Genes Encoding mosquito and silkworm lipophorin receptors

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Lipophorin is the main lipid transport vehicle in the hemolymph of most insects. A characteristic feature of lipophorin is the selective mechanism by which it shuttles its lipid cargo between cells without concomitant degradation of the protein matrix of the lipophorin particle (1). Fat body tissue plays a key role in insect lipid metabolism, as this is the site of both lipid storage and mobilization (1-3).

Lipophorin (Lp) plays a dual role in lepidopteran vitellogenesis, shuttling precursors from the fat body to the ovaries for the deposition of lipid yolk droplets, and in some species becoming one of the major constituents of the protein yolk bodies (4,5). It has been proposed that lipophorin docks via a receptor or binding site at the target tissues, thereby facilitating lipid delivery.

The recently characterized locust lipophorin receptor (LpR) is a homolog of vertebrate very low density lipoprotein receptors and is hypothesized to be the endocytotic receptor for high-density lipophorin (6). In the yellow fever mosquito, *Aedes aegypti* (*Aa*), lipid accumulation in the oocyte during oogenesis is triggered by the ingestion of a blood meal and it is internalized via receptor-mediated endocytosis (4).

We report here splice variants of lipophorin receptor gene products specific to mosquito fat body (*Aa*LpRfb) and ovary (*Aa*LpRov) with molecular masses (Mr) of 99.3 and 128.9 kDa, respectively. Two isoforms, differing in the NH2-terminus, ligand binding domain, and the O-linked sugar domain, were characterized and compared. Partial sequence of silkworm LpR shows unexpected high homology with mosquito LpRfb (98.7%) and LpRov (98.3%).

According to the deduced amino acid sequence of full length cDNA, both

isoforms of mosquito encode a member of the LDL receptor family. There are five recognizable domains: Ⅰ) the first encodes the putative ligand-binding domain consisting of seven (*Aa*LpRfb) and eight (*Aa*LpRov) cysteine-rich ligand binding repeats. Ⅱ) The EGF-precursor domain contains three EGF-precursor repeats and five copies of the characteristic YWXD sequence (8), at approximately 50 amino-acid intervals. Ⅲ) The third domain is a putative O-linked sugar domain with stretches of 63 (*Aa*LpRfb), 71 (*Bm*LpR) and 257 amino acid residues (*Aa*LpRov), rich in serines and threonines. Ⅳ) The fourth domain is a single membrane-spanning hydrophobic stretch of 22 amino acids. Ⅴ)The putataive cytoplasmic tail of the receptor contains a highly conserved internalization signal FDNPVY required for directing the LDL receptor to clathrin-coated pits.

Proposed phylogenetic relationships among LDLR superfamily members suggest that the insect LpRs are more closely related to vertebrate LDLRs and VLDLR/VgRs than to insect VgR/YPRs, with which they share a very distant common ancestor.

Northern blot analyses indicate that *Aa*LpRov gene is expressed throughout the previtellogenic and vitellogenic stages, coincident with rising 20-hydroxyecdysteroid (20E) titer. In contrast, *Aa*LpRfb gene expression is restricted to the late stage of vitellogenesis, coinciding with the termination of Lp synthesis and the onset of lipogenesis in the fat body. Thus, in addition to tissue-specific expression, differential stage-specific expression is characteristic of the LpR splice variants in mosquito as well.

References

1. Law, J. H., and Wells, M. A. (1989) *J. Biol. Chem.* **264**, 16335-16338.
2. Ryan, R. O. (1990) *J. Lipid Res.* **31**, 1725-1739.
3. Van der Horst, D. J. (1990) *Biochim. Biophys. Acta.* **1047**, 195-211.
4. Sun, J., Hiraoka, T., Dittmer, N. T., Cho, K. H., Raikhel, A. S. (2000) *Insect Biochem. Molec. Biol.* **30**,1161-71.
5. Telfer, W. H., Dan, M. L., and Law, J. H. (1991) *Insect Biochem.* **21**, 653-663.

6. Dantuma, N.P., Potters, M. P. J., Tensen, C. P.,Kooiman, F. P., Bogerd, J., and Van der Horst, D. J. (1999) *J. Lipid Res.* **40**, 973-978.
7. Trowbridge, I. S., Collawn, J. F. & Hopkins, C. R. (1993) *Annu. Rev. Cell Biol.* **9**, 129-161.