Research Topic for the ParisTech/CSC PhD Program
(one page maximum)

Subfield: Life Sciences, Biomedical Neuroscience

ParisTech School: ESPCI Paris, PSL Research University, Paris, France

Title: **Role of inflammatory processes and of the gut-brain axis in Parkinson's disease pathogenesis studied in the *Drosophila* model**

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Short description of possible research topics for a PhD:

Parkinson's disease (PD) is the most common neurodegenerative movement disorder that affects ~2% of the population aged over 65. It is characterized by the progressive loss of midbrain dopaminergic neurons, leading to motor symptoms such as resting tremor, slowness of movement (bradykinesia), muscle rigidity and postural instability, and at later stages, cognition decline and dementia. At the neuropathological level, PD is defined by the formation of intraneuronal inclusions known as Lewy bodies (LB) and Lewy neurites. Because our understanding of the molecular pathways underlying its pathogenesis is incomplete, neuroprotective treatments are lacking and current therapies are often palliative by offering only symptomatic relief. The overall goal of this PhD project will be to understand better the pathological mechanisms underlying the progressive degeneration of the dopaminergic neurons and associated decline in locomotor ability in *Drosophila* models of PD, the ultimate goal being to discover novel therapeutic targets for neuroprotection. The project will focus on glia-neuron interactions causing neuroinflammatory processes, as well as the involvement of the gut in PD-like pathogenesis. Understanding the links between brain cells and this distant organ, coupled to the search for beneficial interventions at multiple levels in this model organism, could contribute to the identification of novel disease-modifying therapeutic targets in PD.

Required background of the student: Master's degree in Agriculture or Life Sciences.

A list of 5 (max.) representative publications of the group: (Related to the research topic)

Vaccaro A., Issa A.-R., Seugnet L., Birman S.*, & Klarsfeld A.* (2017) *Drosophila* Clock is required in brain pacemaker neurons to prevent premature locomotor aging independently of its circadian function. **PLOS Genet.** 13(1):e1006507, doi:10.1371/journal.pgen.1006507

Cassar M., Issa A.-R., Riemensperger T., Petitgas C., Rival T., Coulom H., Iché-Torres M., Han K.-A., & Birman S. (2015) A dopamine receptor contributes to paraquat-induced neurotoxicity in *Drosophila*. **Hum. Mol. Genet.** 24(1):197-212, doi:10.1093/hmg/ddu430

Riemensperger T., Issa A.-R., Pech U., Coulom H., Nguyễn M.-V., Cassar M., Jacquet M., Fiala A., & Birman S. (2013) A single dopamine pathway underlies progressive locomotor deficits in a *Drosophila* model of Parkinson disease. **Cell Rep.** 5(4):952–960, doi:10.1016/j.celrep.2013.10.032

Humphrey D. M., Parsons R. B., Ludlow Z. N., Riemensperger T., Esposito G., Verstreken P., Jacobs H. T., Birman S., & Hirth F. (2012) Alternative oxidase rescues mitochondria-mediated dopaminergic cell loss in *Drosophila.* **Hum. Mol. Genet.** 21(12): 2698-2712, doi:10.1093/hmg/dds096

Riemensperger T., Isabel G., Coulom H., Neuser K., Seugnet L., Kume K., Iché-Torres M., Cassar M., Strauß R., Préat T., Hirsh J., & Birman S. (2011) Behavioral consequences of dopamine deficiency in the *Drosophila* central nervous system. **Proc. Natl. Acad. Sci. USA** 108(2):834-39, doi:10.1073/pnas.1010930108