Hematopoietic Growth Factors

Drug		MOA	Administration	Uses	Side Effects	Notes
Recombinant Human Erythropoietin (epoetin-α)		-Stimulates erythroid proliferation and differentiation by interacting with JAK/STAT cytokine receptor on red cell progenitor -Releases reticulocytes from the bone marrow	-IV & subcutaneous injection -In anemia of chronic failure: **50-150** IU/kg three times a week -In primary bone marrow disorders and secondary anemias: patients require higher doses (**100-500** IU/kg)	1. Anemia of chronic renal failure (**most** likely to benefit): failure to respond is usually due to iron or folic acid deficiency 2. Primary bone marrow disorders and secondary anemias: plastic anemia, myeloproliferative and myelodysplastic disorders, multiple myeloma and bone marrow malignancies, anemia of chronic inflammation, AIDS and cancer *Response is generally **incomplete**, better with low baseline erythropoietin levels 3. Anemia of zidovudine treatment 4. Anemia of prematurity 5. Iron overload 6. Unethically, used by athletes	*Toxicity: -Due to rapid increases in hematocrit and hemoglobin: hypertension and thrombotic complications - Allergic reactions are infrequent and mild	-34-39 kDa glycoprotein -Was the first isolated growth factor -Originally purified from urine of patients with severe anemia → elevated in most anemias but lowered in anemia of renal failure -Produced in a mammalian cell expression system -Half-life after IV administration is 4-13 hours -**Darbepoetin α** has longer half life -It is not cleared by dialysis
Megakaryocyte GFs	**IL-11**	Acts through a specific receptor → Stimulates the growth of lymphoid and myeloid cells and primitive megakaryocytic progenitors → Increases the number of peripheral platelets and neutrophils	IV & S.C injection	-**Thrombocytopenia**: for the secondary prevention of thrombocytopenia in patients receiving cytotoxic chemotherapy for nonmyeloid cancers (Platelets transfusion is an alternative)	-Toxicity: Fatigue, headache, dizziness, anemia, dyspnea, transient atrial arrhythmias and hypokalemia	-65-85 kDa protein -Produced by fibroblasts and stromal cells in the bone marrow -Half-life is 7-8 hours after s.c injection.
	Oprelvekin		IV & S.C injection			-Recombinant form of IL-11→ Produced by expression in E.coli

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Megakaryocyte GFs	Thrombo-poietin	-Independently stimulates the growth of primitive megakaryocytic progenitors -Stimulates mature megakaryocytes. Activates mature platelets to respond to aggregation-inducing stimuli			- Toxicity: Fatigue, headache, dizziness, anemia, dyspnea, transient atrial arrhythmias and hypokalemia	- 65-85 kDa glycoprotein - Recombinant form is produced by expression in human cells. - Commercial preparations: **Eltrombopag & Romiplostim**
Myeloid GFs	rHuG-CSF (Filgrastim)	-Works on JAK/STAT receptors. -Stimulates proliferation and differentiation of progenitors committed to the neutrophil lineage -Activates the phagocytic activity of mature neutrophils and prolongs their survival in the circulation -Mobilizes hemopoietic stem cells into the peripheral circulation.	-In mobilization of **PBSCs**: Patients or donors are given GM-CSF for 4 days, then leukapheresis, CD34 is used as a marker for the stem cells. At least 5x106 CD34 cells/kg should be reinfused to ensure effective engraftment	1.Cancer Chemotherapy-Induced Neutropenia: G-CSF accelerates neutrophil recovery, leading to reduced episodes of febrile neutropenia, need for antibiotics and days of hospitalization, but do not improve survival. **(G-CSF is reserved for risky patients)** **(GM-CSF can produce fever on its own)** *Safe even in the post chemotherapy supportive care of patients with AML 2. Congenital neutropenia 3. Cyclic neutropenia 4. Myelodysplasia 5. Aplastic anemia 6. Autologous Stem Cell Transplantation 7. Allogenic Bone Marrow Transplantation 8. Mobilization of peripheral blood stem cells (**PBSCs**)	*Toxicity: -Bone pain -Fever, malaise, arthralgia, myalgia. -Capillary Leak Syndrome: peripheral edema, pleural or pericardial effusions -Allergic reactions. -Splenic rupture. *In Autologous Stem Cell Transplantation: **High** dose chemotherapy regimens cause **extreme myelosuppression** → counteracted by reinfusion of the patient's own hematopoietic stem cells which are collected before the chemotherapy	- Originally purified from cultured human cells - Produced in a bacterial cell expression system – 175 amino acids, 18 kD mol. wt. – Has a half-life of 2-7 hours. – **Pegfilgrastim**: Filgrastim covalently conjugated with polyethylene glycol (Injected once per chemotherapy cycle)
	rHuGM-CSF (Sargramostim)	Has broader actions. Works on JAK/STAT receptors Stimulates proliferation and differentiation of early and late granulocytic progenitor cells as well as erythroid and megakaryocyte progenitors. -With interleukin-2, also stimulates T-cell proliferation. -Mobilizes peripheral blood stem cells, but **less** than G-CSF				- Originally purified from cultured human cells -Produced in a yeast cell expression system – 127 amino acids, 15-19 kD mol. wt -Has a half life of 2-7 hours -Locally, it is an active factor of inflammation

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