NKAML:
Natural **K**iller (cell, and) **A**cute **M**yeloid **L**eukaemia

HSCT:
Haematopoietic **S**tem **C**ell **T**ransplantation

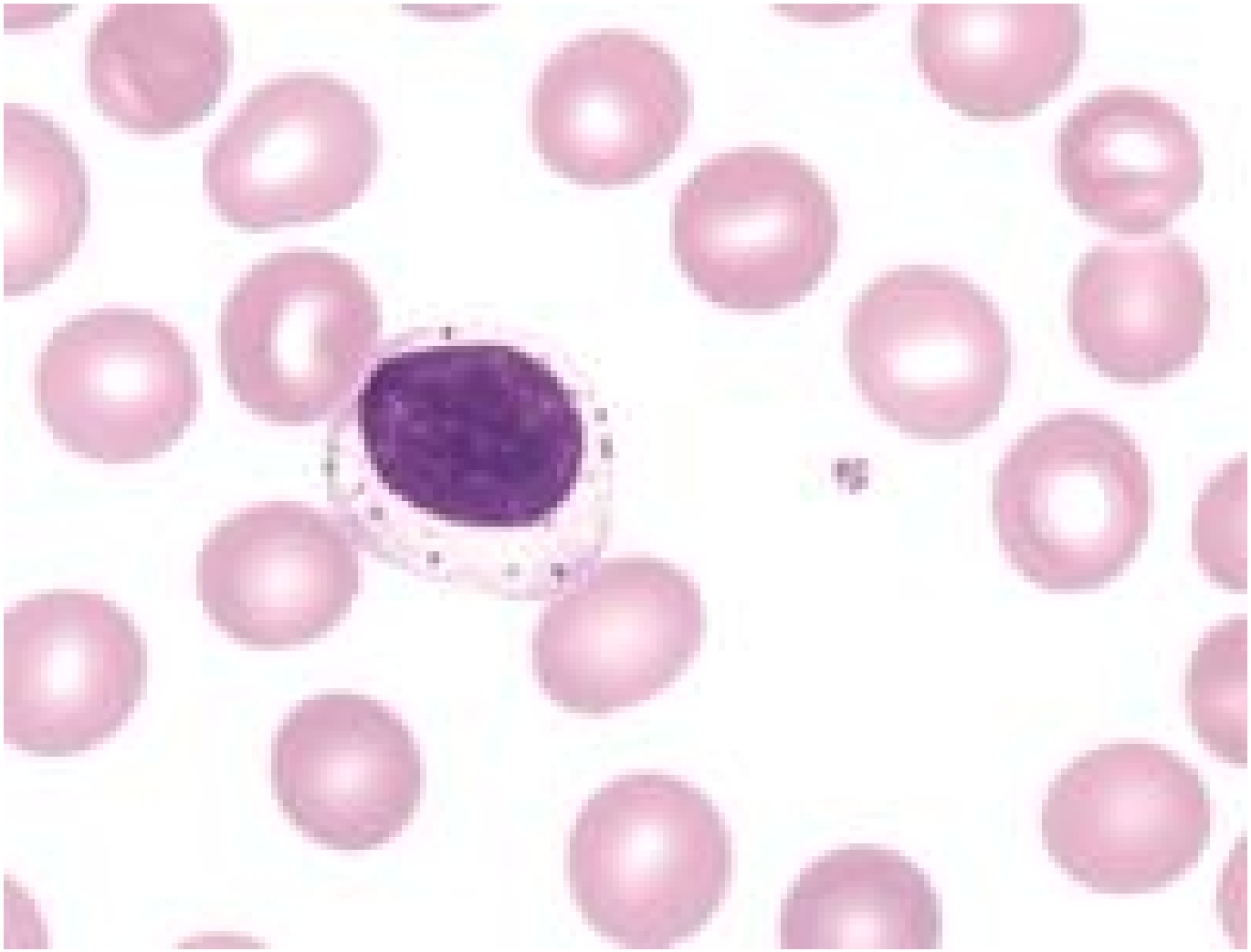
GVHD:
Graft **V**ersus **H**ost **D**isease

GVT:
Graft **V**ersus **T**umor (effect)

GVL:
Graft **V**ersus **L**eukaemia

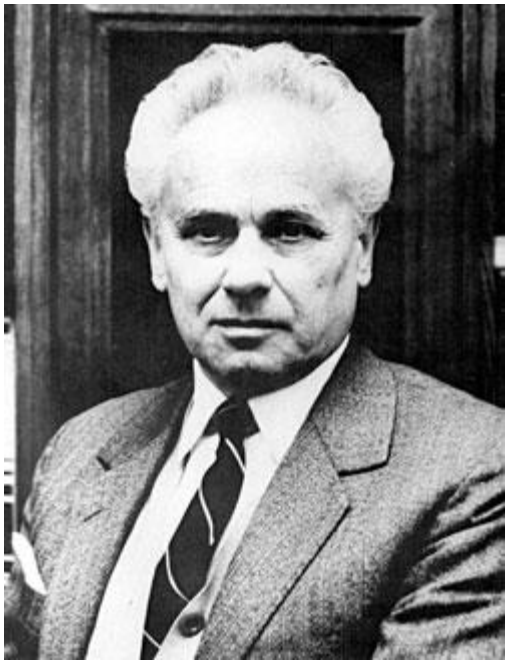
LGL:
Large **G**ranular **L**ymphocyte: **NK** cell

