

POSTER PRESENTATION

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Dll4 blockade interferes with the bone marrow vascular niche and perturbs hematopoietic recovery following myeloablation

Leonor Remédio^{1,2,3*}, Tânia Carvalho^{1,2,3}, Sérgio Dias^{1,2,3}

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The Delta:Notch signaling pathway regulates numerous aspects of differentiation, morphogenesis and cell function, during embryogenesis and throughout adult life. More recently, Delta-like 4 (Dll4) has been shown to regulate adult neo-vascularization (angiogenesis). Consequently, therapeutic strategies to target Dll4 have been put forward for the treatment of different cancers. In the present study, we describe for the first time that Dll4 blockade affects the bone marrow (BM) microenvironment, by perturbing the BM vascular niche. Anti-Dll4 treatment administered 1 day after myeloablation increased the BM vascular content (CD31⁺ cells), promoted megakaryopoiesis and promoted hematopoietic (Sca1⁺) and endothelial progenitor (Flk1⁺CXCR4⁺) cell mobilization to the peripheral blood (PB). Moreover, anti-Dll4 treatment increased BM myeloid content, and induced mobilization of B (B220^{hi}CD19^{lo}) and T (CD3⁺NK1.1⁻) lymphocytes to the PB. Taken together, we show that Dll4 blockade affects the BM vascular niche, and as such affects hematopoietic cell differentiation and mobilization.

Author details

¹Angiogenesis Lab, CIPM, Portuguese Institute of Oncology, IPOFG, EPE, Lisbon, Portugal. ²CEDOC, FCM, Universidade Nova de Lisboa, Lisbon, Portugal. ³Instituto Gulbenkian de Ciência, Oeiras, Portugal.

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* Correspondence: leonor.remedio@gmail.com

¹Angiogenesis Lab, CIPM, Portuguese Institute of Oncology, IPOFG, EPE, Lisbon, Portugal

Full list of author information is available at the end of the article

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