LATE MYELOID PROGENITORS REGENERATE HAEMATOPOIESIS IN SUBMYELOABLATIVELY IRRADIATED MICE

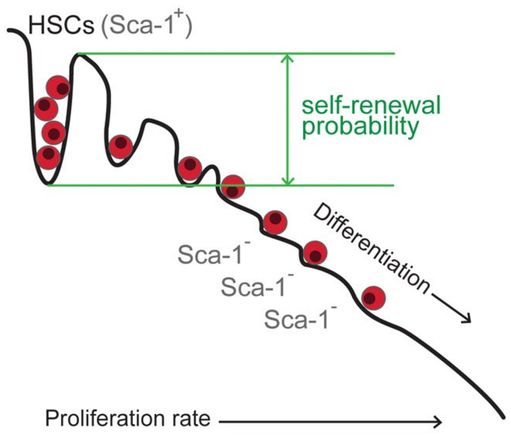
K. Faltusova, P. Paral, M. Molik, C.-L. Chen, L. Sefc, E. Necas

Institute of Pathological Physiology, First Faculty of Medicine, Charles University

FIRST FACULTY OF MEDICINE
Charles University

Introduction

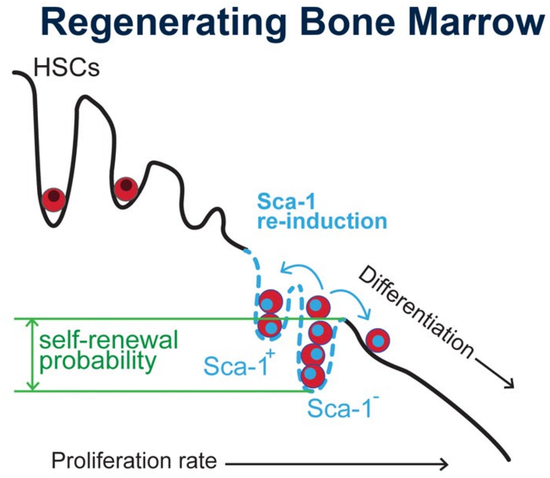
Normal Bone Marrow



In normal adult haematopoiesis only stem cells (HSC) and multipotent progenitors (both Sca-1⁺ cells) mainain their populations by self-renewing cell divisions.

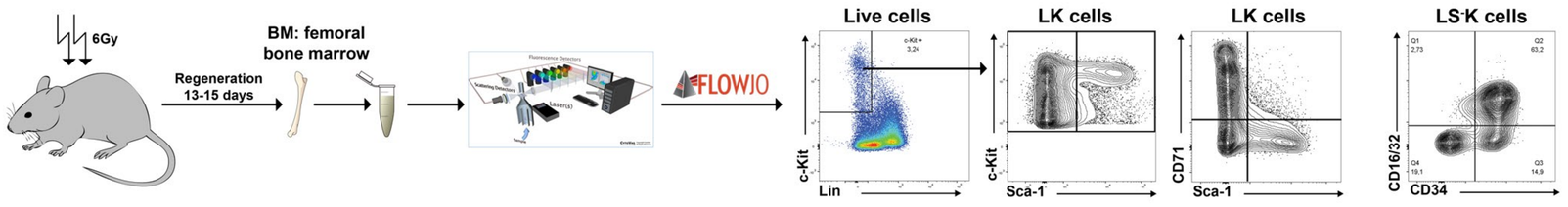
Conclusions

Regenerating Bone Marrow



In damaged haematopoiesis very late myeloid progenitors are activated, expand their populations, and become the first source of red blood cells, granulocytes and platelets.

