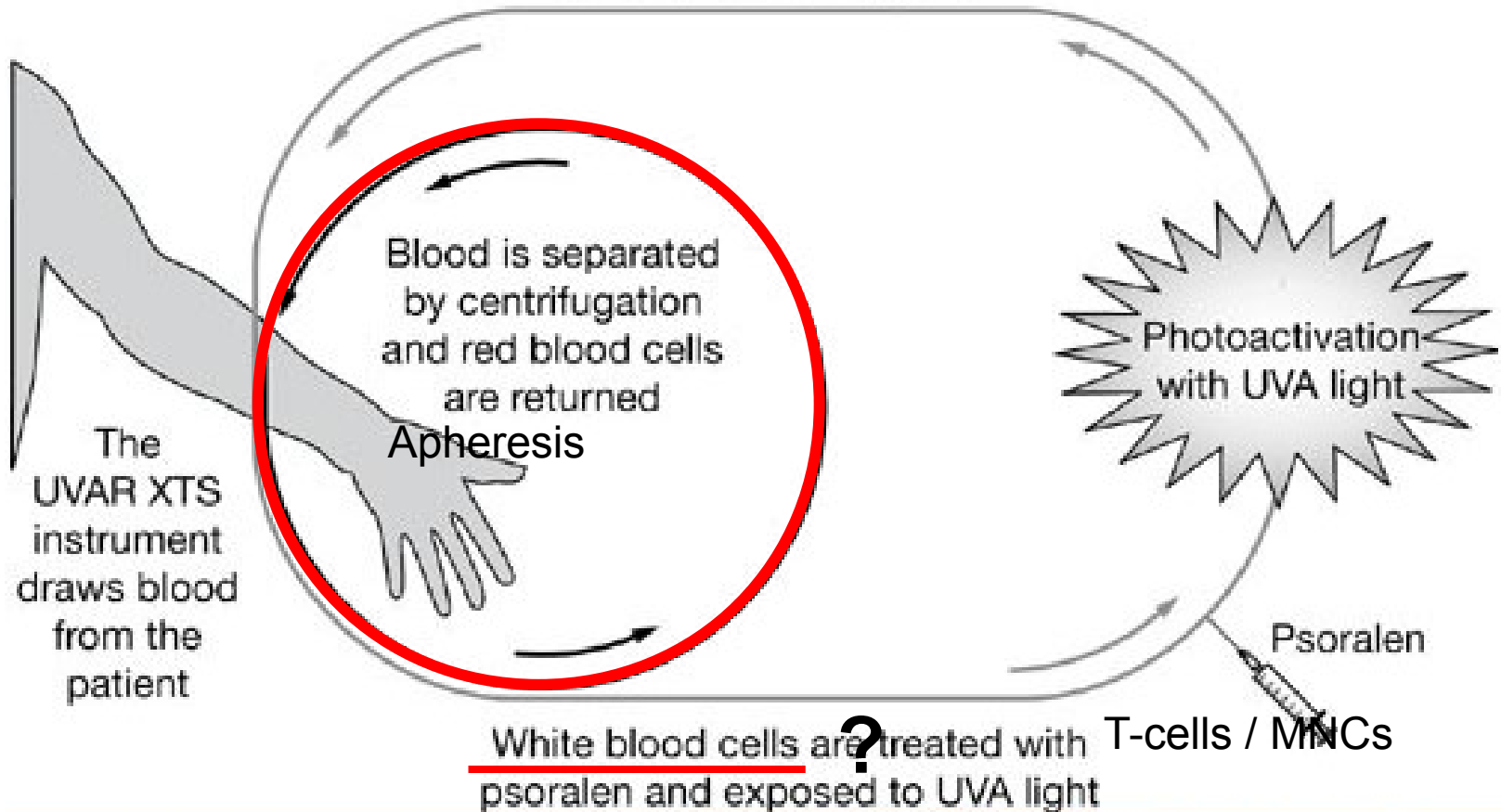




The photoactivated white blood cells
are returned to the patient



White blood cells

- Lymphocytes
 - B-cells
 - T-cells
- HPCs
- Monocytes



MNCs

- Granulocytes
 - Basophils
 - Eosinophils
 - Neutrophils

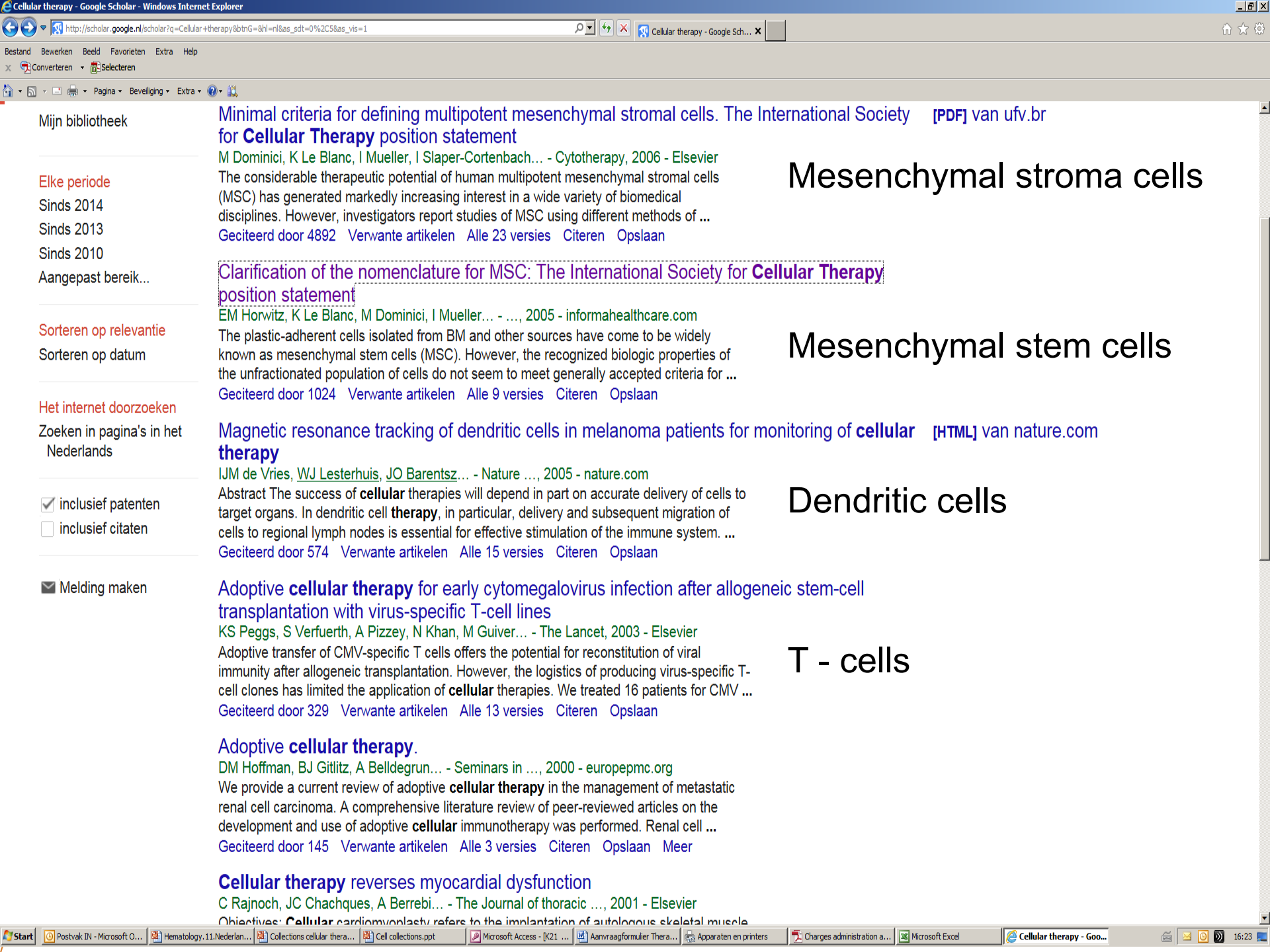


PMNCs

Collections for cellular therapy

Hans Vrielink, MD, PhD

Sanquin Blood Supply, Amsterdam, The Netherlands



Mijn bibliotheek

Elke periode

Sinds 2014

Sinds 2013

Sinds 2010

Aangepast bereik...

Sorteren op relevantie

Sorteren op datum

Het internet doorzoeken

Zoeken in pagina's in het Nederlands

inclusief patenten

inclusief citaten

Melding maken

[Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement](#) [PDF] van ufv.br

M Dominici, K Le Blanc, I Mueller, I Slaper-Cortenbach... - *Cytotherapy*, 2006 - Elsevier

The considerable therapeutic potential of human multipotent mesenchymal stromal cells (MSC) has generated markedly increasing interest in a wide variety of biomedical disciplines. However, investigators report studies of MSC using different methods of ...

Geciteerd door 4892 Verwante artikelen Alle 23 versies Citeren Opslaan

[Clarification of the nomenclature for MSC: The International Society for Cellular Therapy position statement](#)

EM Horwitz, K Le Blanc, M Dominici, I Mueller... - ..., 2005 - informahealthcare.com

The plastic-adherent cells isolated from BM and other sources have come to be widely known as mesenchymal stem cells (MSC). However, the recognized biologic properties of the unfractionated population of cells do not seem to meet generally accepted criteria for ...

Geciteerd door 1024 Verwante artikelen Alle 9 versies Citeren Opslaan

[Magnetic resonance tracking of dendritic cells in melanoma patients for monitoring of cellular therapy](#) [HTML] van nature.com

IJM de Vries, WJ Lesterhuis, JO Barentsz... - *Nature* ..., 2005 - nature.com

Abstract The success of **cellular** therapies will depend in part on accurate delivery of cells to target organs. In dendritic cell **therapy**, in particular, delivery and subsequent migration of cells to regional lymph nodes is essential for effective stimulation of the immune system. ...

