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Alteration of B-cell receptor (BCR) signaling in B-cell lymphomas: New therapeutic targets for lymphoma treatment

Dominique Ledoux
University of Paris, France

This lecture will address the alteration of B-cell receptor (BCR) signaling in B-cell from lymphomas such as Chronic Lymphocytic Leukemia (CLL) and Mantle Cell Lymphoma (MCL) and the emergence of new drugs targeting BCR signaling molecules as promising therapeutic agents. CLL is one of the most common hematologic malignancies in Western countries and MCL is an aggressive malignant lymphoma representing 6-10% of non-Hodgkin's lymphomas. Despite new chemotherapeutic combinations, CLL and MCL remain incurable diseases due to rapid relapse after initial treatment or primary resistance to conventional drugs. Numerous *in vitro* studies indicate that the BCR pathway plays a crucial role in the survival, proliferation, migration and adhesion of CLL cells and we have recently demonstrated a central role for active BCR signals in survival of MCL cells. These data thus suggest that BCR engagement through antigen stimulation could favor the accumulation of proliferative malignant cells within lymphoid tissues such as lymph nodes and contribute to disease progression. Recently, a variety of novel kinase inhibitors have been developed to target various components of the BCR pathway, including spleen tyrosine kinase (SYK), mammalian target of rapamycin (mTOR), phosphoinositide 3-kinase (PI3K) and Bruton's tyrosine kinase (BTK). These inhibitors show clinical efficacy in CLL characterized by a reduction in lymph node size concurrently with a redistribution of lymphocytosis, which likely reflects microenvironment modulation. In 2013, the BTK inhibitor Ibrutinib received breakthrough designation from the FDA for the treatment of CLL and MCL.

Biography

Dominique Ledoux is working as a scientist in the field of oncology since 20 years. He more recently focused his research topics on the role of the stromal and cytokine microenvironment in lymphomas with a particular interest on the impact of B-cell receptor signaling on survival and trafficking of neoplastic B cells from CLL and MCL.

ledoux@univ-paris13.fr