MASTER 2 BMC
PARCOURS GENOPATH
ANNÉE 2018-19

Titre du sujet de stage :
Caractérisation de nouveaux mécanismes impliqués dans la régulation de la sénescence, du cancer et du vieillissement

Nom, adresse de l'Unité d'accueil / Nom du responsable de l'unité :

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Sujet de stage :

Cellular senescence is recognized to be involved in numerous physio-pathological conditions, especially during normal or premature aging. Virtually, all phenotypes linked to aging involve senescence at the cellular level. Senescence response is activated by numerous cellular stresses such as replicative exhaustion, radiation, genotoxic, oncogenic signals, inflammation, metabolic stress as well as oxidative stress, and it results in the acquisition of a specific secretome and is characterized by a stable proliferation arrest.

We have described several new regulators of cellular senescence (see publications below). The research project (details will be directly discussed with the selected M2 candidate) will be targeted towards understanding the mechanisms of action and the role of one of the new regulator of senescence we have described on the regulation of cellular senescence, cancer and/or other age-related diseases. The project will involve various technologies including si/shRNA experiments, senescence characterization, primary cell culture, retroviral infection, cell imaging and eventually in vivo experiments in mice.

We invite highly motivated M2R student wishing to work on aging and cancer biology to contact us to discuss in detail the project.

Technologies utilisées :

Classical cellular and molecular approaches (RNA and protein extraction, RTqPCR, immunoblot, IF, viral transduction, cell culture, confocal microscopy...) and eventually experiments in mice.

Mots clés :
Cellular senescence, Cancer, Aging

Publications d'intérêt:
.Warnier M, Flaman JM, Chouabe C, Wiel C, Gras B, Blanc E, Foy JP, Mathot P, Saintigny P, Van Coppenolle F, Vindrieux D, Martin N, Bernard D. The SCN9A channel and plasma membrane depolarization promote cellular senescence through Rb pathway. Aging Cell. 2018 Jun;17(3):e12736.
.Collin G, Huna A, Warnier M, Flaman JM, Bernard D. Transcriptional repression of DNA repair genes is a hallmark and a cause of cellular senescence. Cell Death & Disease, 2018 Feb 15;9(3):259.
.Griveau A, Devailly G, Eberst L, Navaratnam N, Le Calvé B, Ferrand M, Faull P, Augert A, Dante R, Vanacker JM, Vindrieux D, Bernard D. The PLA2R1-JAK2 pathway upregulates ERRa and its mitochondrial program to exert tumor-suppressive action. Oncogene, 2016;35:5033-42.
.Wiel C, Gras B, Vindrieux D, Warnier M, Gitenay D, Le Calvé B, Ferrand M, Augert A, Bernard D. Multidrug Resistance Protein 3 loss promotes tumor formation by inducing senescence escape. Oncogene, 2016;35:1596-1601.
.Wiel C, Lallet-Daher H, Gitenay D, Gras B, Le Calvé B, Augert A, Ferrand M, Prevarskaya N, Simonnet H, Vindrieux D, Bernard D. Endoplasmic reticulum calcium release through ITPR2 channel leads to mitochondrial calcium accumulation and senescence. Nature Communications, 2014; 5:3792.
.Vindrieux D, Augert A, Girard CA, Gitenay D, Lallet-Daher H, Wiel C, Le Calvé B, Gras B, Ferrand M, Verbeke S, de Launoit Y, Leroy X, Puisieux A, Aubert S, Perrais M, Gelb M, Simonnet H, Lambeau G, Bernard D. PLA2R1 mediates tumor suppression by activating JAK2. Cancer Res, 2013; 73(20):6334-6345.
.Lallet-Daher H, Wiel C, Gitenay D, Navaratnam N, Augert A, Le Calvé B, Verbeke S, Carling D, Aubert S, Vindrieux D, Bernard D. Potassium channel KCNA1 modulates oncogene-induced senescence and transformation. Cancer Res, 2013; 73(16):5253-65.
.Humbert N, Navaratnam N, Augert A, Da Costa M, Martien S, Wang J, Martinez D, Abbadie C, Carling D, de Launoit Y, Gil J, Bernard D. Regulation of ploidy and senescence by the AMPK-related kinase NUAK1. EMBO J, 2010;29(2):376-86.