Geciteerd door 574 Verwante artikelen Alle 15 versies Citeren Opslaan

[Adoptive cellular therapy for early cytomegalovirus infection after allogeneic stem-cell transplantation with virus-specific T-cell lines](#)

KS Peggs, S Verfuert, A Pizzey, N Khan, M Guiver... - *The Lancet*, 2003 - Elsevier

Adoptive transfer of CMV-specific T cells offers the potential for reconstitution of viral immunity after allogeneic transplantation. However, the logistics of producing virus-specific T-cell clones has limited the application of **cellular** therapies. We treated 16 patients for CMV ...

Geciteerd door 329 Verwante artikelen Alle 13 versies Citeren Opslaan

[Adoptive cellular therapy.](#)

DM Hoffman, BJ Gitlitz, A Beldegrun... - *Seminars in* ..., 2000 - europepmc.org

We provide a current review of adoptive **cellular therapy** in the management of metastatic renal cell carcinoma. A comprehensive literature review of peer-reviewed articles on the development and use of adoptive **cellular** immunotherapy was performed. Renal cell ...

Geciteerd door 145 Verwante artikelen Alle 3 versies Citeren Opslaan Meer

[Cellular therapy reverses myocardial dysfunction](#)

C Rajnoch, JC Chachques, A Berrebi... - *The Journal of thoracic* ..., 2001 - Elsevier

Objectives: **Cellular** cardiomyoplasty refers to the implantation of autologous skeletal muscle

Mesenchymal stroma cells

Mesenchymal stem cells

Dendritic cells

T - cells

Agenda

- Collection of specific leukocytes
 - CD34 +ve cells
 - Lymphocytes
 - Monocytes
 - Granulocytes

Apheresis

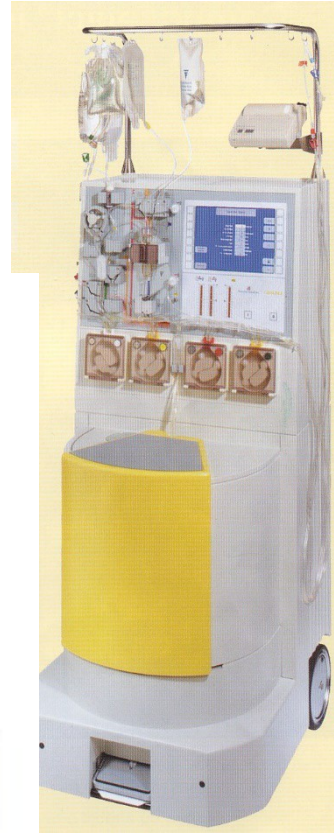
- Donors
- Patients

- To collect blood components
- To collect blood components
- To reduce blood components
- To exchange blood components

