Molecular mechanisms guiding hematopoietic cell development

A permissive role for IL-7 in mouse B cell development

Patients deficient for IL-7 or the IL-7R are practically devoid of T cells but have normal B cell compartments. In mice deficient for IL-7 or the IL-7R both T cell and B cell compartments are dramatically reduced. Based on these findings it was argued that IL-7 plays a redundant role in human B cell development but a non-redundant and may be even an instructive role in mouse B cell development. Now by generating IL-7-deficient mice on a FLTsL transgenic background we found a very significant rescue of all the precursor B cell subpopulations in the bone marrow and the mature B cell populations in the periphery. Thus, increased levels of FLTsL make the role of IL-7 in mouse B cell development largely redundant. Our findings rather suggest that IL-7 mainly acts as a growth factor for pre-B cells and thereby making B cell development more efficient. Yet, another suggestion coming from our studies is that human B cell development is regulated by FLTsL.

Hematopoietic progenitors with multipotent developmental potential: real multipotency or heterogeneity?

Over the past couple of years new hematopoietic progenitors with multipotent developmental potential mainly determined in vitro were described. However, by the generation of so-called reporter mice the multipotency of some of these precursors in vivo was questioned. Moreover, the multipotent developmental potential in vitro of these precursors was tested at the "bulk" but not at the single cell level. Therefore, the in vivo significance of this multipotency is questionable and furthermore the in vitro experiments do not exclude heterogeneity within the tested precursor populations.

Several years ago we have described a small bone marrow derived precursor population with lymphoid and myeloid developmental potential in vitro (Balciunaite G, Ceredig R, Massa S, Rolink AG. Eur J Immunol. 2005 Jul;35(7):2019-30). This population comprises 0.1 – 0.3% of total BM nucleated cells and was characterized as B220+ c-Kit+ CD19- NK1.1-. Now, by identifying new markers and by analyzing newly generated mutant mice we have found that this population can be subdivided into at least 6 subpopulations. The main marker we used for this was Ly5D. Single cell RNA- sequence analysis performed on the Ly5D+ and Ly5D-, B220+ c-Kit+ CD19- NK1.1- cells revealed within the Ly5D+ cells a largely lymphoid restricted transcriptional whereas the Ly5D- cells showed either a transcriptome reminiscent of lymphoid, myeloid or dendritic cells. Thus these findings reveal that B220+ c-Kit+ CD19- NK1.1- cells are very heterogeneous and that lymphoid and myeloid developmental potential is coming from different cells within this population.

Connection to Clinical Practice

The prophylactic and/or therapeutic effects of IL-2 – anti-IL-2 complexes on SLE like cGVHD
cGVHD as can be induced by the injection of DBA/2 T cells into semi-allogeneic (C57Bl6 x DBA/2) F1 (BDF1) mice shows many similarities to SLE in man. Some years ago it was shown that injection of IL-2 anti-IL2 complexes into a semi-allogeneic (C57/Bl6 x DBA/2) F1 (BDF1) mice shows many similarities to SLE in man. Some years ago it was shown that injection of IL-2 anti-IL2 complexes into a semi-allogeneic (C57/Bl6 x DBA/2) F1 (BDF1) mice shows many similarities to SLE in man. Some years ago it was shown that injection of IL-2 anti-IL2 complexes into a semi-allogeneic (C57/Bl6 x DBA/2) F1 (BDF1) mice shows many similarities to SLE in man. Some years ago it was shown that injection of IL-2 anti-IL2 complexes into a semi-allogeneic (C57/Bl6 x DBA/2) F1 (BDF1) mice shows many similarities to SLE in man. Some years ago it was shown that injection of IL-2 anti-IL2 complexes into a...