LABORATORY OF

HAEMATOONCOLOGY

Haematology, haematopoietic stem cells, neutrophilic differentiation, granulocytes, emergency granulopoiesis, inflammation

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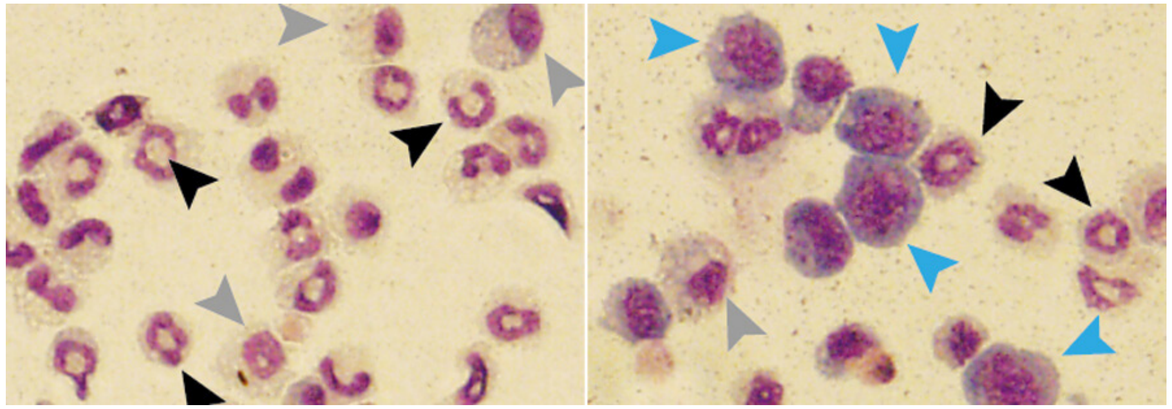
In our research group, we investigate the regulation of haematopoietic stem cell (HSC) maintenance and fate by cell intrinsic as well as cell extrinsic factors. On one hand we focus on transcription factors and their target genes, determine whether these elements are altered in human leukaemias (in particular acute myeloid leukaemia, AML), and elucidate their contribution to leukaemogenesis. On the other hand, we investigate how cell extrinsic factors, mainly originated in inflammatory conditions, regulate HSC self-renewal and how they impact myeloid commitment.

Our three main research lines are:

1. To determine the function of C/EBPa target genes in normal and malignant haematopoiesis.
2. To define the role of the b-catenin-TCF/LEF transcription-mediating complex in normal and aberrant haematopoiesis.
3. To assess the effects of inflammation/infection in HSC fitness, myeloid differentiation, and leukaemogenesis.

To reach these goals, we employ murine and human primary cells, as well as murine models. We perform a variety of in vitro assays to assess cell proliferation, apoptosis, colony-forming potential, re-plating ability, differentiation, and migration. Further, we carry out murine bone marrow cell transplantation assays, challenge mice with infectious agents, and perform HSC mobilization assays in vivo. Using primary cells from patients suffering from AML, we generate PDX models. To get novel insights into the molecular mechanism of stem cell regulation and transformation, we employ molecular biology approaches including RNA-seq, ATAC-seq and ChIP-seq/qPCR.
Together, we aim at understanding the mechanisms that control HSC maintenance and fate, and determine cell intrinsic and extrinsic factors that contribute to myeloid commitment and differentiation. Ultimately, our work will contribute to establishing knowledge for the development of better AML therapies.

In the picture: 1. Kuzmina Maria | 2. Alberich Jorda Meritxell | 3. Vaníčková Karolína | 4. Kosanović Sladana | 5. Ribeiro Bas Irina | 6. Burócziová Monika | 7. Adamcová Miroslava Kari | 8. Grušanović Srdjan | 9. Shaikh Mehak Nihal



Cell morphological analysis assessed on May-Grunwald Giemsa stained cytospins. The left image shows healthy mature granulocytes (black arrows). The right image shows blast cells that were unable to differentiate towards mature granuloctyes (blue arrows). Cells were isolated from cultures favouring growth of murine myeloid cells.

Selected publications:

1. Danek P, Kardosova M, Janeckova L, Karkoulia E, Vanickova K, Fabisik M, Lozano Asencio C, Benoukraf T, Tirado-Magallanes R, Zhou Q, Burocziova M, Rahmatova S, Pytlik R, Brdicka T, Tenen DG, Korinek V, Alberich Jorda M*: β-catenin-TCF/LEF signaling promotes steady-state and emergency granulopoiesis via G-CSF receptor upregulation. Blood 2020 Nov 7:e54729
2. Lobo de Figueiredo-Pontes L, Adamcova MK, Grusanovic S, Kuzmina M, Aparecida Lopes I, Fernandes de Oliveira Costa A, Zhang H, Strnad H, Lee S, Moudra A, Jonasova AT, Zidka M, Welner RS, Tenen DG*, Alberich-Jorda M*: Improved hematopoietic stem cell transplantation upon inhibition of natural killer cell-derived interferon-gamma. Stem Cell Reports 2021 16(8): 1999-2013.
3. Stavast CJ, van Zuijen I, Karkoulia E, Özçelik A, van Hoven-Beijen A, Leon LG, Voerman JSA, Janssen GMC, van Veelen PA, Burocziova M, Brouwer RWW, van IJcken WFJ, Maas A, Bindels EM, van der Velden VHJ, Schliehe C, Katsikis PD, Alberich-Jorda M, Erkeland SJ: The tumor suppressor MIR139 is silenced by POLR2M to promote AML oncogenesis. Leukemia 2022 36(3): 687-700.
4. Lobo de Figueiredo-Pontes L, Adamcova MK, Welner RS, Tenen DG*, Alberich-Jorda M*: Response to NK cell content does not seem to influence engraftment in ex vivo T cell depleted haploidentical stem cell transplantation. Stem Cell Reports 2022 17(3): 446-447.
5. Grusanovic S, Danek P, Kuzmina M, Adamcova MK, Burocziova M, Mikyskova R, Vanickova K, Kosanovic S, Pokorna J, Reinis M, Brdicka T, Alberich-Jorda M*: Chronic inflammation decreases HSC fitness by activating the druggable Jak/Stat3 signaling pathway. EMBO Rep 2022, e54729