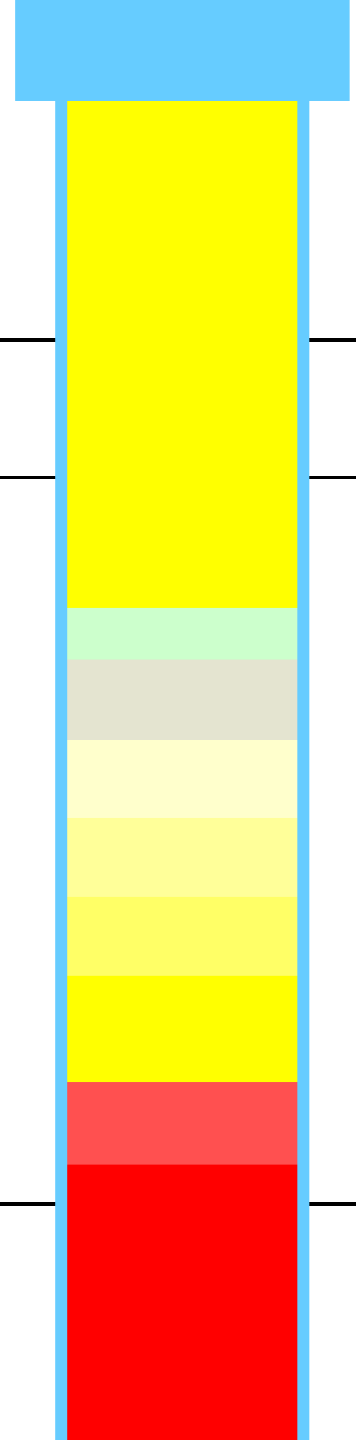
→ WBCs



Apheresis equipment

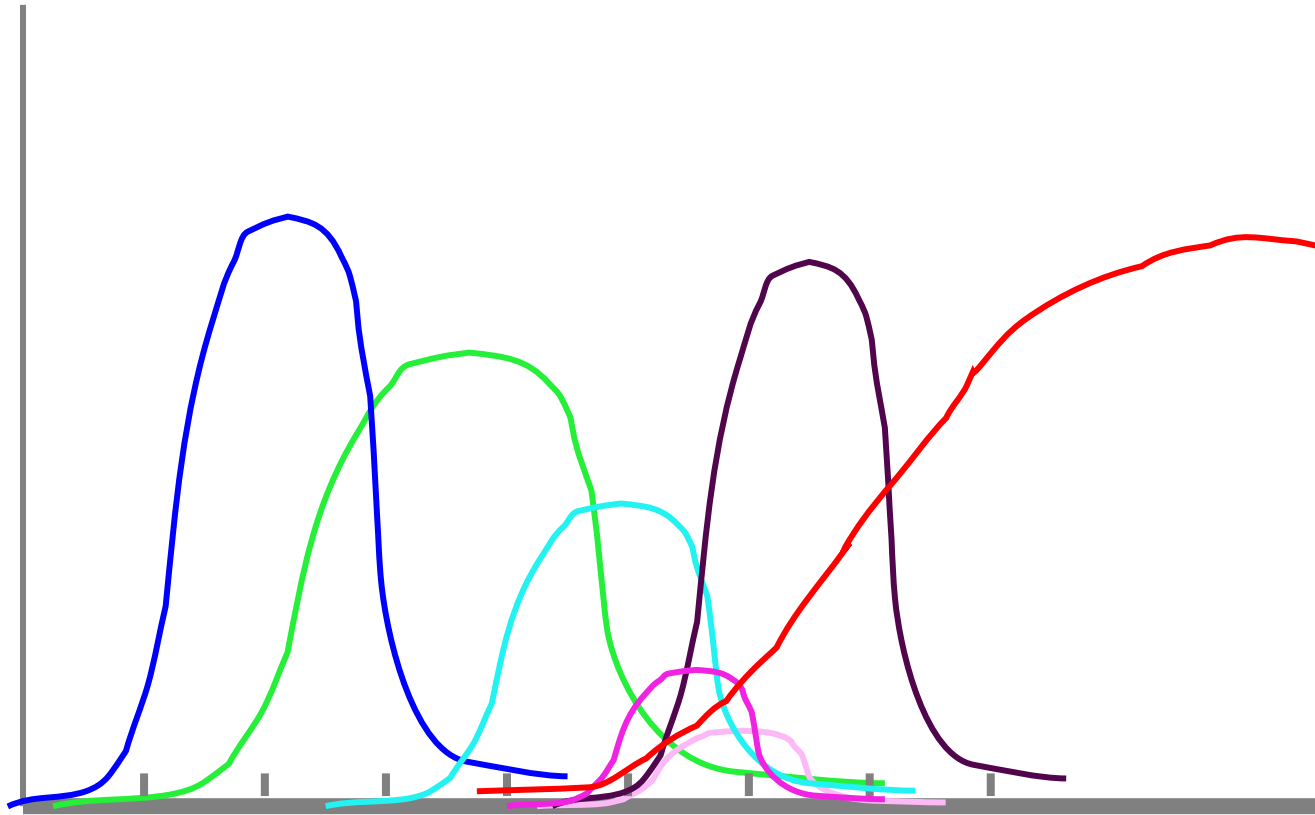


Blood

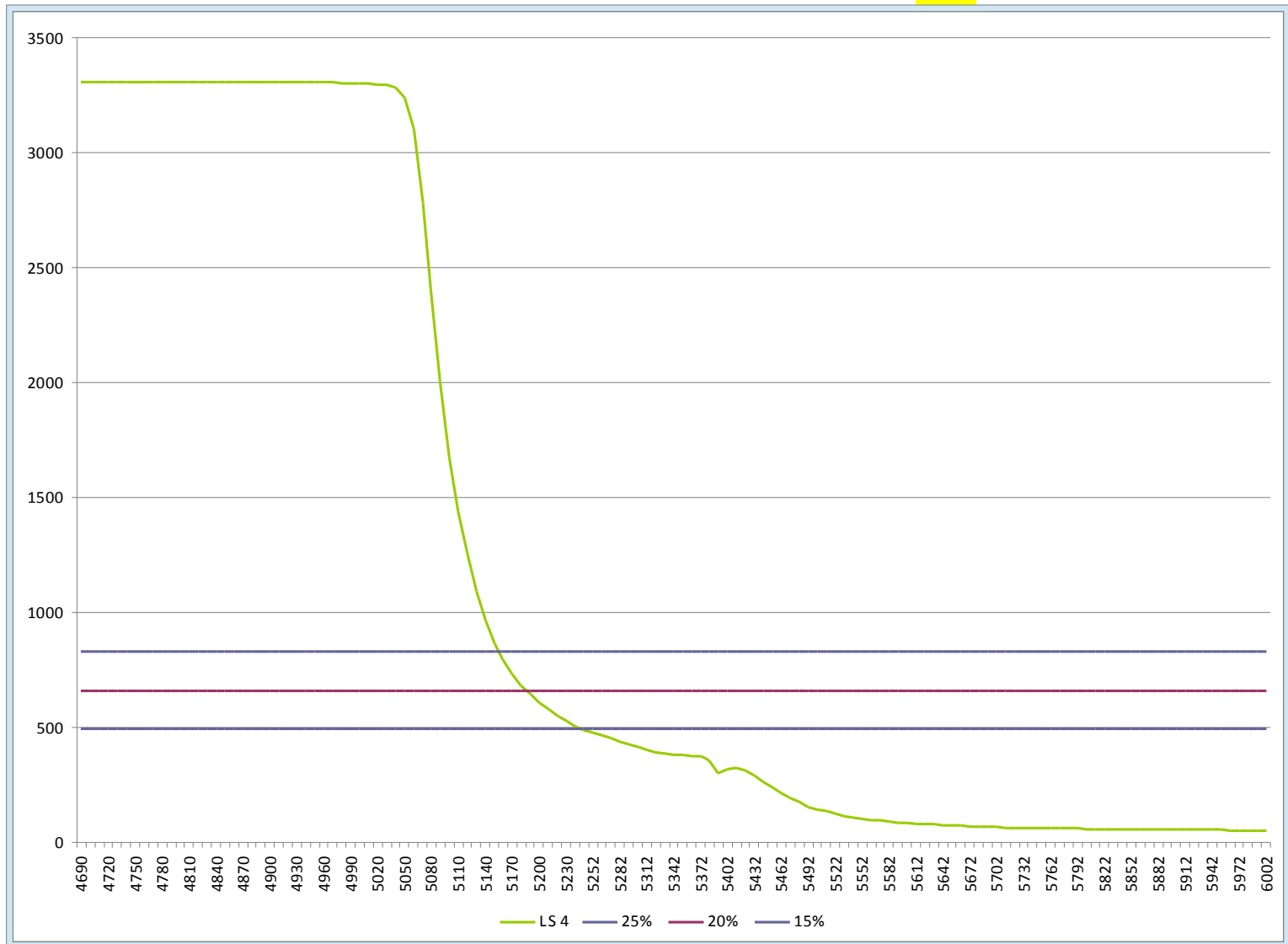


	Specific weight
Plasma	1.026
Platelets	1.040
Lymphocytes	1.050-1.061
Monocytes	1.077
Basophils	1.080
Eosinophils	1.082
Neutrophils	1.088
Erythrocytes	1.100

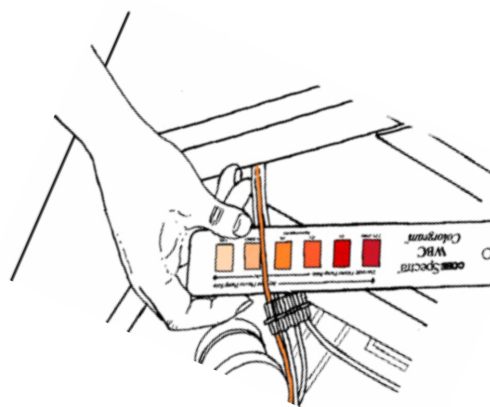
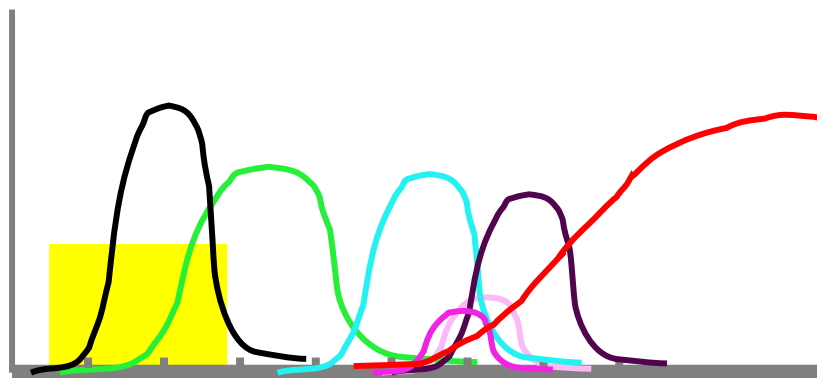
Separation



