

29^{ème} congrès du CHO

11 au 14 octobre 2023

Giens, Var, France

Role of Galectine 1 (Gal1) in the control of leukemogenesis

Marjorie C. Delahaye¹, Jeffrey Pelletier, Cyril Broccardo², Bastien Gerby², Michel Aurrand-Lions¹, and Stéphane J.C. Mancini^{1,3}

1 Aix Marseille Université, CNRS, INSERM, Institut Paoli-Calmettes, CRCM, Marseille, France

2 CRCT, INSERM, Université Toulouse III Paul Sabatier (UPS), Toulouse, France

3 Université de Rennes 1, INSERM, Etablissement Français du Sang Bretagne, Rennes, France

B-Acute Lymphoblastic Leukemia (B-ALL) is the malignant counterpart of developing B cells in the bone marrow and is the leading cause of cancer in children. B-ALL results from differentiation arrest and exacerbated proliferation of B cells. Several studies have shown the influence of soluble factors secreted by the bone marrow microenvironment on normal B cell differentiation. Our laboratory has demonstrated that galectin1 (Gal1), secreted by stromal cells, is able to interact with the pre-BCR, expressed by pre-B cells, inducing their proliferation and differentiation. In the present study, we thus addressed whether Gal1 may play a role in leukemic initiation and maintenance of B-ALL Pre-BCR+, which represent the leukemic counterpart of pre-B cells.

We use mice carrying the chimeric Pax5-Elastin (P5E) gene found in human B-ALL. These mice develop spontaneously B-ALL Pre-BCR+, i.e. pre-B blasts carrying the pre-BCR. We studied P5E mice crossed with Gal1^{-/-} mice in order to address the function of Gal1 in the pathological context.

We found that a large proportion of P5EGal1^{-/-} mice developed B-ALL BCR+ in contrast to P5E mice which developed almost exclusively B-ALL Pre-BCR+. The analysis of 6-week-old mice – devoid of secondary mutations – showed that the proliferation of pre-leukemic cells was impaired in absence of Gal1. Furthermore, while pre-leukemic cells accumulate at the pro-B/pre-B cell transition in young P5E mice, a block at the later pre-B/immature B transition could be observed in P5EGal1^{-/-} mice. scRNAseq of pre-leukemic B cells isolated from P5E

29^{ème} congrès du CHO

11 au 14 octobre 2023
Giens, Var, France

and P5EGal1^{-/-} mice has been performed and will be discussed with respect to signaling pathways downstream of Gal1/pre-BCR in pre-leukemic context.

Our results suggest that Gal1⁺ stromal cells dictate the leukemic fate of pre-B cells at least partially through pre-BCR dependent proliferation.