PhD project No. 22, Prof. Orian-Rousseau

Scientific Area	Immune-related diseases
Two project titles	A) Contribution of CD44 expressed on tumour associated macrophages, to progression of pancreatic cancer B) The CD44/CXCR4 interplay in immune suppression of pancreatic cancer
Host country	Germany
Supervisor, institution	Prof. Veronique Orian-Rousseau, Karlsruhe Institute of Technology, Germany
Co-Supervisor, institution	A) and B) Dr. Gertraud Orend, Institut d´Hématologie et d´Immunologie, Strasbourg, France
Mentor, institution	A) and B) to be determined later
Secondment institution	A) and B) Institut d´Hématologie et d´Immunologie, Strasbourg, France

Short description of the supervisor's lab with introduction to the topic

The Orian-Rousseau lab is focussed on the role of cell adhesion molecules, amongst which CD44, in tumour progression and metastasis. We have identified several CD44 isoforms as co-receptors for receptor tyrosine kinases (MET, VEGFR-2, EGFR), G-Protein coupled-receptor (CXCR4) and Wnt receptors. The study of these interactions led to the design of inhibitors of tumour progression. One such inhibitor, the CD44v6 peptide is in clinical trial.

Topic description, including techniques to be used

Project A)

Pancreatic cancer shows one of the highest mortality rate. Yet, using a CD44v6 peptide inhibiting the co-receptor functions of CD44v6 for receptor tyrosine kinases on cancer cells, we observed a drastic decrease in tumour growth and metastasis in several mouse models of pancreatic cancer. The pancreatic tumour stroma is comprised of cancer-associated-fibroblasts, stellate, immune and endothelial cells, as well as extracellular matrix. In the present project, we will assess the contribution of CD44 on immune cells and specifically on macrophages using a *Cd44*$^{fl/fl}$*;Csfr1cre* mouse.

Techniques: mouse genetics, flow cytometry, qPCR, all basic molecular and cellular biology techniques, isolation of primary cells.

Project B)

We have shown that CD44 augments CXCL12-induced CXCR4 signalling thereby inducing angiogenesis. We also have implicated the CD44/HA/CXCR4/CXCL12 axis in resistance of leukemic cells to chemotherapy. We have detected a direct interaction between CD44 and CXCR4 upon CXCL12 induction. Here, we plan to investigate the CD44/CXCR4 interplay in the CD8$^+$ T cell-mediated killing in pancreatic ductal adenocarcinoma.

Techniques: mouse genetics, flow cytometry, co-immunoprecipitation, qPCR

Recommended applicant's training (technical expertise and knowledge)

Techniques: mouse genetics, flow cytometry, qPCR, molecular and cellular biology
Knowledge: Tumour biology, immunology, cell biology, signalling

Maximum two relevant publications

Morath et al., 2018, Oncogene: Differential recruitment of CD44 isoforms by ErbB ligands reveals an involvement of CD44 in breast cancer
Matzke-Ogi et al., 2016, Gastroenterology: Inhibition of Tumour growth and metastasis in pancreatic cancer by interference with CD44v6 signaling

The EURIdoc programme has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement number 101034170.

Ethics description

1. Humans	
This research involves human participants.	YES ☐ / NO ☒
This research involves physical interventions on the study participants.	YES ☐ / NO ☒
2. Human Cells /Tissues	
This research involves human cells or tissues, such as blood.	YES ☒ / NO ☐
3. Personal Data	
This research involves personal data collection and/or processing.	YES ☐ / NO ☒
This research involves further processing of previously collected personal data (secondary use).	YES ☐ / NO ☒
4. Animals	
This research involves animals, such as mice.	YES ☒ / NO ☐

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