Tackling oncogenic signaling and tumor-stroma crosstalk in aggressive B-cell lymphoma

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Aggressive B-cell lymphomas are clinically and pathologically diverse and reflect multiple pathways of transformation involving, among others, oncogenic signalling, lymphoma-stroma crosstalk and intrinsic protein homeostasis. Alterations in these highly regulated processes play a key role in the progression of the malignant clone and correlate with a high failure rate in treatment protocols. In the last decade, new therapies applied to the treatment of B-cell lymphoma have significantly improved the overall survival of these patients, but so far, no single agent can cure these diseases. At the origin of the gap between promising preclinical results and failure in clinical phase II/III, conventional preclinical models lack predictive value in the main trials carried out in these cancer subtypes.

To foster the bench-to-bedside translation of innovative therapeutic strategies more selective and more suited to the biology of B-cell lymphoma, our team has been focused on the development of innovative *in vitro* (2D and 3D multicellular co-cultures) and *in vivo* (mice and chicken embryo xenografts) models of the most prevalent and/or aggressive subtypes of B-cell non-Hodgkin lymphoma (NHL). In the last 10-15 years, these models allowed us to unravel some crucial aspects of the interplay between lymphoma cells and their stroma, and to decipher the mechanism of action of several agents directed against specific tumour-associated processes like protein homeostasis, microenvironment signalling, or epigenetic control of cancer cell growth (1–4).

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Biography:

Dr Roué is a specialist in Cellular and Molecular Biology with a 20-year experience in the design, management and execution of scientific research projects in the field of hemato-oncology. He obtained his PhD degree in 2002 at the University of Caen (France) and worked between 2002 and 2004 as a postdoctoral researcher within the Department of Immunology, at the Pasteur Institute in Paris, France. In September 2004, he initiated a second postdoc at the Hospital Clínic's Hematopathology Unit in Barcelona, Spain, characterizing the MoA of a first set of targeted therapies for B-lymphoid neoplasms, including the proteasome inhibitor bortezomib, and the immunodulatory drug and $CRL4^{CRBN}$ E3 ubiquitin ligase modulator, lenalidomide. Between 2008 and 2017, he held a Miguel Servet tenure track (ISCIII) at the Hemato-Oncology Department, IDIBAPS Research Institute in Barcelona, where he supervised the development of a high-throughput flow cytometry-based platform for therapeutic drug screening and the set-up of innovative animal models representative of the main subtypes of B-cell non-Hodgkin lymphoma (B-NHL). Between 2017 and 2019, Dr Roué was co-head of the Molecular Hematological Genetics Unit of the Vall d'Hebron university hospital, in Barcelona, and at the same time he developed a first-in-kind model of 3D B–cell lymphoma co-culture at the Vall d'Hebron Institute of Oncology. Since November 2019, he leads the Lymphoma Translational Research group at the Josep Carreras Leukemia Research Institute, in Badalona (Barcelona), with a special interest in oncogenic and epigenetic signaling, B-cell receptor (BCR) pathway and in the role of protein homeostasis in the control of the interaction between the malignant B cells and their stroma.