第 563 回 難研セミナー
第 136 回 難治疾患共同研究拠点セミナー

下記により難研セミナーを開催しますので、多数御来聴下さい。

記

日　時：　平成 29 年 7 月 11 日（火） 17:00 ～ 18:00
場　所：M&D タワー21 階　セミナー室

演　者：Lionel LARUE
(Institut Curie, Section de Reshershe)

演　題：**From Melanoblast to Melanoma: a Stressed Journey**

要　旨：Melanoma is known as a radioresistant tumor. Melanoma is intra-tumorally highly heterogeneous due to its genetic instability and plasticity. This heterogeneity may explain, at least in part, the natural neo and acquired resistance of melanoma against therapies. In a two dimensional biological world, cells may switch from “proliferative” to “invasive”, and vice versa. Two transcription factors, Mitf and Brn2, may be of great importance in this switch. Brn2 is a POU transcription factor belonging to the Oct family. In vitro studies have shown that Brn2, as well as Mitf, is transcriptionally controlled by the Lef/β-catenin complex and indirectly controlled by Braf. Moreover, the level of Brn2 mRNA is controlled by miR-211, which is directly induced by Mitf. This switch would be modulated by the transcriptional activity of Brn2 on Mitf, but also on other crucial proteins of the melanocyte lineage such as Pax3. In human melanoma metastasis, it appears that melanoma cells are mainly Brn2-positive or Mitf-positive. However some cells express both or none of these two proteins. Here, we evaluated the importance of Brn2 during the establishment, the renewal and transformation of melanocytes using genetically modified mouse models, human genetics and cell lines. It appears that Brn2 is dispensable during the establishment and the renewal of melanocytes. The specific lack of Brn2 in the melanocyte lineage reveals that this protein is important for melanoma resistance against ionizing irradiation, which consequently results in the disappearance of melanocyte stem cells over time. Moreover, mouse melanoma models relevant for humans were generated, showing that Brn2 plays an important role during melanoma initiation and can be better used to improve melanoma therapies.

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The 563th Medical Research Institute Seminar

The 136th Joint Usage/Research Program of Medical Research Institute Seminar

Date: **September 11th , 2017 (Tue) 17:00 – 18:00**

Venue: **21F M&D Tower　Seminar Room**

Lecturer: **Lionel LARUE（Institut Curie, Section de Reshershe）**

Title: **From melanoblast to melanoma: a stressed journey**

Summary: Melanoma is known as a radioresistant tumor. Melanoma is intra-tumorally highly heterogeneous due to its genetic instability and plasticity. This heterogeneity may explain, at least in part, the natural neo and acquired resistance of melanoma against therapies. In a two dimensional biological world, cells may switch from “proliferative” to “invasive”, and vice versa. Two transcription factors, Mitf and Brn2, may be of great importance in this switch. Brn2 is a POU transcription factor belonging to the Oct family. In vitro studies have shown that Brn2, as well as Mitf, is transcriptionally controlled by the Lef/β-catenin complex and indirectly controlled by Braf. Moreover, the level of Brn2 mRNA is controlled by miR-211, which is directly induced by Mitf. This switch would be modulated by the transcriptional activity of Brn2 on Mitf, but also on other crucial proteins of the melanocyte lineage such as Pax3. In human melanoma metastasis, it appears that melanoma cells are mainly Brn2-positive or Mitf-positive. However some cells express both or none of these two proteins. Here, we evaluated the importance of Brn2 during the establishment, the renewal and transformation of melanocytes using genetically modified mouse models, human genetics and cell lines. It appears that Brn2 is dispensable during the establishment and the renewal of melanocytes. The specific lack of Brn2 in the melanocyte lineage reveals that this protein is important for melanoma resistance against ionizing irradiation, which consequently results in the disappearance of melanocyte stem cells over time. Moreover, mouse melanoma models relevant for humans were generated, showing that Brn2 plays an important role during melanoma initiation and can be better used to improve melanoma therapies.

Organizers: Department of Stem Cell Biology・Emi Nishimura(4651)

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