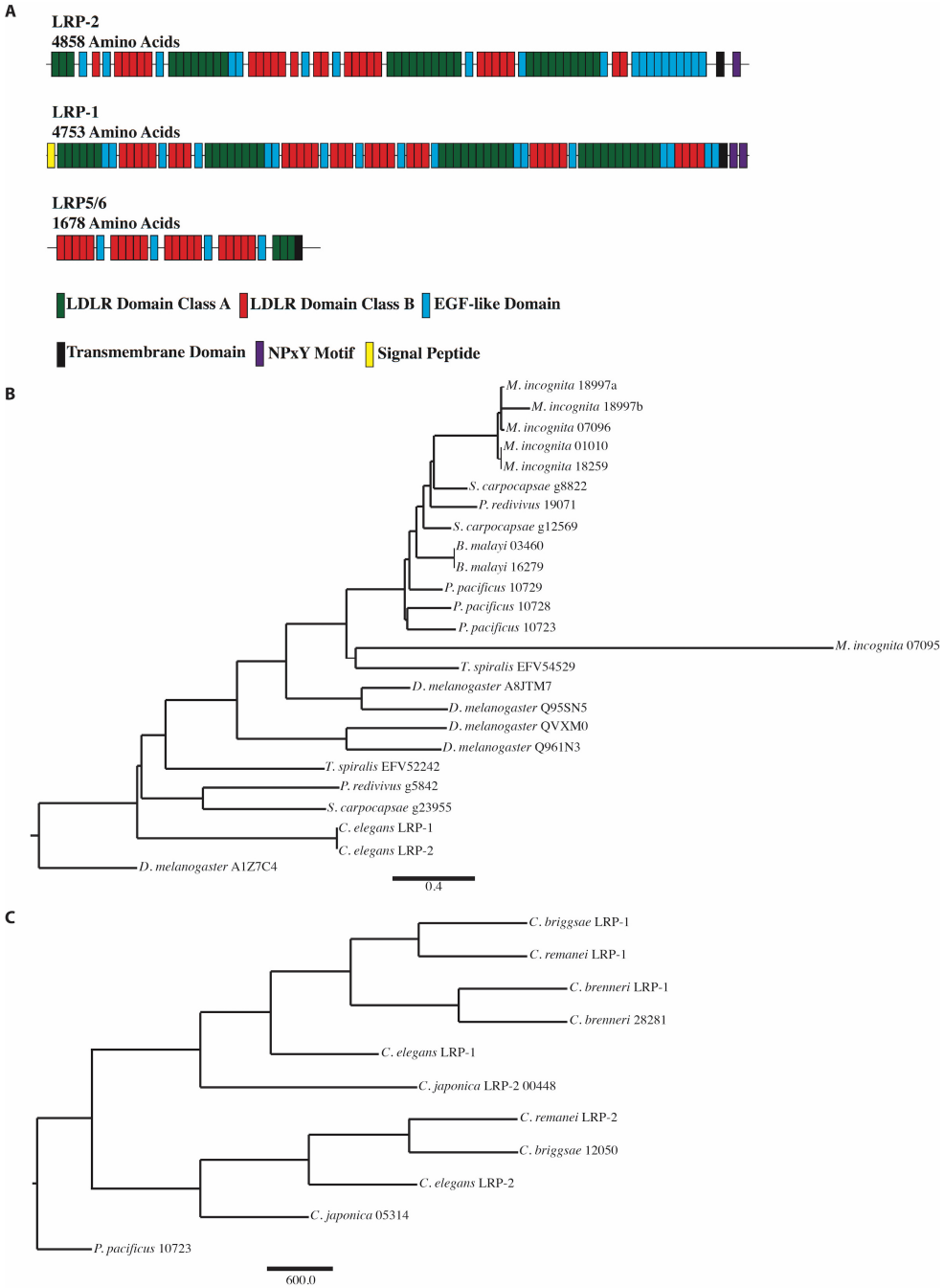

Figure 1. LRP-2 domains and phylogeny: (A) Protein domains of LRP-2, LRP-1, and *Drosophila* Arrow. *C. elegans* does not possess a true ortholog of Arrow (LRP5/6); however, it does possess multiple megalin-like proteins that contain LDLR Class A repeats, LRDR Class B repeats, and EGF-like domains that are found in varieties of low density like lipoprotein receptors such as megalin and Arrow. All domains are color-coded and drawn to approximate scale according to the SMART database. (B) An evolutionary tree based on the protein sequence of LRP-1 and LRP-2 in nematodes and megalin in *Drosophila melanogaster*. Based on sequence similarity, position in the genome, and clustering, it appears that LRP-2 is the

result of a recent duplication in *Caenorhabditis*. (C) Within *Caenorhabditis*, LRP-1 orthologs cluster together and LRP-2 orthologs cluster. *Pristionchus pacificus* is used as the outgroup.

Description

The regulation of vulval cell lineage polarity is controlled by Wnt signaling. Previously known components involved in the regulation of vulval cell lineage polarity include LIN-17, LIN-18, CAM-1, and VANG-1 (Inoue *et al*., 2004; Gleason *et al*., 2006; Green *et al*., 2008). A directed bioinformatics screen of known Wnt pathway components was performed to find additional genes involved in directing vulval orientation. A BLAST was run using other known Wnt receptors and it was determined that *C. elegans* does not contain a true ortholog of *Drosophila* LRP5/6 (Arrow) (He *et al*., 2004; Eisenmann, 2005), but does have multiple low-density lipoprotein receptors, including LRP-1 and LRP-2 (Figure 1). Like other low-density lipoprotein receptors, both LRP-1 and LRP-2 contain many LDLR Domain Class A and Class B repeats, EGF-like domains, and a transmembrane domain. However, having approximately three times as many amino acids, LRP-1 and LRP-2 are more similar to megalin than LRP5/6 (Yochem *et al*., 1999). The absence of