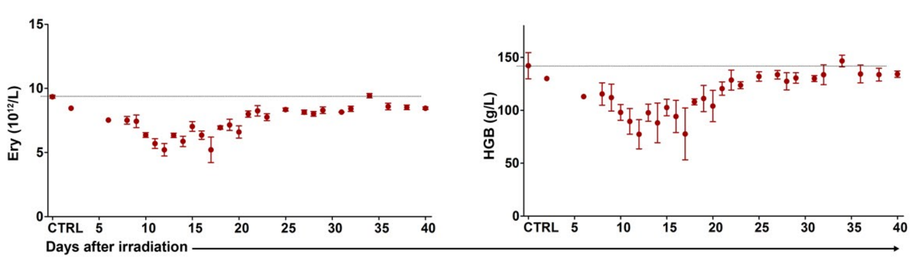
Materials and methods

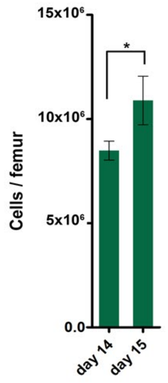


Mice: C57BL/6J
Irradiation: ^{60}Co irradiator - 6Gy
Flow cytometry: BD FACS Canto II
Antibodies: Lineage coctail (anti-B220, -CD3, -Gr-1, Mac-1, Ter119), Sca-1, c-Kit, CD71, IL7R, CD16/32, CD34
Flow Cytometry data analysis: Flow Jo software

Results

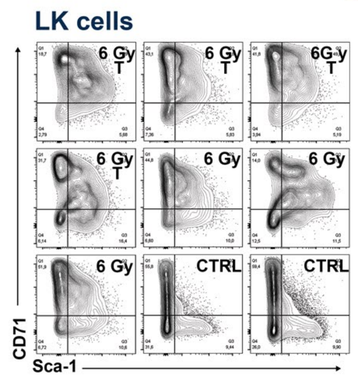
Two weeks after irradiation of mice haematopoiesis rapidly expanded



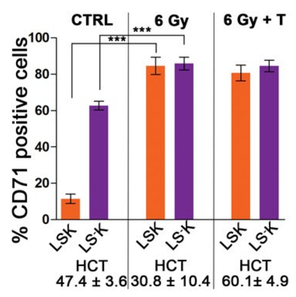


Red blood cell production exceeded their losses after 12 days.
Cellularity of BM increased between day 14 and 15 after irradiation.

Two weeks after irradiation with 6Gy a majoritiy of Lin⁻ Sca-1⁺ c-Kit⁺ cells became CD71 (transferrin receptor) positive and were organized in cell clusters.

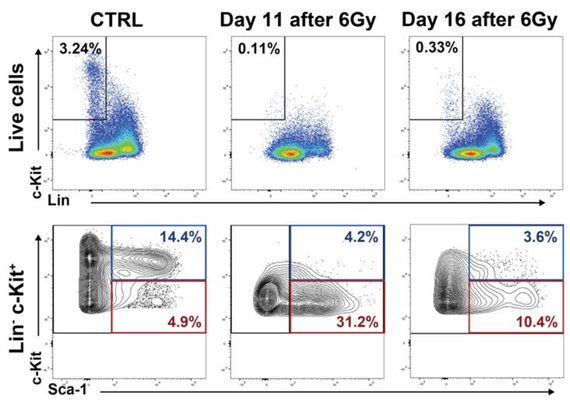


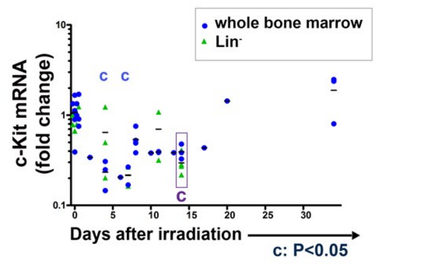
High CD71 positivity in LSK cells was not affected by post-transfusion polycythaemia.

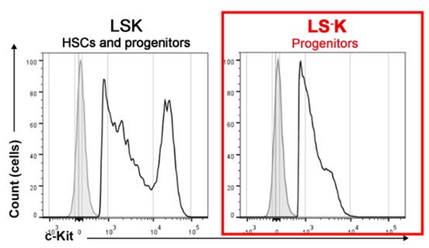


T: transfusions of RBCs

Immature Lin⁻c-Kit⁺ cells had decreased c-Kit expresion level and c-Kit mRNA in regenerating BM.



