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Project Title: Neuro-vascular communication in the central nervous system

Project leader: Carmen Ruiz de Almodóvar

Lab website: http://www.bzh.uni-heidelberg.de/ruiz_de_almodovar/

Application Deadline: 30th Sept 2017

Start of PhD and/or Postdoc project: From October/November 2017

Project Description:

The central nervous system (CNS) (brain and spinal cord) is composed of different neural cell types organized in a very stereotyped pattern and localized in defined compartments. Apart of the neuronal cell types, the CNS is also composed of blood vessels, responsible for providing oxygen and nutrients to the neuronal tissue. Similar to neurons, during development, blood vessels also follow defined pathways to enter and invade the CNS in order to assure proper oxygen and nutrient delivery to all parts of the tissue.

We recently found that the typical angiogenic factor Vascular Endothelial Growth Factor (VEGF) is important for vessel growth into the developing central nervous system. However, neurons regulate VEGF availability by expression a VEGF trapping receptor and like that making sure that blood vessels follow a stereotypic patterning of vascularization (Himmels et al. *Nat Commun* 2017). We could also show that VEGF regulates angiogenesis by the activation of the Hippo pathway effectors YAP/TAZ (Wang et al. *Dev Cell* 2017).

Based on those results, we now aim to further understand how different neuronal populations control CNS vascularization and how the vasculature integrates into the CNS. We aim to identify the molecular mechanisms of this regulation.

References:

Wang X, Freire Valls A, Shermann G, Shen X, Moya IM, Castro L, Urban S, Solecki GM, Winkler F, Riedemann Lm Jain RK, Mazzone M, Schmidt T, Fischer T, Halder G, Ruiz de Almodovar C. YAP/TAZ orchestrate VEGF signaling during developmental angiogenesis. *Dev Cell*. 2017(accepted).

Himmels P, Paredes I, Adler H, Karakatsani A, Luck R, Marti HH, Ermakova O, Rempel E, Stoeckli ET & Ruiz de Almodovar C. Motor neurons control blood vessel patterning in the developing spinal cord. *Nat Commun*. 2017 Mar 6;8:14583.

Chen S, Tisch N, Kegel M, Yerbes R, Hermann R, Hudalla H, Zuliani C, Gülcüler GS, Zwadlo K, von Engelhardt J, Ruiz de Almodóvar C, Martin-Villalba A. CNS Macrophages Control Neurovascular Development via CD95L. **Cell Rep.** 2017 May 16;19(7):1378-1393

Lange C, Storkebaum E, Ruiz de Almodovar C, Dewerchin M & Carmeliet P. Vascular endothelial growth factor: a neurovascular target in neurological diseases. **Nat Rev Neurol.** 2016 Jul 1.

Ruiz de Almodovar, C*, Fabre, P*, Knevels, E, Coulon, C, Segura, I, Haddick, PCG, Aerts, L, Delattin, N, Strasser, G, Oh, WJ, Lange, C, Vinckier, S, Haigh, JJ, Fouquet, C, Henderson, C, Gu C, Alitalo K, Castellani V, Tessier-Lavigne M, Chedotal A, Charron F* and Carmeliet P*. (2011). VEGF mediates commissural axon chemoattraction through its receptor Flk1. **Neuron**, June 9 (70):966-78.

Methods that will be used:

Mouse genetics
Chicken electroporation
Micro-dissections
Ex vivo 3D cell culture
In vitro cell culture
Cell Biology
Biochemistry and Molecular Biology techniques
Histology
Immunohistochemistry
Light and fluorescent microscopy
Confocal microscopy

Profile of candidate's qualification:

The candidate should be an enthusiastic and motivated scientist willing to join a young international research group in a highly dynamic working environment (with English as main language). The ideal candidate should have a biomedicine or a biochemical and molecular biology background.

Application: For further details on the application procedure, please send an email with your CV, letter of motivation and contacts for references to:

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