LRP5/6 within *C. elegans* but presence in flies and all other higher order organisms suggests that the gene encoding LRP5/6 arose after nematodes, potentially from either LRP1 or LRP2/megalin, as both receptors contain the entire extracellular portion of LRP5/6 in a single contiguous sequence block (Figure 1).

Our examination of the protein sequence of LRP-1 and LRP-2 indicates that most nematodes have at least two copies of LRP-like proteins with *C. elegans* LRP-1 and LRP-2 being highly similar possibly due to a recent duplication and divergence (Figure 2). Comparing the sequences across *Caenorhabditis* we find that LRP-1 proteins cluster together and LRP-2 proteins also form their own cluster. Based on location in the genome and sequence similarity from protein alignment, we believe that *Caenorhabditis lrp-2* is a recent duplication and divergence of *lrp-1* (Figure 2).

Methods

Request a detailed protocol

Available predicted protein datasets from nematodes were obtained from WormBase release WS225 (www.wormbase.org). Other sequences were obtained from the NCBI/NIH repository (ftp://ftp.ncbi.nih.gov/genomes). Maximum likelihood (ML) analyses with 1,000 bootstraps were done using the RAxML BlackBox server (http://phylobench.vital-it.ch/raxml-bb). Protein domain analysis performed using the SMART protein domain analysis website (http://smart.embl-heidelberg.de)

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Funding: Howard Hughes Medical Institute, with whom PWS was an Investigator. The National Institute of Neurological Disorders and Stroke of the National Institutes of Health under award number 1F32NS098658-01A1 awarded to PJM.

Reviewed By: David Eisenmann

History: Received July 29, 2019 **Accepted** August 26, 2019 **Published** August 27, 2019

8/27/2019 - *Open Access*

Citation: Minor, PJ; Sternberg, PW (2019). Low density lipoprotein receptors LRP-1 and LRP-2 in C. elegans. microPublication Biology. https://doi.org/10.17912/micropub.biology.000154