Année de publication : 2017

Christine Tran Quang, Benedetta Zaniboni, Jacques Ghysdael (2017 Mar 31)
**A TCR-switchable cell death pathway in T-ALL.**
*Oncoscience* : 17-18 : DOI : 10.18632/oncoscience.342

**Résumé**

Rocchetti F, Tran Quang C, Maragno AL, Nguyen J, Lasgi C, Ghysdael J. (2017 Jan 1)
**The calcineurin protein phosphatase is dispensable for BCR-ABL-induced B-ALL maintenance, propagation and response to dasatinib.**
*Leukemia* : DOI : 10.1038/leu.2016.269

**Résumé**

Année de publication : 2016

Amélie Trinquand, Nuno R Dos Santos, Christine Tran Quang, Francesca Rocchetti, Benedetta Zaniboni, Mohamed Belhocine, Cindy Da Costa de Jesus, Ludovic Lhermitte, Melania Tesio, Michael Dussiot, François-Loïc Cosset, Els Verhoeyen, Françoise Pflumio, Norbert Ifrah, Hervé Dombret, Salvatore Spicuglia, Lucienne Chatenoud, David-Alexandre Gross, Olivier Hermine, Elizabeth Macintyre, Jacques Ghysdael, Vahid Asnafi (2016 Sep 6)
**Triggering the TCR Developmental Checkpoint Activates a Therapeutically Targetable Tumor Suppressive Pathway in T-cell Leukemia.**

**Résumé**

Cancer onset and progression involves the accumulation of multiple oncogenic hits, which are thought to dominate or bypass the physiologic regulatory mechanisms in tissue development and homeostasis. We demonstrate in T-cell acute lymphoblastic leukemia (T-ALL) that, irrespective of the complex oncogenic abnormalities underlying tumor progression, experimentally induced, persistent T-cell receptor (TCR) signaling has antileukemic properties and enforces a molecular program resembling thymic negative selection, a major developmental event in normal T-cell development. Using mouse models of T-ALL, we show that induction of TCR signaling by high-affinity self-peptide/MHC or treatment with monoclonal antibodies to the CD3ε chain (anti-CD3) causes massive leukemic cell death. Importantly, anti-CD3 treatment hampered leukemogenesis in mice transplanted with either mouse- or patient-derived T-ALLs. These data provide a strong rationale for targeted therapy based on anti-CD3 treatment of patients with TCR-expressing T-ALL and demonstrate that endogenous developmental checkpoint pathways are amenable to therapeutic intervention in cancer cells.
Résumé

Intensive chemotherapy regimens have led to a substantial improvement in the cure rate of patients suffering from T-cell acute lymphoblastic leukemia (T-ALL). Despite this progress, about 15% and 50% of pediatric and adult cases, respectively, show resistance to treatment or relapse with dismal prognosis, calling for further therapeutic investigations. T-ALL is an heterogeneous disease, which presents intrinsic alterations leading to aberrant expression of transcription factors normally involved in hematopoietic stem/progenitor cell development and mutations in genes implicated in the regulation of cell cycle progression, apoptosis, and T-cell development. Gene expression profiling allowed the classification of T-ALL into defined molecular subgroups that mostly reflects the stage of their differentiation arrest. So far this knowledge has not translated into novel, targeted therapy. Recent evidence points to the importance of extrinsic signaling cues in controlling the ability of T-ALL to home, survive, and proliferate, thus offering the perspective of new therapeutic options. This review summarizes the present understanding of the interactions between hematopoietic cells and bone marrow/thymic niches during normal hematopoiesis, describes the main signaling pathways implicated in this dialog, and finally highlights how malignant T cells rely on specific niches to maintain their ability to sustain and propagate leukemia.