Internship Proposition
(one page max)
Master 2 GP Immunology & ImmunoIntervention (I^3)
2024-2025

Lab: Tanaka lab

Team: Functional Genomics and Bioinformatics Research Unit, Maisonneuve-Rosemont Hospital Research Centre

Name and position of the supervisor: Yoshiaki Tanaka, Assistant Professor

Email of the supervisor: Yoshiaki.tanaka@umontreal.ca

Candidate (if internship filled):

Title of the internship: Delineation of glioblastoma-mediated angiogenesis

Summary of the internship proposal:

Glioblastoma multiforme (GBM) is characterized by microvascular hyperplasia and a glomeruloid vascular structure. Newly-formed blood vessels deliver nutrients and other growth factors to GBM cells that support tumor growth and invasion. Although inhibition of GBM-mediated blood vessel formation represents a promising treatment option, conventional anti-angiogenic therapies show only transitory/incomplete efficacy. Thus, elucidation of the molecular basis for GBM-mediated angiogenesis is important toward establishing long-term suppression of tumor progression and invasion. Recently, we identified 3 critical transcriptional/epigenetic factors (ESRRB, TET1 and ID2) that are highly expressed in GBM and potentially associated with tumor angiogenesis. In this project, **we will elucidate how these genes contribute to angiogenesis in GBM cells.**

To address the angiogenic effect of these factors, we will co-cultivate primary human brain microvascular endothelial cells (BMEC) and patient-derived GBM cells with doxycycline (Dox)-inducible shRNA. We will then evaluate angiogenesis in each fraction with respect to 1) growth rate and 2) blood vessel-like structure formation of BMEC. We will also overexpress these genes and assess whether these factors can increase endothelial gene expression to facilitate BMEC proliferation and vascular format. To further dissect the molecular mechanisms of GBM-mediated angiogenesis by these factors, we will perform ChIP-seq on GBM cells and identify binding sites for each factor. We anticipate that ESRRB, TET1 and ID2 bind regulatory sites of angiogenesis-related genes (e.g. VEGFA) GBM cells to govern angiogenesis of the surrounding microenvironment. Taken together, the proposed study will delineate the molecular basis underlying GBM-mediated angiogenesis, and explore if these transcriptional/epigenetic factors can become potential therapeutic targets to attenuate the cancer growth.

Option(s) linked to the project:

☐ Clinical Research Profile (Recherche Clinique)
☑ Data Analyst Profile (Recherche et Analyse de Données Biologiques)
☑ Experimental Biology Profile (Recherche Expérimentale)

Form to be sent by email to : gpi3@univ-nantes.fr