The MeLiM pig: a model for cutaneous melanoma
Emmanuelle Bourneuf, Josef Janda, Silvia Vincent-Naulleau

To cite this version:

HAL Id: hal-01608081
https://hal.science/hal-01608081
Submitted on 3 Jun 2020
Cutaneous melanoma has been a public health concern for several decades, with a growing incidence in Caucasian populations. Tumors arise from skin melanocytes, the pigment-producing cells. The only efficient therapy described so far is an early resection of the primary tumor, as treatment options for invasive melanoma have been limited until recently. Novel molecular and immune therapies are now improving patient outcomes, nevertheless complementary insights from melanoma biology and immunology research must be pursued. Like most neoplasms, genetic and environmental factors favor melanoma development. Most tumors are a consequence of UV exposure, which damages skin cells DNA and favors cell transformation. Nevertheless, a significant proportion (10-20%) of patients carries a genetic susceptibility to melanoma. Despite huge efforts of the scientific community to decipher melanoma mechanisms, animal models are still needed to accelerate the discovery of the genetic basis of the disease and investigate potential therapeutic approaches.

The MeLiM pig (melanoblastoma-bearing Libechov Minipig) is a highly relevant model for many aspects of melanoma. Piglets develop tumors spontaneously at birth or within the first two months of life, without any human intervention. Following a tumor progression phase, and eventually a metastatic process, all lesions undergo a spontaneous regression, leading to an absence of malignant cells in adult animals. A histological and clinical comparison of the lesions observed in the MeLiM pig with human tumors has shown similarities between the two species. Obviously, discrepancies exist as well, such as the early-onset of tumors and the spontaneous regression process. However, these phenomena can provide exciting research lines. The model is maintained both in the Institute of Animal Physiology and Genetics of Libechov (Czech Republic), and in the National Institute of Agronomical Research in Jouy-en-Josas (France). Several research programs are developed, aiming at a better understanding of melanoma appearance and regression.

For example, we could evidence, in the MeLiM genome, loci that carry genes and variants predisposing to melanoma. Based on very promising results, a precise cross-species comparison with human and dog genetic data is underway. Concerning oncogenesis, a transcriptomic survey of purified melanocytes and melanoma cells gives insight into early mechanisms of transformation. Molecular investigations performed on the regression phenomenon have shown a precocious cell cycle arrest of tumor cells, in parallel of an efficient immune response, leading to tumor regression and eventually a local or systemic vitiligo-like depigmentation of the animals. Current investigations are based on the precise characterization of the tumor-infiltrating immune cells.

Finally, the MeLiM model has been used to study the effect of therapeutic molecules, and to test innovative imaging methods for example.

Funding: French Research Agency, National League Against Cancer, Cancer Research Association, French National Cancer Institute, INRA, CEA.