MCS+: line sensor signal



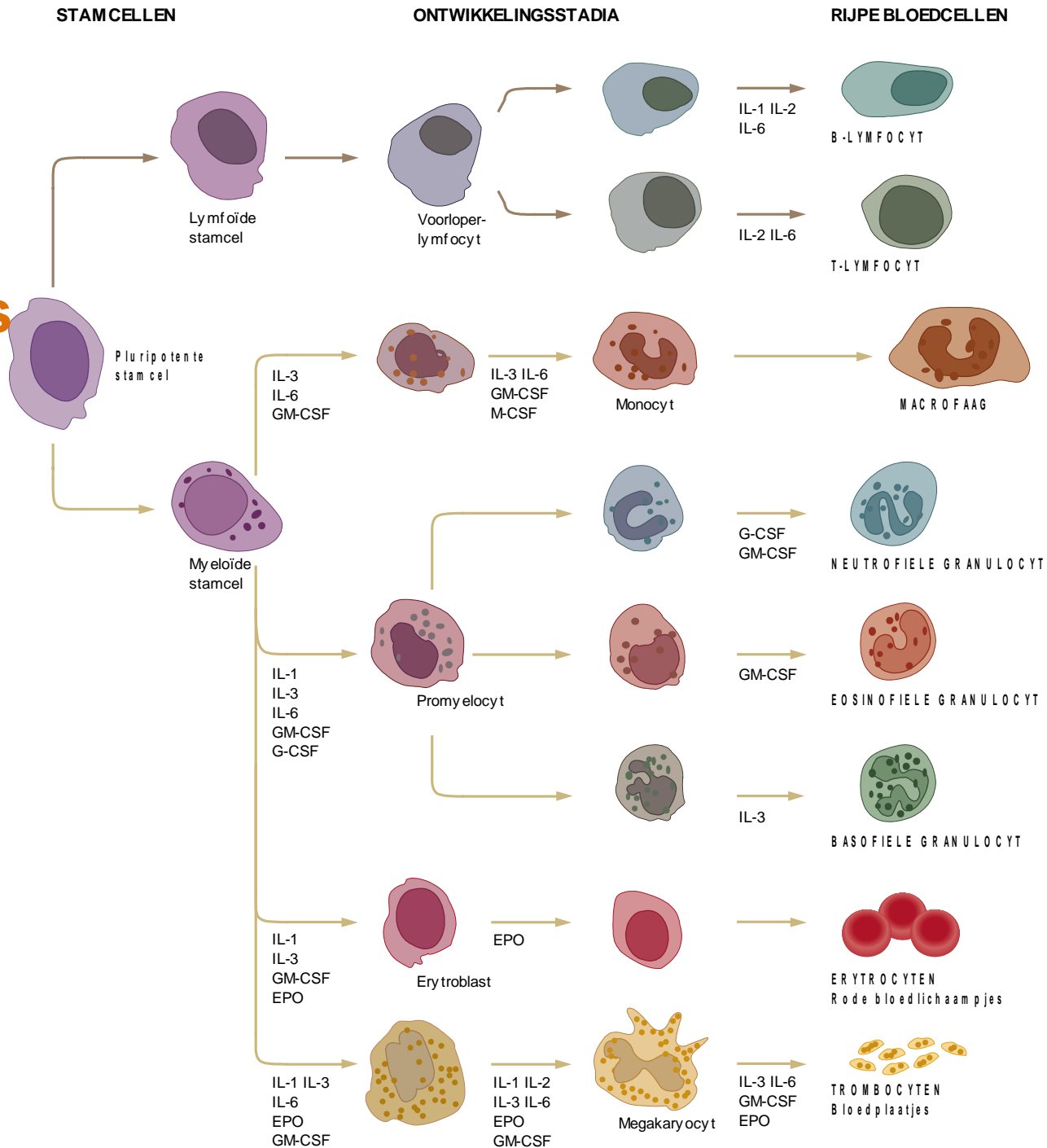
WBC collection



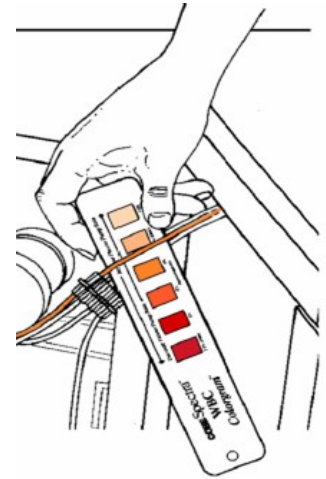
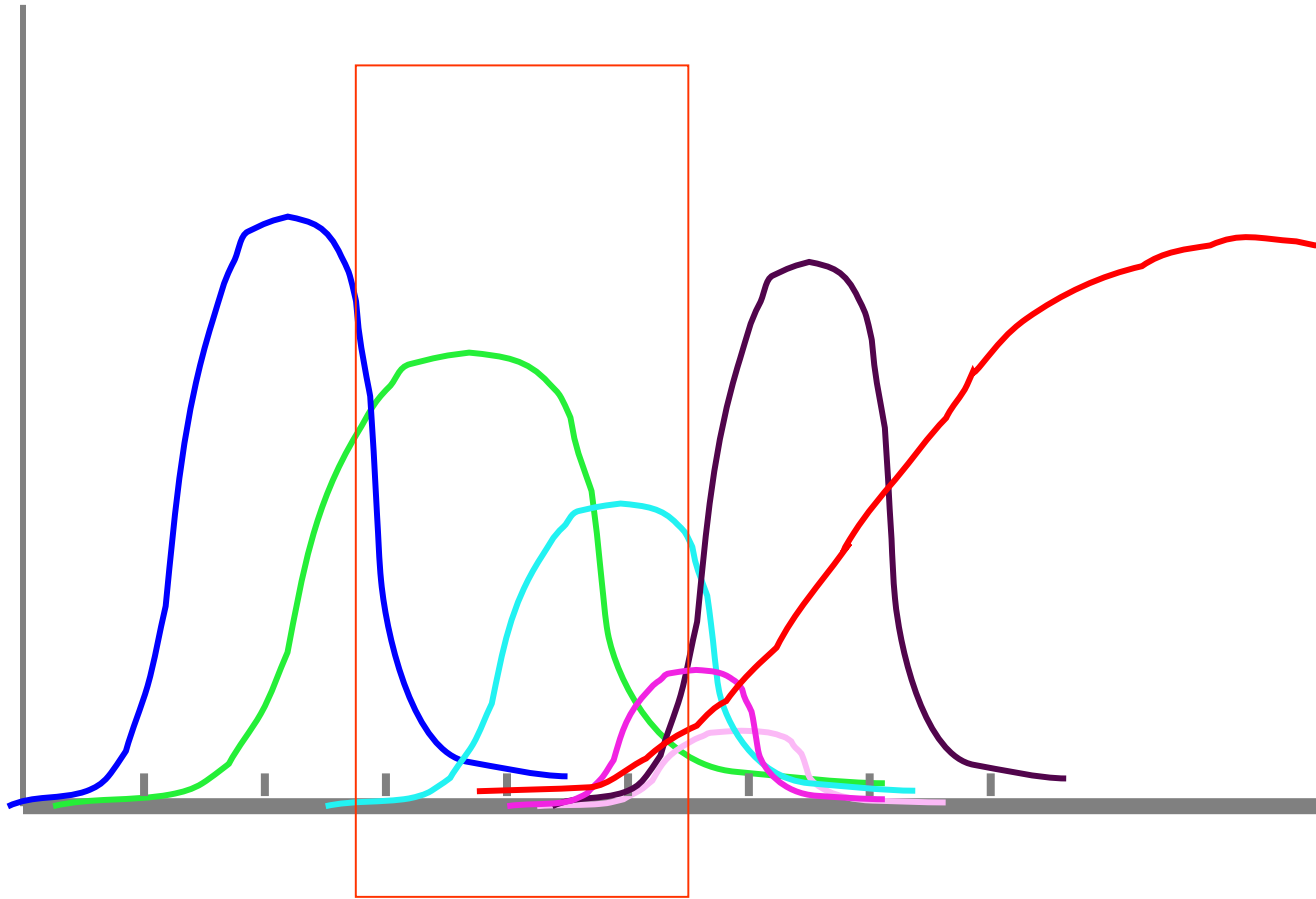
Agenda

- Collection of specific leukocytes
 - CD34 +ve cells
 - Lymphocytes
 - Monocytes
 - Granulocytes

Hematopoiesis



MNC collections → CD34+ve cells



MNC collections → CD34+ve cells

Hematopoietic Progenitor Cell (HPC), apheresis

- Mobilized
- Collected by apheresis
- Minimally invasive
- Autologous, Allogenic, Syngeneic (identical twins)
- CD34 +ve cells / kg
- Faster engraftment

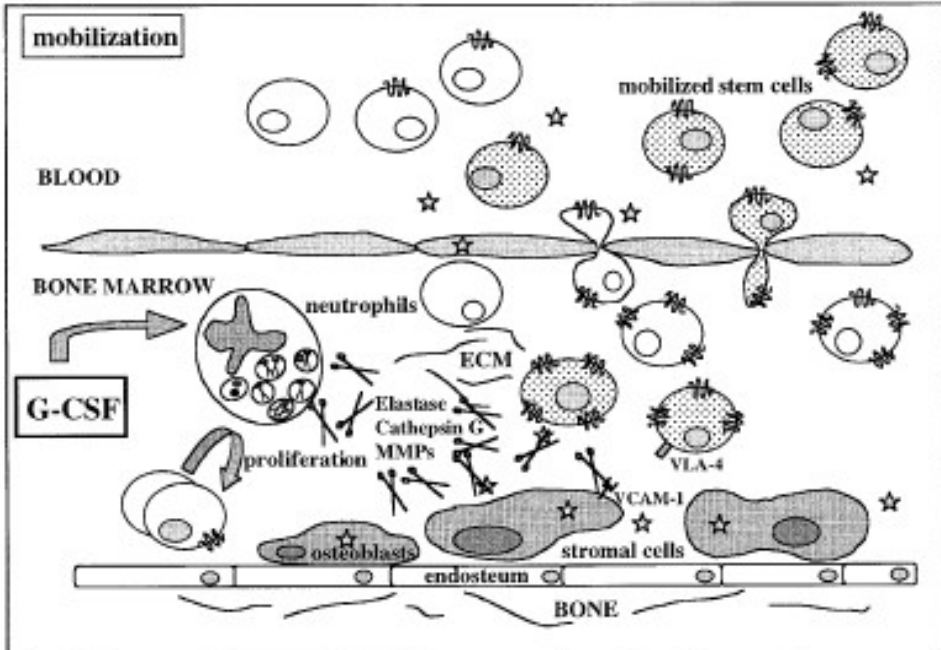
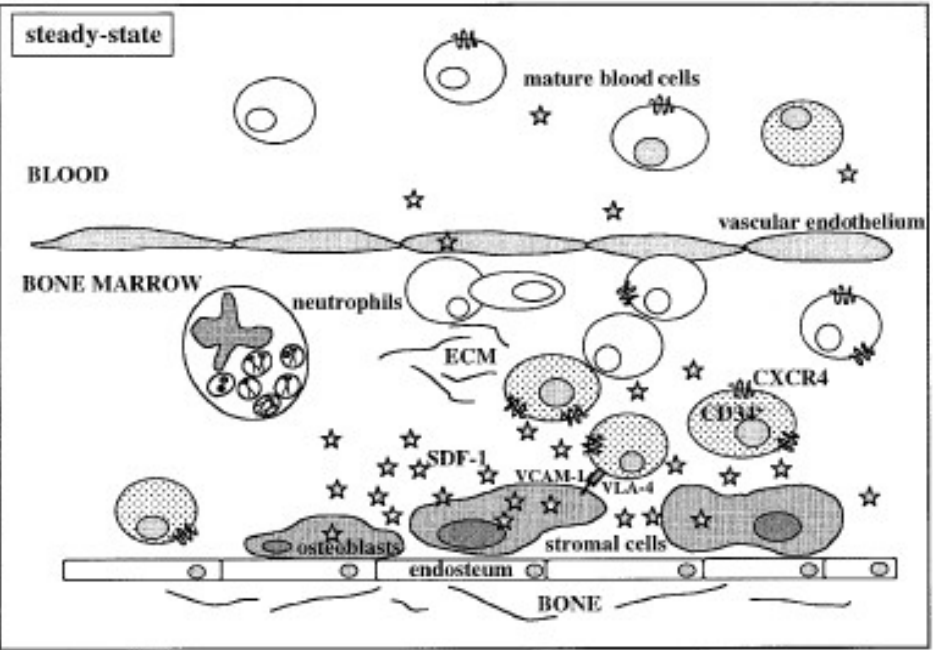
CD34+ve stem cells

- HPC
- CD34 +ve cell and regenerative medicine
 - Myocardial infarction



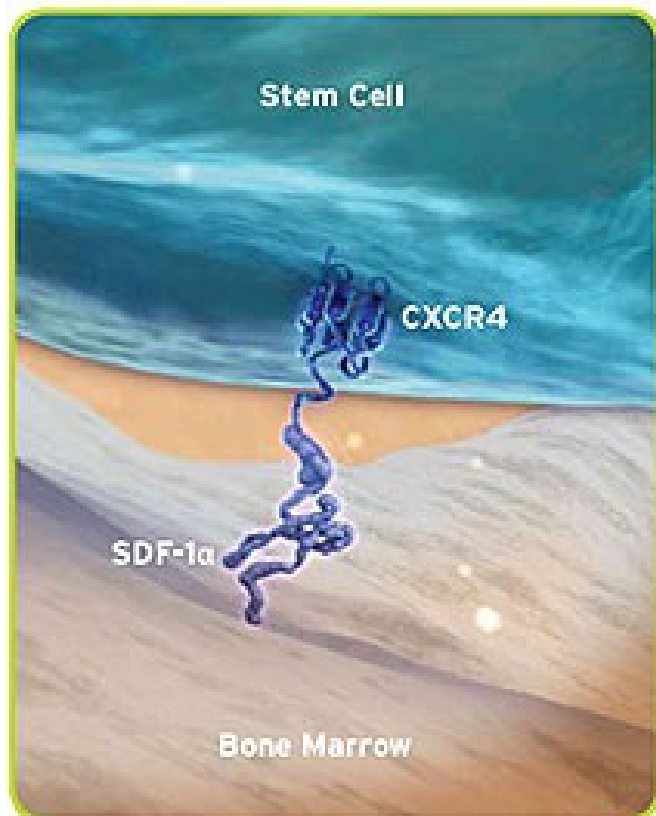
Research / Trials

Mobilization by G-CSF



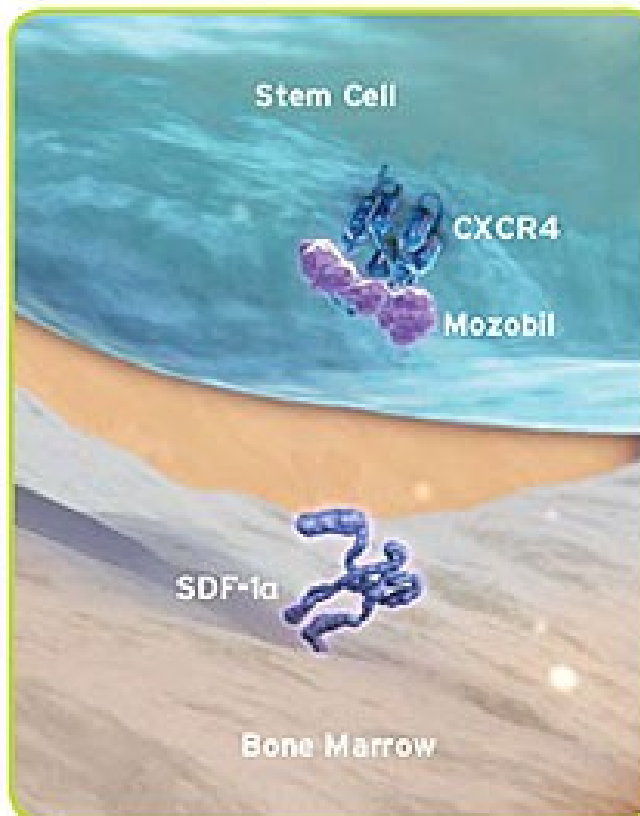
Mobilization by Plerixafor

Stem Cell Trafficking and Retention²



Stromal cell derived factor-1 alpha (SDF-1α) and CXCR4 play key regulatory roles in stem cell trafficking to, and retention by, the bone marrow.

