Vessel Formation in Development and Disease Group

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An ANR funded PhD position is available in the Vessel Formation in Development and Disease group at the iBV

The role of p16-dependent cellular senescence in healthy aging

Description : Cellular senescence attracts attention as a key player contributing to organismal aging. The accumulation of senescent cells is dramatically increased with aging, however their precise contribution to aging-related phenotypes remains largely unclear. In collaboration with the team of D. Bulavin we showed p16-dependent senescent cells are required for healthy aging. We used different novel inducible mouse lines to characterise the role of p16 expressing cells in different organs. Currently, we focussed mainly on liver. The project aims at identifying the cell repertoire linked to aging-induced senescence and to investigate the impact of senescent cells on liver functions and to understand molecular pathways modulated by senescence. For these purposes we will use p16-Cre and p16-Cre-ERT2 mice crossed either with Rosa26-mTmG reporter or Rosa26-DTA ablator mice. The animals will be investigated by histological and immunohistological methods and RNA sequencing will be performed at different ages. This project will help to understand the molecular mechanism responsible for aging-induced activation of senescence and hopefully identify potential molecular targets to manipulate senescence through reprogramming and/or selective elimination of subsets of senescent cells.

Required Skills : The working language is English.
Experience in molecular biology, cellular biology and/or mouse genetics would be a plus.
Motivation to work with mouse models and team orientation are required. Animal experimentation training is part of the project.

Related publications:

Grosse, L, Wagner, N, Emelyanov, A, Molina, C, Lacas-Gervais, S, Wagner, KD et al.. Defined p16High Senescent Cell Types Are Indispensable for Mouse Healthspan. **Cell Metab**. 2020:. doi: 10.1016/j.cmet.2020.05.002. PubMed PMID:32485135 .

Wagner, KD, Du, S, Martin, L, Leccia, N, Michiels, JF, Wagner, N et al.. Vascular PPARβ/δ Promotes Tumor Angiogenesis and Progression. **Cells**. 2019;8 (12):. doi: 10.3390/cells8121623. PubMed PMID:31842402 PubMed Central PMC6952835.

Wagner, KD, El Maï, M, Ladomery, M, Belali, T, Leccia, N, Michiels, JF et al.. Altered VEGF Splicing Isoform Balance in Tumor Endothelium Involves Activation of Splicing Factors Srpk1 and Srsf1 by the Wilms' Tumor Suppressor Wt1. **Cells**. 2019;8 (1):. doi: 10.3390/cells8010041. PubMed PMID:30641926 PubMed Central PMC6356959.

Wagner, KD, Ying, Y, Leong, W, Jiang, J, Hu, X, Chen, Y et al.. The differential spatiotemporal expression pattern of shelterin genes throughout lifespan. **Aging** (Albany NY). 2017;9 (4):1219-1232. doi: 10.18632/aging.101223. PubMed PMID:28437249 PubMed Central PMC5425123.

Wagner, KD, Cherfils-Vicini, J, Hosen, N, Hohenstein, P, Gilson, E, Hastie, ND et al.. The Wilms' tumour suppressor Wt1 is a major regulator of tumour angiogenesis and progression. **Nat Commun**. 2014;5 :5852. doi: 10.1038/ncomms6852. PubMed PMID:25510679 .

El Maï, M, Wagner, KD, Michiels, JF, Ambrosetti, D, Borderie, A, Destree, S et al.. The Telomeric Protein TRF2 Regulates Angiogenesis by Binding and Activating the PDGFRβ Promoter. **Cell Rep**. 2014;9 (3):1047-60. doi: 10.1016/j.celrep.2014.09.038. PubMed PMID:25437559 .

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