ERYTHROPOIESIS or RBC DEVELOPMENT

Breed Aw — HLA is different allele for different blood group.
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Human lymphotic Antigen.

MCF-7 – Breast cancer cell. It is breast epithelial cell.

→ Hemangioblast – These produces both blood forming cell (hematopoietic cell) as well as epithelial cells which forms the blood vessels.

① Erythropoiesis involves the differentiation of hematopoietic stem cells into erythroid blast and ends in final enucleation to form erythrocytes. The process is regulated by physiological stimulus called hypoxia that promote the synthesis of erythropoietin or (Epo) from the foetal liver or adult kidney.

② Epo signalling regulates erythroid development by preventing apoptosis and promoting terminal erythroid proliferation and differentiation. Deprivation of Epo induces the apoptotic demise (death) of cultured erythroid progenitors which could be reversed by forced

Double positive T cells — CD^+, CD^+, $CD8^+$

CD3ε and CD3ζ — two markers present on all cells.

expression of $Bcl-X_L$

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Bcl & Bcl_2 is group of protein, members of which are anti-apoptotic as well as pro-apoptotic.

Pro apoptotic Bcl family members are –

Bim
Bax
Bak
Bid
$Bcl-X_S$

Anti apoptotic members are
$Bcl-X_L$ (— large) — most imp.
Mcl-1

$Bcl-X_L$ is that protein which help in cell proliferation.
$Bcl-X_L$ deficient mouse embryo dies prematurely because of a combination of neuronal and erythroid defect. Absence of $Bcl-X_L$ results in severe anaemia and also hyperplasia of megakaryocytic and erythroid progenitors in bone marrow and spleen.

③ The apoptosis observed in $Bcl-X_L$ deficient mouse during erythroid differentiation could not be circumvented by genetic loss of pro-apoptic Bax, suggesting the pro-apoptotic Bak may be redundant during the embryonic development of erythrocytes.

④ Another Bcl_2 family members called Nix play imp role in terminal stages of erythropoiesis. It was observed that erythroid differentiation induces expression of Nix which is a pro-apoptotic Bcl_2 family member. Nix binds to $Bcl-X_L$ and induces apoptosis when over expressed. It is expected that $Bcl-X_L$ inhibit the Nix

during normal erythroid development. The genetic deletion of Nix revealed the cuential role of Nix in regulation of erythropoiesis. Nix deficient mouse are viable and fertile but shows profound defect w.r.t. reticulocytosis, thromocytosis or splenomegaly (large spleen)

Transcriptional Contol of Erythropoiesis (Role of Transcriptional factors)

① Development and differentiation of erythropoiesis is blocked in GATA-1 deficient mouse causing lethal anaemia. Expression of GATA-2, GATA-3 transgene (forced expression) induces the development of erythroid lineage and rescued from defect in GATA-1 deficient mouse.

② GATA-1 collaborate with FOG-1 (friend of GATA-1) during erythropoiesis. Loss of FOG-1 partially blocks the erythropoiesis and also causes complete loss of megakaryocyte.

Development of Granulocytes

① Granulocytes are developed from CMP (common myleoid progenitors) which gives rise to granulocyte, monocyte precursors (or GMP). GMP in turn gives rise to monocyte and granulocytes. The granulocytes includes neutrophils, eosinophiles and basophils.

A model proposed by Jacobson et al implies that granulocyte macrophage cell (GM cells) can be generated by two distinct pathways.

(I) One via classical common myleoid progenitor
(II) Other via lymphomyelomonocytic lineages without the megakaryocyte potential.

Cytokines & Growth factors in GM cells development.

① Granulocyte macrophage colony stimulating factor is responsible for

generating & differentiating both granulocyte and macrophages

② Dendritic cell can also be generated from bone marrow macrophage prog by using GM-CSF treatment.

③ G-CSF (Granulocyte Colony Stimulating factor) induces development of neutrophils.

Transcription factor in GM cells development-

① GATA-1 is imp. for megakaryocytic development. Many macrophage and granulocyte-macrophage lineage depends upon PU.1. PU.1 co-operates regulation of genes encoding the myeloid growth factor receptor like - M-CSF-R, G-CSF-R etc.

Hemangioblast

① The concept of emergence of hematopoietic cell and endothelial precursor has been documented with gene expression along circumstantial evidences of commonality of cells found the cases. This is the concept of hemangioblast.

② Deficiency in TGF-β1 (Transforming Growth Factor β-1) and resulted into selective defect in organization of both blo as well as vascular cells, revealing the facts of appa dependence of hematopoiesis and vasculogenesis through development.

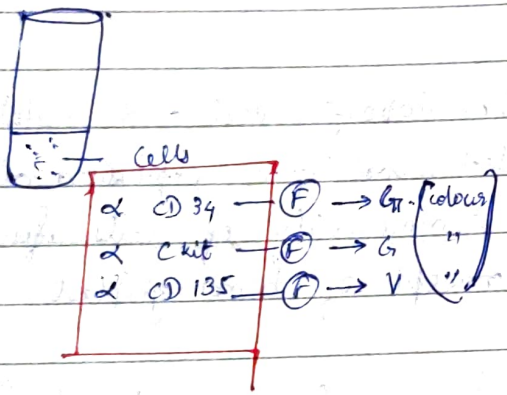
③ Evidence for hemangioblast activity in developing embryo from studies of cultured mouse embryonic stem c population of Vascular Endothelial Growth Factor precursor (VEG bipotent potential of hematopoietic and endothelial cell develo documented.

② Haematoporetic stem cell plasticity or Plasticity of Hpc cell

① Hematopoietic stem cell can produce multiple unexpected type of cells : include [neuronal cells], [skeletal muscles] cell, [cardiac cell] [blood cells] ~~lymphocyte~~ etc. [gut inner lining cell], [hepatocytes] etc.

② This transdifferentiation of bone marrow hematopoietic stem cells understood the fact of ~~as~~ multipotency or multipotential nature of HSC (Hemetopoietic stem cells)

③ One of the drawback in study of hemetopoiesis is presence of contaminating precursor cells which could be responsible for variation in result often observed in these tissue culture practices.



Pure population = >99% of cells are of one type.

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100% pure could n't be obtained.

1% contamination. (not considered at smaller level)

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On amplification this creates a problem.

④ Most studies have assayed partially purified population of cells which is the source of contamination in consequent variability in the result obtained.