Mechanism of Action of Mozobil³



Mozobil blocks the CXCR4-SDF-1α interaction, releasing stem cells from the bone marrow into the circulating blood.



Side effect of medication / apheresis?

Filgrastim

- Headache
- Gastrointestinal disorders
 - Nausea / Vomiting
 - Diarrhea
- Chest pain, musculoskeletal pain
- Fatigue, weakness
- Splenomegaly

Plerixafor

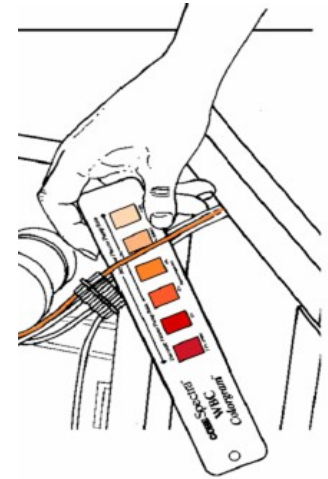
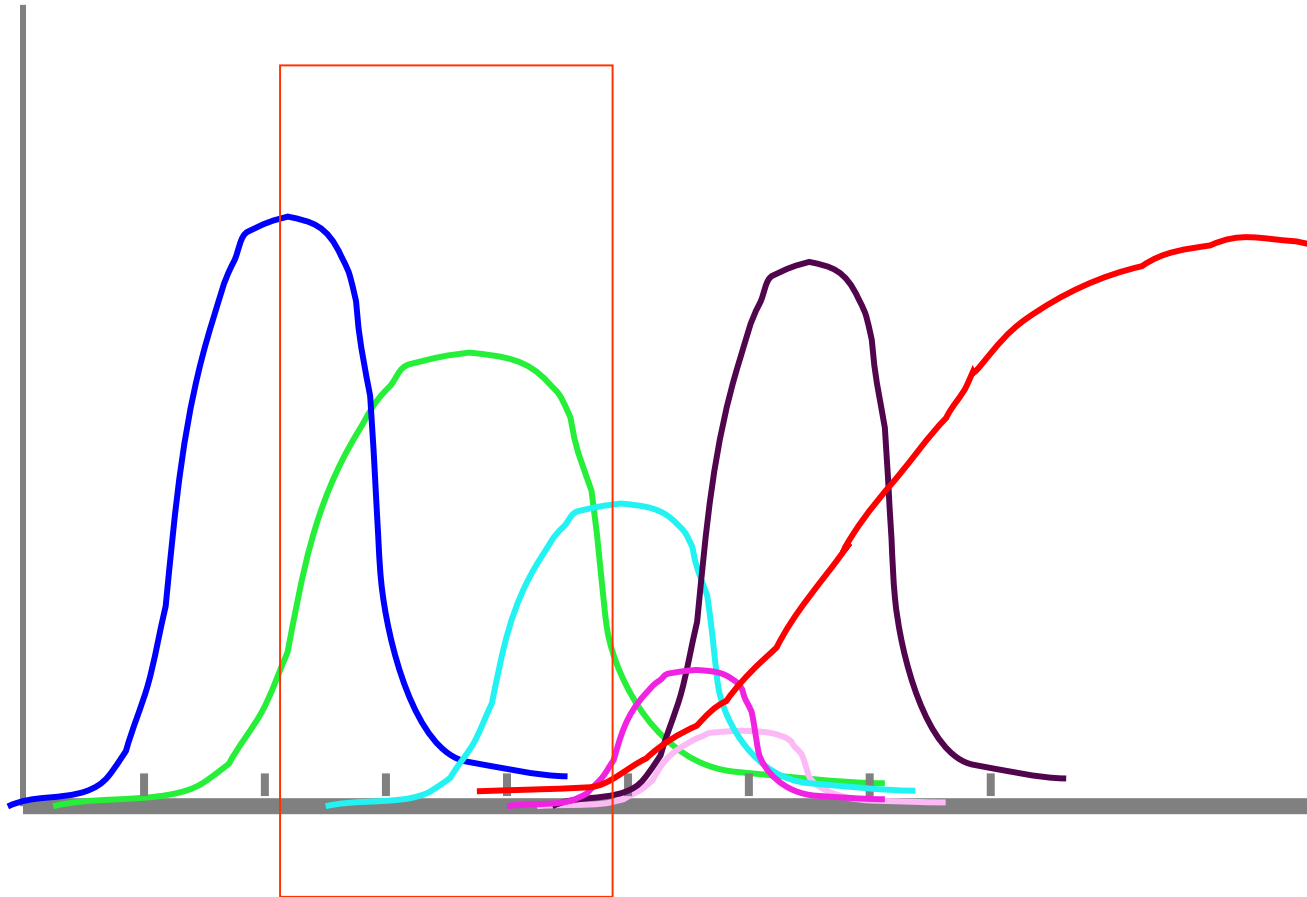
- Headache
- Dizziness
- Gastrointestinal disorders
 - Nausea / Vomiting
 - Diarrhea
- Erythema
- Arthralgia, musculoskeletal pain
- Fatigue, malaise

MNC collections (2)

Therapeutic cells, apheresis

- Non-mobilized
- Lymphocytes / Monocytes
 - Donor lymphocyte infusion
 - Extra corporeal phototherapy
 - T-cell / NK-cell therapy
 - Dendritic vaccination therapy

MNC collections → T - cells



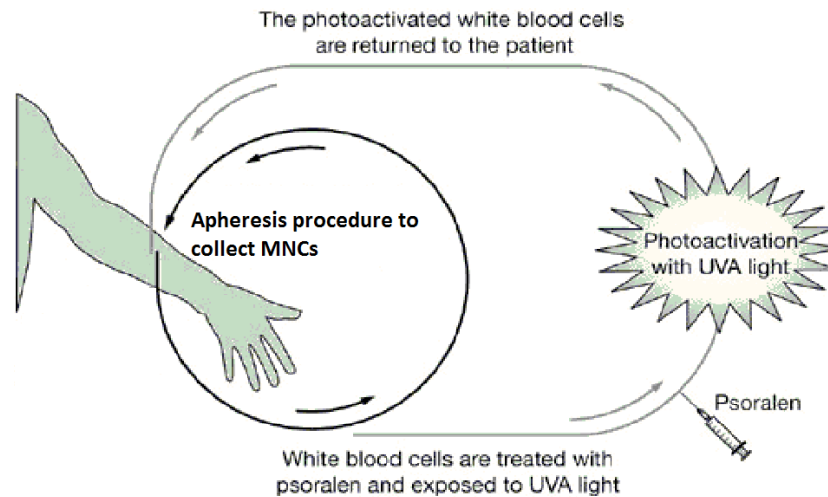
T-lymphocytes

DLI (donor lymphocyte infusion)

- Original donor CD34 +ve cells
- No mobilization needed
- Graf versus leukemia effect
- Treatment of opportunistic viral infections (EBV / CMV)

Extra corporeal photo therapy

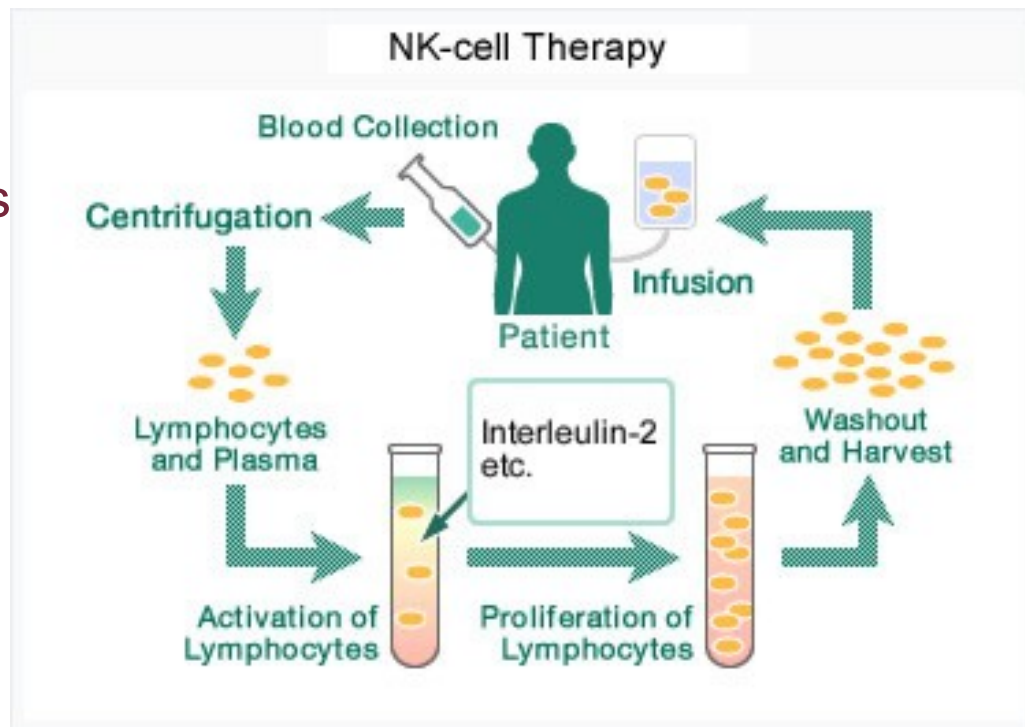
- T-lymphocytes
- Treatment with 8-methoxypsoralen and UVA light
- Indications
 - CTCL
 - Scleroderma
 - GvHD



