

Fear of intimacy – a close LIV-1 acquaintancy?

A recent paper in *Development* by Mathews and colleagues demonstrates the essential role of *Drosophila* Fear of Intimacy (FOI) in gonad morphogenesis (Mathews et al., 2006) that is linked to its ability to transport zinc. FOI is a member of the LIV-1 subfamily of the Zrt, IRT-like protein (ZIP) family of ion transporters. Given the increasing interest in this family of zinc transporters, we wish to highlight certain points of nomenclature in the Mathews et al. paper, which do not reflect on its conclusions.

The ZIP family of ion transporters divides into four subfamilies that belong to solute carrier family 39 (SLC39A) (Eide, 2003). LIV-1 is designated SLC39A6 or ZIP6. FOI belongs to the LIV-1 subfamily (Taylor and Nicholson, 2003), which contains nine human sequences in total.

We question the designation of FOI as dSLC39A6/dZIP6, which suggests that it is the *Drosophila* equivalent of LIV-1, which is already known as SLC39A6 (Eide, 2003). There appears to be no evidence to justify this, and an examination of the phylogenetic tree of over 110 members of the SLC39A

family (Taylor and Nicholson, 2003) clarifies this view. There are four *Drosophila* sequences in the LIV-1 subfamily termed Dm1-4. Dm4 represents FOI.

The section of the tree that includes both FOI and LIV-1 also contains another *Drosophila* molecule and five human ones. The two *Drosophila* sequences, Dm3 and Dm4 (FOI), are present in a different branch to that containing the human sequences: ZIP10/SLC39A10, ZIP5/SLC39A5, LIV-1/ZIP6/SLC39A6, ZIP14/SLC39A14 and ZIP8/SLC39A8. Additionally, when the LIV-1 subfamily sequences alone are aligned (Taylor et al., 2004), Dm3 and FOI (Dm4) again locate in a separate branch, whereas LIV-1, ZIP10/SLC39A10 and ZIP5/SLC39A5 locate in another. Furthermore, an alignment of the family sequences across transmembrane domains IV and V (Taylor and Nicholson, 2003), containing the zinc transport active site, shows the FOI sequence to be closest to ZIP5/SLC39A5 and ZIP10/SLC39A10, although there is also good sequence similarity with LIV-1, ZIP12/SLC39A12,

ZIP8/SLC39A8 and ZIP14/SLC39A14. In light of this, it is our opinion that it is inappropriate to assign FOI to any individual SLC39A family member, especially LIV-1, until further research clarifies the situation.

References

- Eide, D. J.** (2003). The SLC39 family of metal ion transporters. *Pflügers Arch.* **447**, 796-800.
- Mathews, W. R., Ong, D., Milutinovich, A. B. and Van Doren, M.** (2006). Zinc transport activity of Fear of Intimacy is essential for proper gonad morphogenesis and DE-cadherin expression. *Development* **133**, 1143-1153.
- Taylor, K. M. and Nicholson, R. I.** (2003). The LZT proteins; the new LIV-1 subfamily of zinc transporters. *Biochim. Biophys. Acta* **1611**, 16-30.
- Taylor, K. M., Morgan, H. E., Johnson, A. and Nicholson, R. I.** (2004). Structure-function analysis of HKE4, a member of the new LIV-1 subfamily of zinc transporters. *Biochem. J.* **377**, 131-139.

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