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Speaker

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Titolo

***Les liaisons dangereuses: autologous recognition and signaling by B-cell receptors in chronic lymphocytic leukemia***"

Abstract

Cell-autonomous B-cell receptor (BcR)-mediated signaling is a hallmark feature of the neoplastic B-lymphocytes in chronic lymphocytic leukemia (CLL)<sup>1</sup>, the most common of leukemia in the Western

world. A combination of biochemical, structural, and cellular techniques were used to elucidate the structural basis of autonomous activation of CLL B-

cells. BcR immunoglobulins from CLL patients interact homotypically to initiate intracellular signaling through structural epitopes that are specific for each subgroup of patients<sup>2</sup>. The molecular details of the BcR-

BcR interactions apparently dictate the clinical course of disease, with stronger affinities and longer half-lives in indolent cases, and weaker, short-

lived contacts mediating the aggressive ones. The high-

resolution description of the diverse homotypic BcR contacts leading to cell-

autonomous signaling explains clinical heterogeneity of CLL, albeit under a common pathogenetic mechanism, and offers opportunities for innovative treatment strategies.

<sup>1</sup> Dühren-von Minden M, *et al.* Chronic lymphocytic leukaemia is driven by antigen-independent cell-autonomous signalling. *Nature* **489**, 309-312 (2012)

<sup>2</sup> Minici C, *et al.*, Distinct homotypic B-

cell receptor interactions shape the outcome of chronic lymphocytic leukaemia. *Nat Commun* **8**, 15746 (2017)