IBMM
Institut des
Biomolécules
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MASTER2 PROJECT - CDKs as predictive biomarkers in lymphoma and pancreatic cancers

Diffuse large B cell lymphoma (DLBCL) and follicular lymphoma (FL) are the most common lymphomas worldwide accounting for 30% and 20% respectively of all non-Hodgkin's lymphomas (1). In DLBCL, the reported 5-year overall survival rates is 46%. Although considered as an indolent neoplasm the median survival of patients with FL is about 12 years (1) and FL may transform into DLBCL. Furthermore, chemoresistance is a challenge in DLBCL as about one third of patients have either refractory disease or relapse after the initial therapy. Therefore, new prognostic markers and new therapeutic approaches to improve the long-term outcome are needed.

Several cyclin-dependent kinases have been reported to be hyperactivated and contribute to cancer progression in different types of lymphoma, in particular CDK4 and CDK6, for which FDA-approved inhibitors constitute promising therapeutics (2, 3). Transcriptional CDKs such as CDK7 and CDK9 have also been identified as pharmacological targets to circumvent resistance (4,5). More recently the prognostic significance of CDK1 expression in DLBCL has been reported (6).

We have developed a toolbox of fluorescent peptide biosensors that report on CDK activities and characterized a panel of 40 follicular lymphomas (7). Interestingly and quite unexpectedly, we found that CDK1 activity constitutes a marker, which is inversely correlated with the age of patients. We wish to explore this further in DLBCL in a joint collaboration between Dr. Morris at the IBMM and Dr. Lacheretz Szablewski at the CHU Montpellier.

In this project, the Master student will use the CDKACT Biosensor technology developed by Dr. Morris to characterize and compare CDK activities in different DLBCL cell lines with different genetic backgrounds in order to investigate CDK1 activity, but also to characterize other CDK activities prior to and following treatment with different drugs targeting these kinases, to assess whether any compensation activities may promote subsequent activation of CDKs in line with the recent report by Knudsen et al., thereby seeking to identify characteristic biomarker signatures (8). Results obtained from these studies will be extended to address whether similar biomarkers can be identified in pancreatic cancer cell lines, where CDK kinases have been reported to be hyperactivated and constitute attractive targets for therapeutics (9, 10). Finally, CDKACT biosensors will be implemented to profile CDK activities in a panel of biopsies derived from cancer patients selected from the CRB-CHU collection, so as to investigate correlations between kinase dysregulation and patient characteristics described in the medical reports (sex, age, genetic mutations, immunohistochemical markers). Statistical analyses of data will be performed in collaboration with the biostatistics facility of Montpellier (Biocampus, M.Pastore & C. Reynes).

Bibliography

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This project will be developed under supervision of Dr. May C. Morris at the Max Mousseron Insitute of Biomolecules (IBMM). It is funded by the MUSE call for Interdisciplinary Master Projects.

Starting date : Jan/Feb 2026

Candidates should have experience in cell biology and biochemistry, as well as interest and background in oncology.

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