- Inline procedure
- Offline procedure

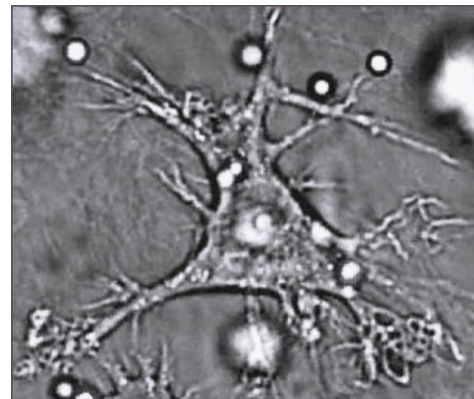
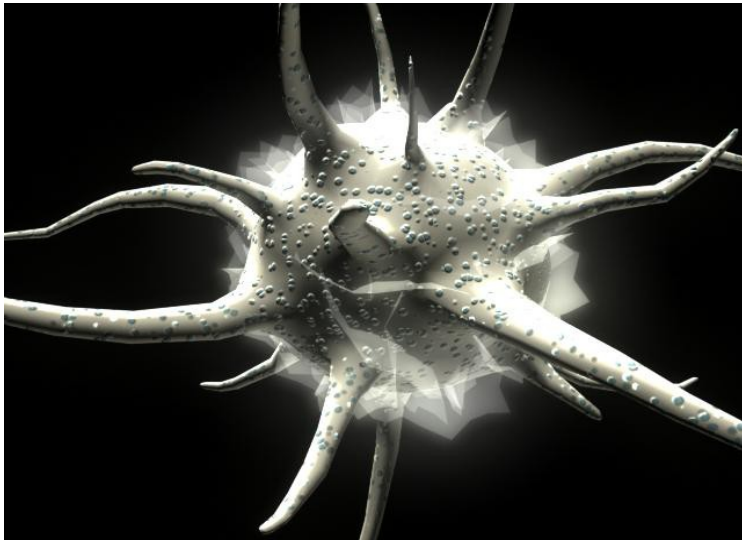
NK-cells

