Uveal melanoma (UM) is the most frequent eye cancer in adults. The primary tumor can be treated efficiently with either proton therapy or surgical removal (enucleation).

Despite these treatment options the prognosis of this cancer is still poor due to the development of secondary tumors or metastases in 20-50% of patients. These metastases appear the most frequently in the liver and are particularly resistant to treatment.

Current therapeutic approaches (chemotherapies or targeted therapies) show very few or no results in clinical trials highlighting the need to identify more effective therapeutic strategies using combination approaches in particular.

Institut Curie is an international reference center and a world leader for UM. As such, despite the rareness of this cancer, we have access to a large number of clinical cases and samples which is a strength for the development of our preclinical cancer research.

Our team’s goal is to identify new therapeutic approaches for metastatic uveal melanoma.

Our research focuses on two main areas:

- Development of preclinical models

We have already established a unique panel of cell lines and mouse models (patient derived xenografts or PDX) which represent the cancer and display the genomic alterations associated with a metastatic risk (loss of chromosome 3, lack of BAP1 expression).
Our current efforts are concentrated in particular on models from hepatic metastases with the development of cell lines, PDX and ex vivo cultures.

**Identification of new treatment combinations and studies of the action mechanism**

On one hand we are carrying out *in vitro* tests of drug molecules as simple agents or combinations targeting various recognized signaling pathways in uveal melanoma. On the other hand we are working with Novartis (Cambridge, USA) on large scale screens to identify new targets and therapeutic combinations.

For this we use dose-response systems (curve or matrix) and study the effect of compounds on cell viability. When an approach is validated different studies are carried out: study of the cellular phenotype, analysis of pharmacodynamic markers and research of the mechanisms of action to identify predictive and/or response biomarkers as well as the *in vivo* combination on PDXs (collaboration with the Preclinical Investigation Laboratory).

**Collaborations**

- Institut Curie/Research: Preclinical Investigation Laboratory (LIP); U830 (M.H. Stern); U932 (O. Lantz)
- Institut Curie/Hospital: S. Piperno-Neumann, P. Mariani, L. Desjardins, N. Cassoux, M. Rodrigues, R. Barnhill
- Novartis Institutes for Biomedical Research (Cambridge, USA)

**Key publications**

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