Skin cancers and especially melanomas are constantly increasing in western countries with their incidence doubling every 12 years. Epidemiological reasons are quite clear: sun, pollution, ethnic migration and lifestyle.

However, the molecular mechanisms associated with this transformation are not yet fully elucidated, even though proteins belonging to the MAP-kinase, PI3K and β-catenin pathways were clearly shown to be involved. In order to better understand melanomagenesis, cellular heterogeneity and plasticity, and melanoma resistance we investigate the establishment and the renewal of the melanocyte lineage, as well as melanomagenesis.

It is becoming very clear that the MAP-kinase pathway induces melanocyte proliferation and senescence. Similarly, the lack of PTEN or p16, or the activation of b-catenin allows the bypass of senescence. However, the vast majority of the cells which are mutated for two of these types of proteins are not able to initiate a melanoma. This indicates that melanoma initiation is still not fully understood. Melanoma
initiation is followed by progression (involving most probably CDH1) and associated molecular heterogeneity (involving most probably MITF and BRN2).

In order to understand/improve prevention, early diagnosis, cellular transformation and therapy, we believe that it is crucial to know better the molecular and cellular mechanisms occurring during the normal and pathological development of this lineage and during melanoma initiation/progression in a cell autonomous and cell non-autonomous manner. Human genetics information associated with the production/study of murine melanoma models will allow for a better understanding of the molecular and cellular events occurring during oncogenesis.

In this respect, our general goal is to better understand the cellular and molecular mechanisms associated with the normal and pathological development of melanocytes. This general goal has five main aims:

1. To better understand the β-catenin signaling during the establishment and renewal of the melanocyte lineage.
2. To better understand the cooperation between UV and Wnt/β-catenin signaling.
3. To induce cooperation of signaling pathways during melanomagenesis.
4. To evaluate the respective importance of MITF and BRN2 during melanoma initiation and progression.
5. To produce relevant melanoma models for humans.

Key publications

Year of publication 2020

Julie U Bertrand, Eirikur Steingrimsson, Fanélie Jouenne, Brigitte Bressac-de Paillerets, Lionel
Normal and Pathological Development of Melanocytes
UMR 3347/U1021 - Signaling, Radiobiology and Cancer

Larue (2020 Apr 30)
**Melanoma Risk and Melanocyte Biology.**
*Acta dermato-venereologica*: adv00139 : [DOI: 10.2340/00015555-3494]

Year of publication 2019

Zackie Aktary, Andre Corvelo, Camille Estrin, Lionel Larue (2019 Nov 4)
**Sequencing two Tyr::CreER transgenic mouse lines.**
*Pigment cell & melanoma research*: 426-434 : [DOI: 10.1111/pcmr.12842]

Year of publication 2018

Véronique Delmas, Lionel Larue (2018 Dec 12)
**Molecular and cellular basis of depigmentation in vitiligo patients.**

**A histopathological classification system of Tyr::NRAS murine melanocytic lesions: A reproducible simplified classification.**
*Pigment cell & melanoma research*: 423-431 : [DOI: 10.1111/pcmr.12677]

**Simulation of melanoblast displacements reveals new features of developmental migration.**
*Development (Cambridge, England)* : [DOI: dev160200]

Veronica A Kinsler, Lionel Larue (2018 Jan 31)
**The patterns of birthmarks suggest a novel population of melanocyte precursors arising around the time of gastrulation.**
*Pigment cell & melanoma research*: 95-109 : [DOI: 10.1111/pcmr.12645]