LGL

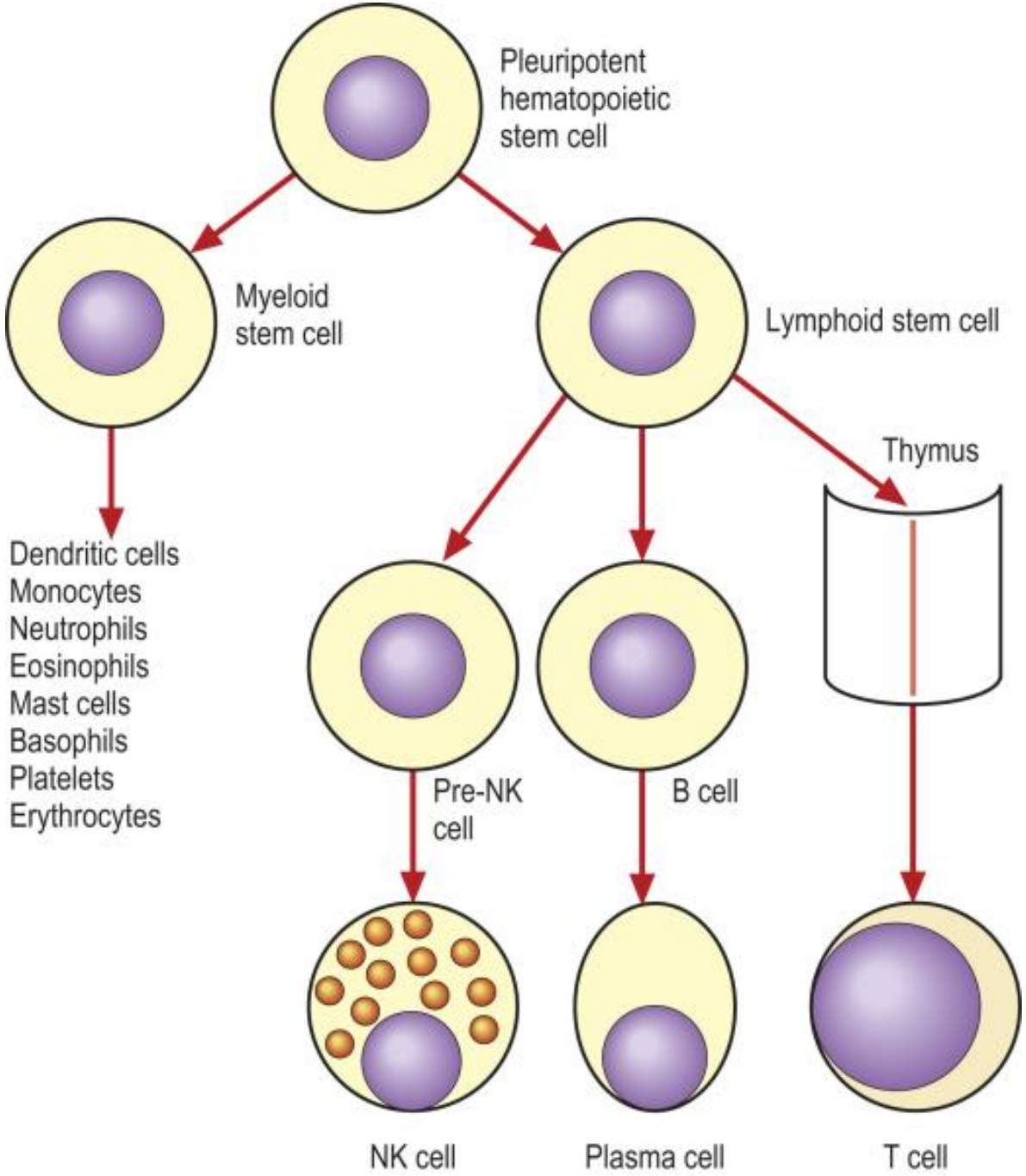


A higher power view reveals distinct azurophilic granules in the cytoplasm. The pattern of chromatin in the nucleus is that found in a differentiated lymphoid cell.

... kiemelkedő tehetségét korán felismerte első professzora, Hetényi Géza, akinek szegedi klinikáján kezdte orvosi pályáját, és ahol rendkívül fiatalon, 29 éves korában elnyerte az egyetemi magántanári címet. Ragyogóan ívelő pályáját átmenetileg megtörte a kommunista diktatúra, amikor az 1956-os forradalomban vállalt szerepe miatt eltávolították a Szegedi Orvostudományi Egyetemről. Egy másik nagy klinikus tanár, Magyar Imre, akit nézetei, szellemisége miatt ugyancsak eltiltottak a medikusok oktatásától, az Orvostovábbképző Intézetben nyújtott számára kutatási lehetőséget, majd a Semmelweis Orvostudományi Egyetem I. sz. Belklinikájára történt visszahelyezése után osztályt és laboratóriumot biztosított számára klinikáján.