- Treatment for malignancies?
 - Solid tumours
 - Hematologic malignancies



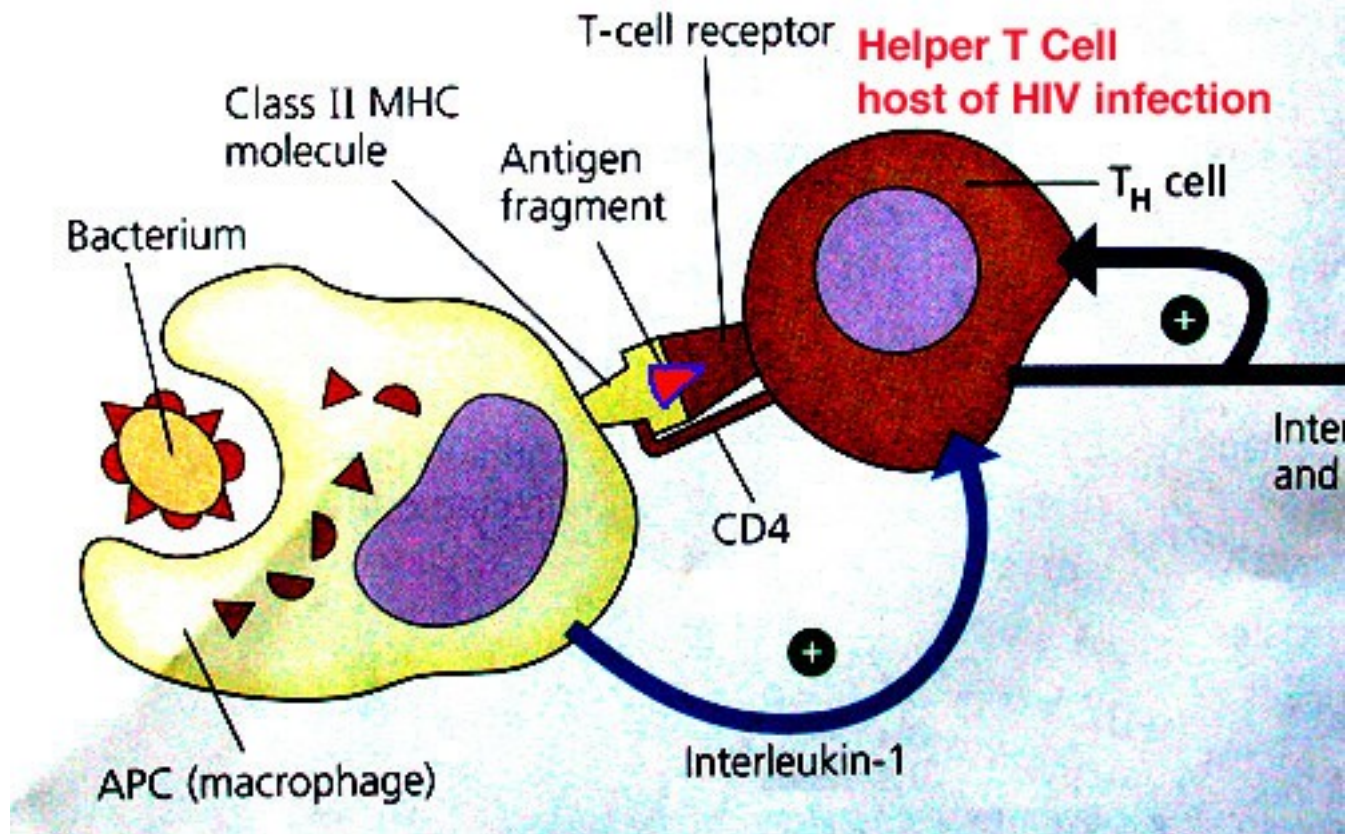
Monocyte

- Macrophage
- Dendritic cell



Function

•Antigen presentation

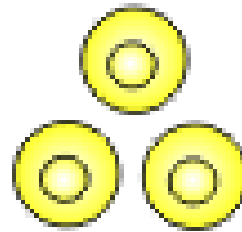




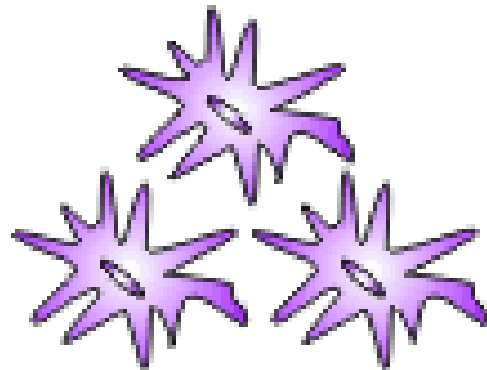
Generation of immature dendritic cells



Isolation of monocytes from peripheral blood



Loading of dendritic cells with whole cell tumor-lysate



Mature, antigen-presenting dendritic cells

Lysate preparation

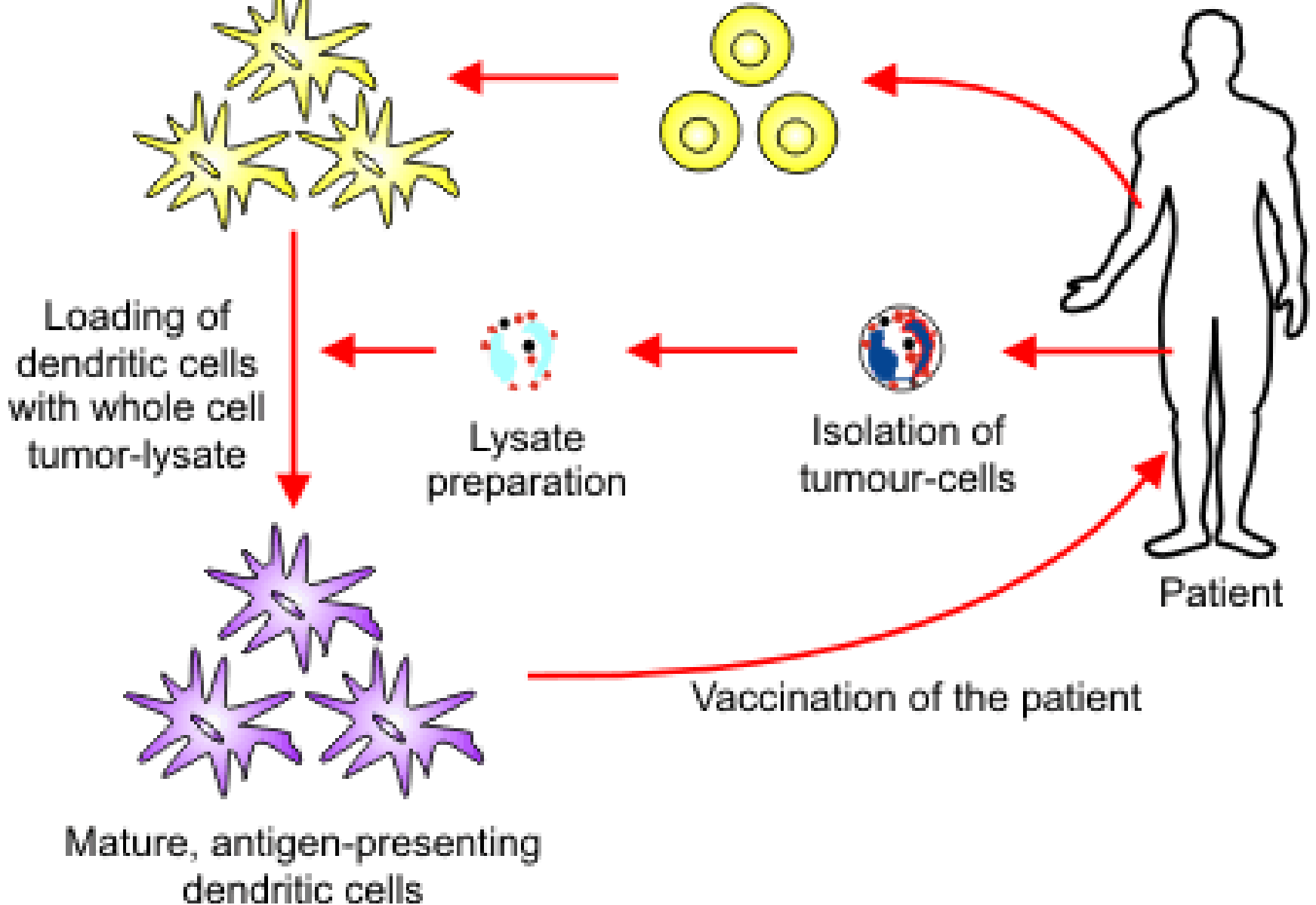


Isolation of tumour-cells

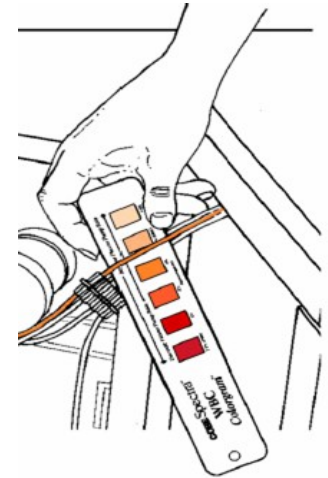
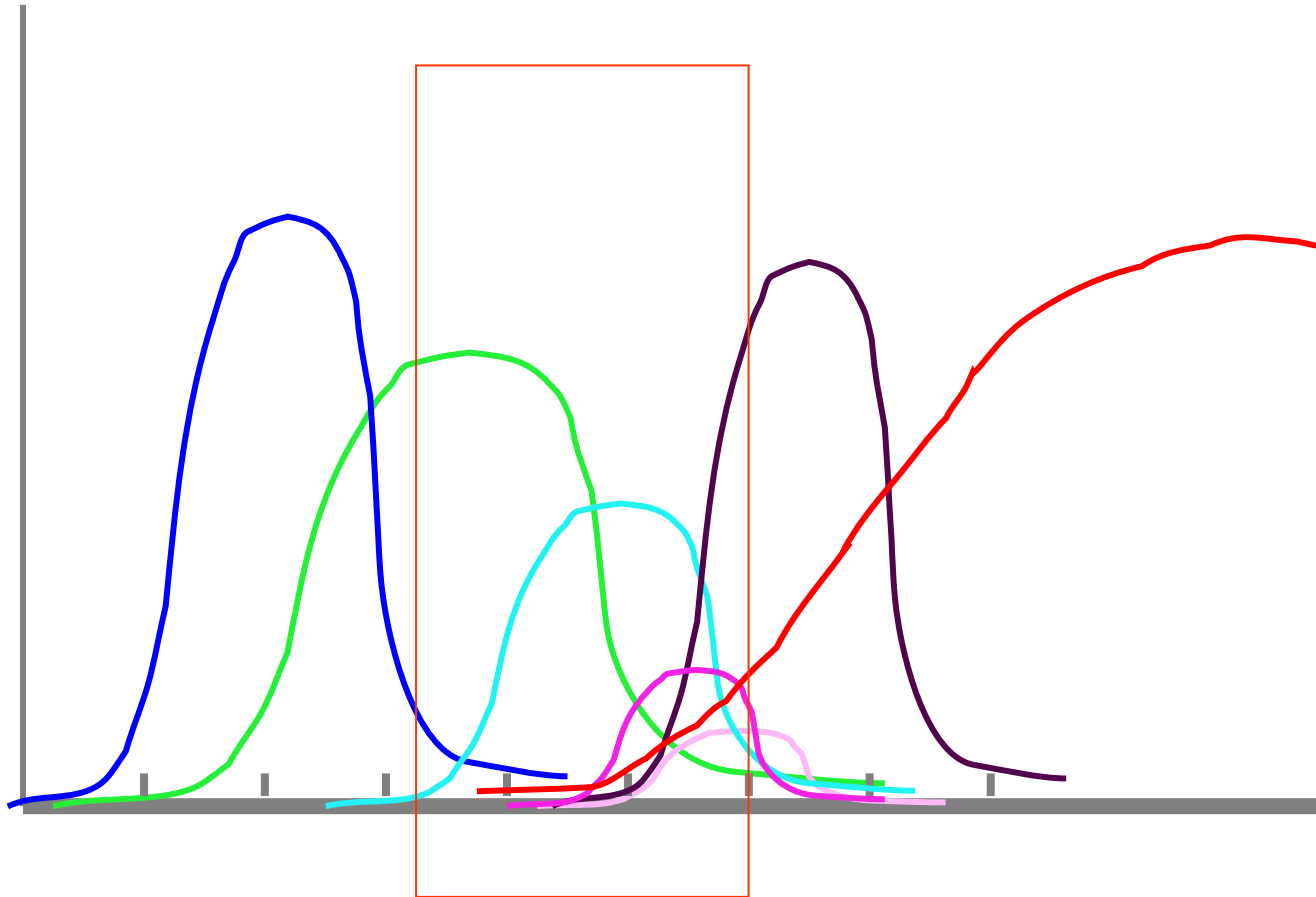


