

## Whole Body Integration of Gene Expression and Morphology Using Correlative Volume EM

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Early in the evolution of bilaterian animals cell types diversified, giving rise to a wide range of cell type families which allow for the complexity of animals. Animal bodies can be composed of hundreds of cell types, which differ in their location, morphology and physiology. These individual cellular traits result from the distinct sets of genes which are expressed in different cell type families<sup>1</sup>. *Platynereis dumerilii*, an annelid worm, is a powerful model for studying the evolution of cell types due to its phylogenetic location relative to other model organisms. At 6dpf the cells of *Platynereis* have differentiated into a set of types comparable to other bilaterians. Additionally, *Platynereis* develops stereotypically<sup>2,3</sup>, opening the door for correlative multimodal exploration where multiple techniques cannot be conducted on a single individual.

Here we establish a link between gene expression and morphology for the entire body of *Platynereis* by combining whole animal volume electron microscopy (from serial blockface scanning electron microscopy) with whole mount in situ hybridization for over 200 genes (using the technique of profiling by signal probably mapping<sup>4</sup>) of *Platynereis* at 6dpf. The data is integrated into an open access atlas, The 'Multimodal Platy Browser', to explore the cells of *Platynereis* (approximately 12000 cells). Additionally the Browser provides a platform that can be expanded to include additional data from different modalities at vary scales, including further electron microscopy sources, such as subvolumes from FIBSEM (Focused ion beam scanning electron microscopy), and x-ray tomography.

This multimodal atlas is a unique resource to unravel cell types and their gene expression and morphology profiles while also retaining information on their precise location within the full body plane. Used as a reference, it serves as a map for targeting specific sites in individuals at the same stage. Applying multimodal correlations, which incorporates x-ray tomography, we are developing new workflows to investigate individual cell or tissue types.

A case study for a single cell type investigation which benefits from correlative workflows is the photoreceptors. *Platynereis* possess both rhabdomeric and ciliary photoreceptor cell types<sup>5,6</sup>, which is also proposed to be the case for the common ancestor of bilaterians, Urbilateria. The larval eye of *Platynereis* is of particular interest as it undergoes considerable morphological changes during early development (48hpf - 6dpf). Effective targeting and correlative methods are required for clear identification of cells, based on morphology and expression of gene which code for light sensitive opsin proteins. The potential

for an eye to shift from rhabdomeric to ciliary based photoreceptor would have significant implications for the evolution of photoreceptors.

#### References

- <sup>1</sup> [Arendt, D., Musser, J.M., Baker, C.V.H., Bergman, A., Cepko, C., Erwin, D.H., Pavlicev, M., Schlosser, G., Widder, S., Laubichler, M.D., et al. \(2016\). The origin and evolution of cell types. \*Nat. Rev. Genet.\* \*17\*, 744–757.](#)
- <sup>2</sup> [Tomer, R., Denes, A.S., Tessmar-Raible, K., and Arendt, D. \(2010\). Profiling by image registration reveals common origin of annelid mushroom bodies and vertebrate pallium. \*Cell\* \*142\*, 800–809.](#)
- <sup>3</sup> [Asadulina, A., Panzera, A., Verasztó, C., Liebig, C., and Jékely, G. \(2012\). Whole-body gene expression pattern registration in \*Platynereis\* larvae. \*Evodevo\* \*3\*, 27.](#)
- <sup>4</sup> [Vergara, H.M., Bertucci, P.Y., Hantz, P., Tosches, M.A., Achim, K., Vopalensky, P., and Arendt, D. \(2017\). Whole-organism cellular gene-expression atlas reveals conserved cell types in the ventral nerve cord of \*Platynereis dumerilii\*. \*Proc Natl Acad Sci USA\* \*114\*, 5878–5885.](#)
- <sup>5</sup> Arendt, D., Tessmar, K., de Campos-Baptista, M., Dorrensteign, A., Wittbrodt, J. 2002. Development of pigment-cup eyes in the polychaete *Platynereis dumerilii* and evolutionary conservation of larval eyes in Bilateral. *Development* *129*, 1143-54
- <sup>6</sup> Arendt, D., Tessmar-raible, K., Snyman, H., Dorresteijn, A.W., (2014) Ciliary photoreceptors with a vertebrate type opsin in an invertebrate brain. *Science* *306*, 869-871