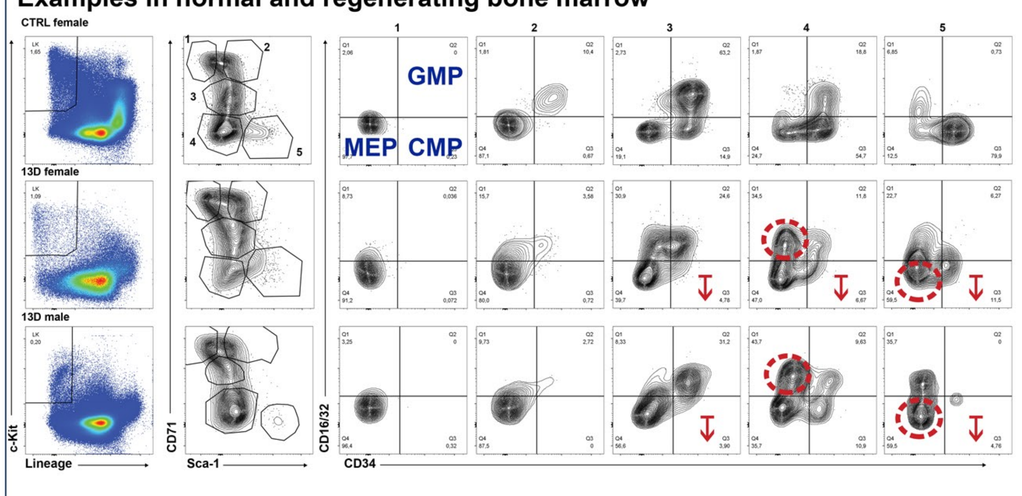


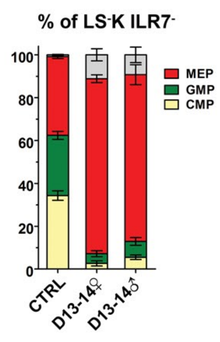


c-Kit expression level is normally low in Sca-1⁻ myeloid progenitors.

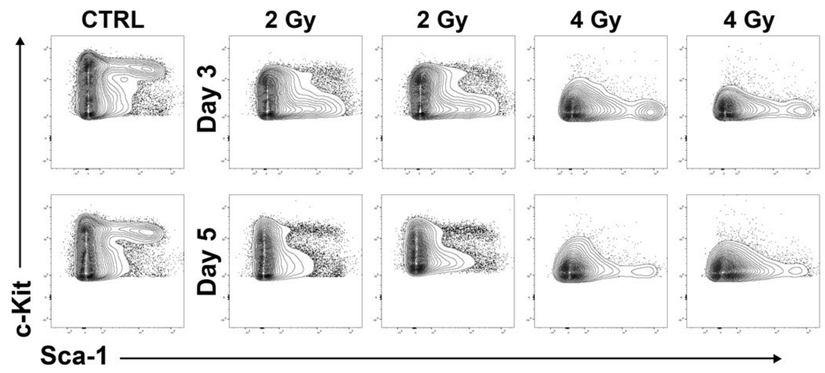
More differentiated granulocyte-macrofage (GMPs) and megakaryocyte-erythroid (MEPs) progenitors dominated over less differentiated common myeloid (CMPs) progenitors.

Examples in normal and regenerating bone marrow

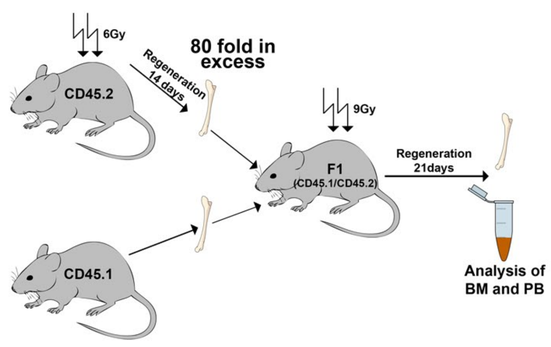


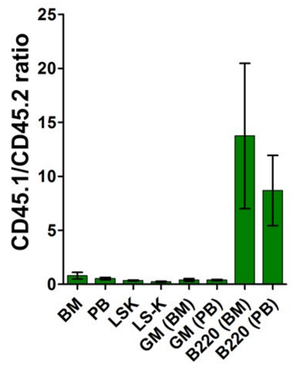


Irradiation with a low dose (2Gy or 4Gy) induced Sca-1 expression in a part of Sca-1⁻ c-Kit^{low} cells.



Regenerating BM competitively transplanted with normal BM produced granulocytes but not B-lymphocytes (in contrast to normal BM which produced boths types of cells).





ACKNOWLEDGMENT: Study was supported from the Grant Agency of Czech Republic (GACR 14-25515S)