Patient

Vaccination of the patient

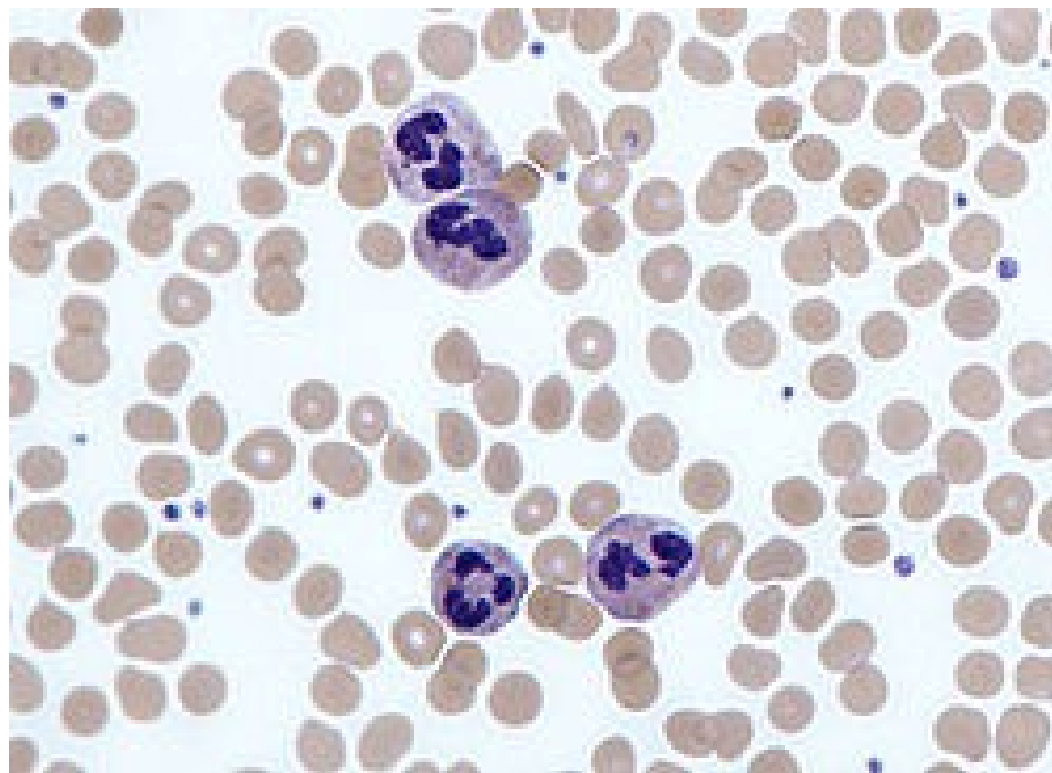


MNC collections → Monocytes

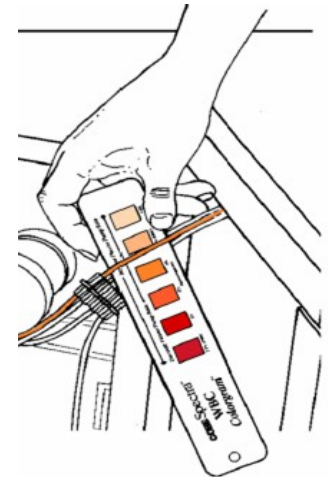
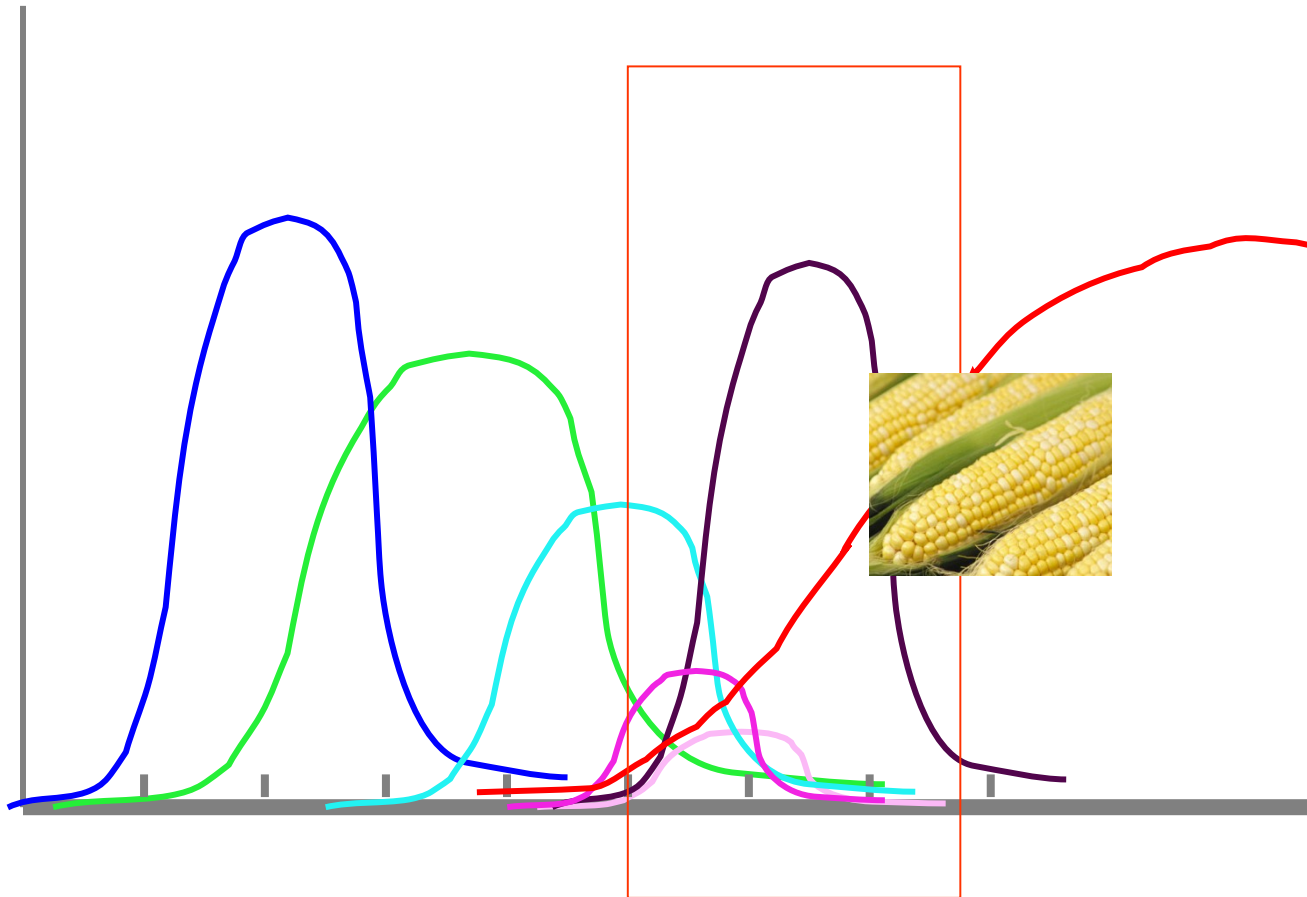


Granulocytes

→ Neutrophils



MNC collections → Granulocytes



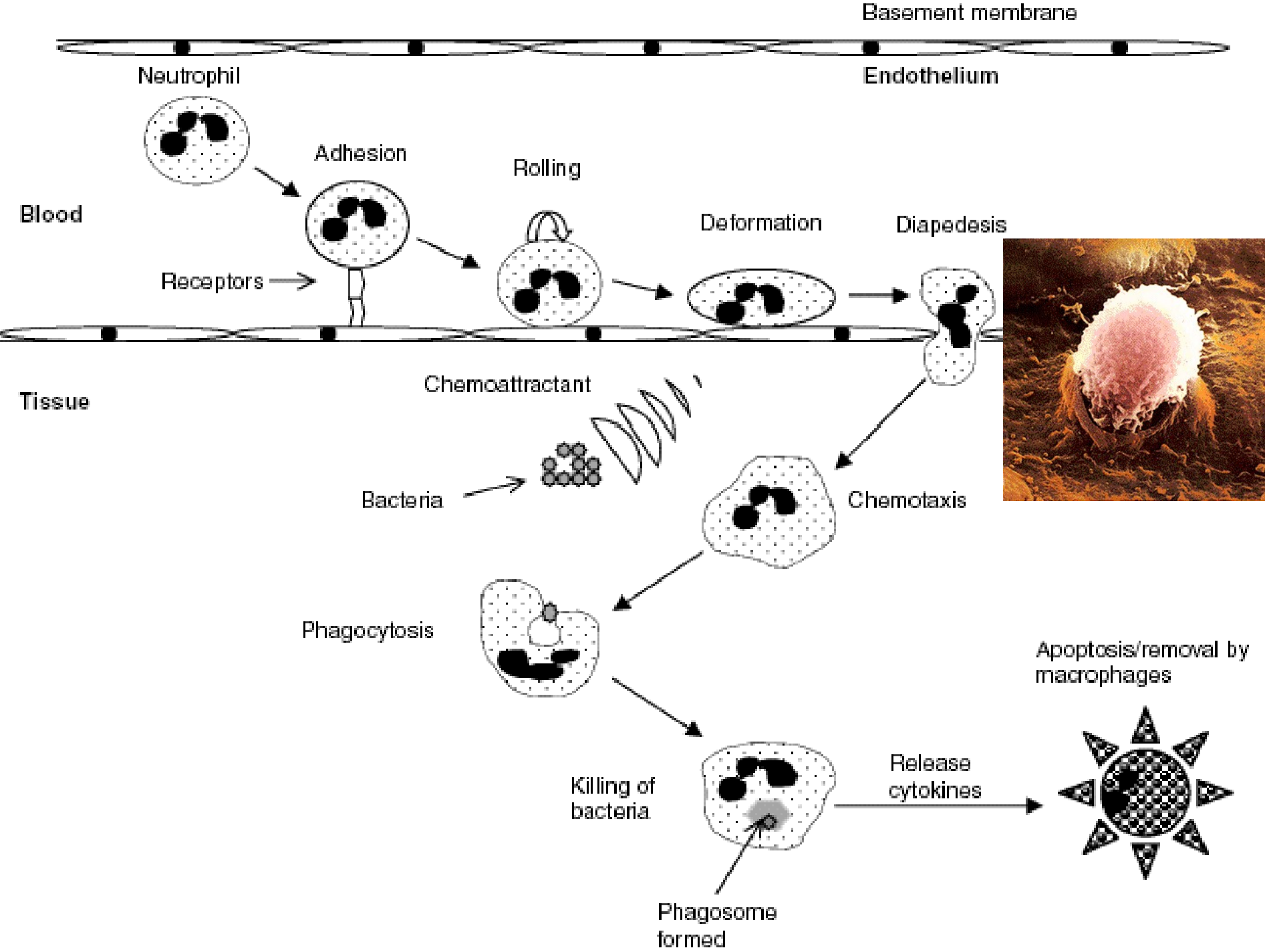
Clinical response to GTX



Pseudomonas & Citrobacter infection before GTX – unresponsive to ceftazadime, tobramycin and meronem

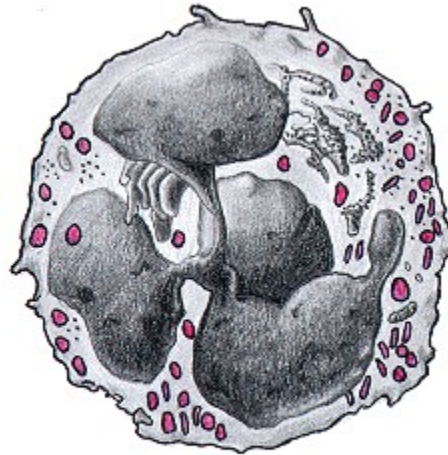


Pseudomonas & Citrobacter infection following total 7 GTX and 3 weeks of antibiotic treatment. Blood and wound culture negative. Tissue regeneration and healing



Granulocyte transfusion

- Severely neutropenic patient with life-threatening bacterial and/or fungal infection unresponsive to conventional therapy.
- Pre-emptive



Collection of granulocytes → donors

- Not stimulated $3.5 \pm 1.3 \times 10^9/L$ (2.1 – 6.9)
- G-CSF $20.8 \pm 2.3 \times 10^9/L$ (14.8 – 36.9)
- G-CSF + dexamethasone $42.5 \pm 12.7 \times 10^9/L$ (19.7 – 82.0)

‘G-CSF mobilized neutrophils have normal function when tested in assays of respiratory burstchemiluminescence, phagocytosis, chemotaxis, and superoxide anion production.’

Granulocyte concentrates: prolonged functional capacity during storage in the presence of phenotypic changes. Drewniak A., et al. Haematologica 2008.

In summary

- Therapeutic cells can be collected by apheresis
 - MNCs
 - Granulocytes
- Autologous / allogeneic
- For some cell types molecular fractionation of cells needed

