**Team “Telomere and Chromatin”**

**Project title: Deciphering the role of telomerase in the occurrence of metabolic syndrome through the regulation of hypothalamic neurogenesis**

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**Concept and Objectives.**

Metabolic syndrome represents the pathological condition that combines the obesity and its associated-metabolic disorders (1). In the brain, the hypothalamus (HpT) has a key role in maintaining the energy homeostasis. Evidence has accumulated that hypothalamic neurogenesis can be regulated by diet and hormonal signals, and that obesity caused by overnutrition can damage the HpT by promoting inflammation (2). We found that mice (p21+/Tert) expressing the catalytic subunit of telomerase (TERT) under the control of the promoter of the stress protein p21Cdkn1a become obese with age with gender disparities, a phenotype never observed in previous systems of TERT expression (3). Monitoring the behavior of these mice revealed that theyshowed an increase in food intake associated with a massive increase in hypothalamic neurogenesis, thus making the p21+/Tert mouse a unique model for its study. The M2 student project will be to determine the consequences of the HpT dysfunction on the whole-body metabolism and onset of obesity. The project will reveal the respective contribution of the canonical and non-canonical functions of telomerase in these processes (4). The M2 student will use a number of techniques including FACS, RNA-seq and tissue immunostainings.

**References**

1. Després JP, Lemieux I. Abdominal obesity and metabolic syndrome. *Nature*. 2006;444(7121):881-887.
2. Cai D, Khor S. "Hypothalamic Microinflammation" Paradigm in Aging and Metabolic Diseases. *Cell Metab*. 2019;30(1):19-35.
3. Breau M, Cayrou C, Churikov D, ... Adnot S, Geli V. Conditional expression of telomerase prevents emphysema in old mice. bioRxiv ; 2020.
4. Ségal-Bendirdjian E, Geli V. Non-canonical Roles of Telomerase: Unraveling the Imbroglio. *Front Cell Dev Biol*. 2019;7:332.