PhD Position : Neurobiology of Obesity and Diabetes

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Title of Project

Molecular and functional mapping of POMC neurons in obesity: a multi-modal approach

Summary of thesis project

The hypothalamus orchestrates several metabolic and behavioral outputs, including, but not limited to, food intake, energy balance, and systemic glucose homeostasis. A population of hypothalamic neurons expressing the neuropeptide proopiomelanocortin (POMC) plays key roles in this context. When POMC neuronal activity is altered, for instance following long-term feeding with hypercaloric diets, this can trigger hyperphagia, systemic glucose intolerance, and ultimately obesity.
Under physiological conditions, POMC neuronal cells are highly heterogeneous, at both molecular and functional levels. However, whether or not such heterogeneity may be implicated in the pathogenesis of obesity, remains unknown. Moreover, the main cellular and molecular mechanisms linking cell-specific POMC neuronal alterations with metabolic control and obesity progression have yet to be fully elucidated.
The main goals of this thesis are 1) to characterize the impact of diet-induced obesity on POMC neuronal dysfunction at a single-cell resolution, and 2) to identify the main molecular factors linking POMC neuronal dysfunction with the establishment and the progression of diet-induced obesity. Different approaches will be used to explore molecular and functional changes induced by obesity in different subpopulations of POMC neurons in murine models of metabolic disease, including single-cell mRNA sequencing, *ex-vivo* patch-clamp recordings, *in vivo* calcium imaging, neuroanatomical tracing studies, and analysis of feeding behavior and systemic energy metabolism.
This project will shed new light on the neurobiological mechanisms underlying the etiology of obesity and its associated metabolic complications.

We are seeking for : highly motivated candidate and strongly interested in experimental neuroscience, neurophysiology, hypothalamus, energy balance regulation, and obesity.

Relevant publications:

1) Quarta C, Claret M, Zeltser LM, Williams K, Yeo GSH, Tschöp MH, Diano S, Brüning JC, Cota D. POMC neuronal heterogeneity in energy balance and beyond: an integrated view. Nature Metabolism. 2021 Mar;3(3):299-308

2) Saucisse N., Mazier W., Simon V., Binder E., Catania C, Zizzari P., Leon S., Quarta C, Clark S, Becker J.M., Yeo G.S.H., Merkle F.T., Wardlaw S.L., Harkany T., Massa F., Marsicano G., Cota D. POMC neurons functional heterogeneity relies on mTORC1 signaling. bioRXIV, 26 March (2020). doi: https://doi.org/10.1101/2020.03.25.007765

3) Quarta C, Fisette A, Xu Y, Colldén G, Legutko B,Tseng YT, Reim A, Wierer M, De Rosa MC, Klaus, Rausch R, Thaker V,Graf E, Strom TM, Poher AL, Gruber T, Le Thuc O,Cebrian-Serrano A, Kabra D, Bellocchio L, Woods SC, Pflugfelder GO, Nogueiras R, Zeltser L, Grunwald Kadow IC, Anne Moon A, García-Cáceres C, Mann M, Treier M, Doege CA, Tschöp MH. (2019). Functional identity of hypothalamic melanocortin neurons depends on Tbx3. Nature Metabolism. 2019 Feb;1(2):222-235

4) Quarta C, Fioramonti X, Cota D. POMC Neurons Dysfunction in Diet-induced Metabolic Disease: Hallmark or Mechanism of Disease? Neuroscience. 2019; 2:S0306-4522(19)30676-1.