

**Project Title**  
**Neuroendocrine control of development**

**Supervisor:** Alisson Gontijo

Institution: CEDOC, NMS | FCM, UNL, Lisbon

<http://cedoc.unl.pt/integrative-biomedicine-laboratory/>

Contact: [alisson.gontijo@nms.unl.pt](mailto:alisson.gontijo@nms.unl.pt)

**Location of research lab/research center:** Lisbon

**Summary:**

The aim of this project is to understand the molecular mechanisms underlying how organ growth and developmental timing are coordinated in animals both in normal conditions and when damage or abnormal growth of tissues occurs during development. Towards this objective, our group employs an integrative approach to study the evolution, biology and mechanism of action of Dilp8, the key insulin-like peptide coordinating growth and maturation time in *Drosophila* (Garelli et al., *Science* 2012; Colombani et al., *Science* 2012). Recent results have shown that Dilp8 acts via a subpopulation of CNS neurons expressing the relaxin receptor Lgr3, which is required to transduce the Dilp8 signal from the periphery to the endocrine gland controlling the onset of metamorphosis (Garelli et al., *Nat Commun*, 2015; Colombani et al., *Curr Biol*, 2015; Vallejo et al., *Science*, 2015; Jaszczak et al., *Genetics*, 2016). This points to an ancient role for neuronal relaxin receptors for sensing peripheral stress and promoting developmental stability. The student will use state-of-the-art molecular genetics and imaging tools to better understand how these Lgr3-positive neurons sense abnormal peripheral tissue growth and respond to control developmental timing. By elucidating how Dilp8 evolved and got integrated into a conserved growth and tissue-stress-sensing pathway, we expect to provide insights into the molecular mechanisms coordinating human organ growth and maturation during normal development and disease.

**Bibliographic references:**

- Colombani J, Andersen DS, Léopold P. Secreted peptide Dilp8 coordinates *Drosophila* tissue growth with developmental timing. *Science*. 2012 May 4;336(6081):582-5.
- Colombani J, Andersen DS, Boulan L, Boone E, Romero N, Virolle V, Texada M, Léopold P. *Drosophila* Lgr3 Couples Organ Growth with Maturation and Ensures Developmental Stability. *Curr Biol*. 2015 Oct 19;25(20):2723-9.
- Garelli A, Gontijo AM, Miguela V, Caparros E, Dominguez M. Imaginal discs secrete insulin-like peptide 8 to mediate plasticity of growth and maturation. *Science*. 2012 May 4;336(6081):579-82.
- Garelli A, Heredia F, Casimiro AP, Macedo A, Nunes C, Garcez M, Dias AR, Volonte YA, Uhlmann T, Caparros E, Koyama T, Gontijo AM. Dilp8 requires the neuronal relaxin receptor Lgr3 to couple growth to developmental timing. *Nat Commun*. 2015 Oct 29;6:8732.
- Jaszczak JS, Wolpe JB, Bhandari R, Jaszczak RG, Halme A. Growth Coordination During *Drosophila melanogaster* Imaginal Disc Regeneration Is Mediated by Signaling Through the Relaxin Receptor Lgr3 in the Prothoracic Gland. *Genetics*. 2016 Oct;204(2):703-709.
- Vallejo DM, Juarez-Carreño S, Bolivar J, Morante J, Dominguez M. A brain circuit that synchronizes growth and maturation revealed through Dilp8 binding to Lgr3. *Science*. 2015 Nov 13;350(6262):aac6767.