Anatomical and functional plasticity of tanycytes in the control of seasonal physiology

Seasonal adaptation of physiology is a key mechanism in the survival of many species in temperate latitudes. These adaptations are triggered by plastic changes in the brain driven by external cues such as the photoperiod (day length). The endocrine consequences of these seasonal adaptations then feed back on the brain triggering further changes in brain connectivity. Seasonal brain plasticity is therefore a particularly interesting model to study brain plasticity and its functional consequences. The signaling pathways uncovered by studying seasonal brain plasticity might be relevant for treating human diseases such as Seasonal Affective Disorder or in the control of human fertility.

In mammals, seasonal physiology is driven by changes in pineal melatonin production, which are translated into changes in thyroid stimulating hormone (TSH) production by the pituitary *pars tuberalis*. These changes in TSH are then transduced into the brain by a particular glial cell type of the hypothalamus, the tanycytes. We have shown that *pars tuberalis* TSH controls the balance of two key enzymes of thyroid hormone metabolism in tanycytes, Deiodinase 2 that activates T4 to T3 and Deiodinase 3 which inactivates both T4 and T3. Furthermore, seasonal changes of this signaling pathway trigger plastic changes in the morphology of tanycytes and their interaction with neurosecretory terminals in the median eminence.

The aim of this PhD project is to analyze the relationships between the hormonal changes and tanycyte morphology, and to determine the functional involvement of this neuroglial plasticity in seasonal physiology. This PhD project involves in vivo experimentation in seasonal hamsters as well as in vitro experiments on cultured tanycytes to analyze the involved signaling pathways.

We will provide training in seasonal physiology, animal experimentation, stereotaxic surgery, endocrinology, molecular biology, and both confocal and electron microscopic techniques. The candidate will apply for a PhD Fellowship of the French Ministry of National Education, Higher Education and Scientific Research in June 2020. Training for the selection process will be provided by the host research laboratory. The candidate should have a good working knowledge in Cell Biology and Endocrinology. An interest for functional neuroanatomy is a plus.

Send your application (cover letter with motivations, CV with academic grades) to Dr. Paul Klosen Klosen@inci-cnrs.unistra.fr and to Dr. Valérie Simonneaux simonneaux@inci-cnrs.unistra.fr

Selected Publications from the host laboratory

* Cázarez-Márquez F., Milesi S., Laran-Chich M.P., Klosen P., Kalsbeek A. & Simonneaux V. (2019) Kisspeptin and RFRP3 modulate body mass in Phodopus sungorus via two different neuroendocrine pathways. *Journal of Neuroendocrinology* **31**: e12710

* Milesi S., Klosen P. & Simmoneaux V. (2017) Seasonal Control of the GnRH Neuronal Network as a Means of Uncovering Novel Central Mechanisms Governing Mammalian Reproduction. in "The GnRH neuron and its Control" Masterclass book/e-book series edited by Herbison A. & Plant T., Chapter 16, pp 411-441

* Milesi S., Simonneaux V. & Klosen P. (2017) Downregulation of Deiodinase 3 is the earliest event in photoperiodic and photorefractory activation of the gonadotropic axis in seasonal hamsters. *Scientific Reports* **7**: 17739

* Rasri-Klosen K., Simonneaux V. & Klosen P. (2017) Differential response patterns of kisspeptin and RFamide-related peptide to photoperiod and sex steroid feedback in the Djungarian hamster (Phodopus sungorus). *Journal of Neuroendocrinology* **29**: e12529

* Klosen P., Sébert M.E., Rasri K., Laran-Chich M.P. & Simonneaux V. (2013) TSH restores a summer phenotype in photoinhibited mammals via the RF-amides RFRP3 and kisspeptin. *FASEB Journal* **27**: 2677-2686

* Bolborea M., Laran-Chich M.P., Rasri K., Hildebrandt H., Govitrapong P., Simonneaux V., Pévet P., Steinlechner S. & Klosen P. (2011) Melatonin controls photoperiodic changes in tanycyte vimentin and neural cell adhesion molecule expression in the Djungarian hamster (Phodopus sungorus). *Endocrinology* **152**: 3871-3883