

Human melanoma brain metastasis and the mechanisms of adaptation

Melanoma is one of the most aggressive skin cancers because of its high metastatic potential, including to the brain. Increasing evidence suggests that the brain microenvironment regulates the pathogenesis of brain metastasis. While mouse models have been instrumental in modeling metastasis, much remains unknown about the cellular cross-talks in the human brain microenvironment. There are, in fact, challenges due to significant species-specific differences between human and mouse brains. For instance, astrocytes differ in size and complexity, and microglia differ in several receptors, determining their reaction to specific stimuli. However, challenging access to human brain cells and difficulties maintaining those cells in culture have hampered the study of cancer cells in the human brain context. This project addresses the need for a humanized, physiologically relevant, well-defined system to identify driver candidates responsible for melanoma adaptation to the human brain microenvironment.