„Gondot viselj magadról és a tudományról; maradj meg azokban; mert ezt cselekedvén, mind magadat megtartod, mind a te hallgatóidat.”
(Pál 1. levele Timótheushoz, 4:16)


Pleuripotent
hematopoietic
stem cell
Myeloid
stem cell
Lymphoid stem cell
Thymus
Dendritic cells
Monocytes
Neutrophils
Eosinophils
Mast cells
Basophils
Platelets
Erythrocytes
Pre-NK
cell
B cell
NK cell
Plasma cell
T cell

Kliegman: Nelson Textbook of Pediatrics, 18th ed.

Section 5 – Hematopoietic Stem Cell Transplantation

Andrea Velardi Franco Locatelli

Chapter 134 – Principles and Clinical Indications

Thousands of children have received an infusion of **allogeneic** or **autologous** (from the same individual) hematopoietic stem cells to cure malignant and non-malignant disorders. **Autologous** transplantation is employed as a rescue strategy after delivering otherwise lethal doses of radiotherapy and chemotherapy. **Allogeneic** transplantation is used to treat children with genetic diseases of blood cells, such as thalassemia and primary immunodeficiency diseases, as well as hematologic malignancies, such as leukemia and lymphoma. Bone marrow had represented the only source of hematopoietic progenitors employed. Growth factor (G-CSF)-mobilized peripheral blood hematopoietic stem cells and umbilical cord blood hematopoietic progenitors are also used to perform hematopoietic stem cell transplantation (HSCT). For many years, an HLA-matched sibling was the only type of donor employed. More recently, matched unrelated volunteers, full-haplotype mismatched family members, and unrelated cord blood donors have been largely employed to transplant patients lacking an HLA-identical relative.

Immunological aspects of **haploidentical** stem cell transplantation in children.
Handgretinger R, Lang P, Schumm M, Pfeiffer M, Gottschling S, Demirdelen B, Bader P, Kuci S, **Klingebiel T, Niethammer D.**
Ann N Y Acad Sci. 2001 Jun;938:340-57; discussion 357-8.PMID: 11458522

Haploidentical stem cell transplantation **in leukemia.**
Aversa F, **Velardi A,** Tabilio A, Reisner Y, Martelli MF.
Blood Rev. 2001 Sep;15(3):111-9. Review

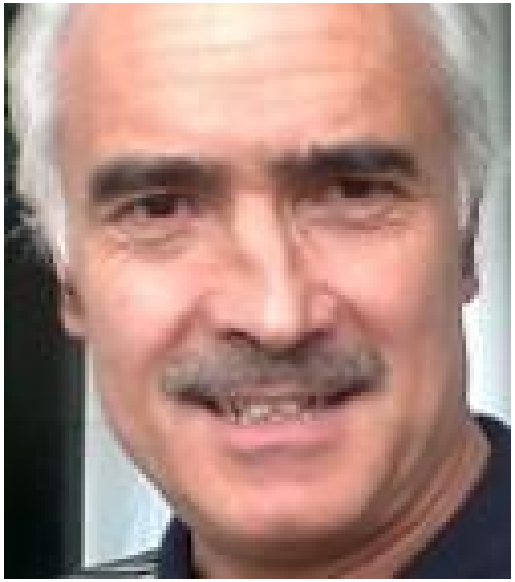
Evaluation of **KIR** ligand incompatibility in **mismatched** unrelated donor hematopoietic transplants. Killer immunoglobulin-like receptor.
Davies SM, Ruggieri L, DeFor T, Wagner JE, Weisdorf DJ, Miller JS, **Velardi A,** Blazar BR.
Blood. 2002 Nov 15;100(10):3825-7. Free article

Survival advantage with KIR ligand incompatibility in hematopoietic stem cell transplantation from unrelated donors.
Giebel S, Locatelli F, Lamparelli T, **Velardi A,** Davies S, Frumento G, Maccario R, Bonetti F, Wojnar J, Martinetti M, Frassoni F, Giorgiani G, Bacigalupo A, Holowiecki J.
Blood. 2003 Aug 1;102(3):814-9. Free article

Immunotherapy with alloreactive natural killer cells in haploidentical haematopoietic transplantation.
Velardi A, Ruggeri L, Capanni M, Mancusi A, Perruccio K, Aversa F, Martelli MF.
Hematol J. 2004;5 Suppl 3:S87-90. Review.

Donor natural killer cell **allorecognition of missing self** in haploidentical hematopoietic transplantation for acute myeloid leukemia: challenging its predictive value.
Ruggeri L, Mancusi A, Capanni M, Urbani E, Carotti A, Aloisi T, Stern M, Pende D, Perruccio K, Burchielli E, Topini F, Bianchi E, Aversa F, Martelli MF, **Velardi A.**
Blood. 2007 Jul 1;110(1):433-40. Free article

Donor T cells in hematopoietic allografts are vital for promoting engraftment, eradicating malignant cells (graft-vs.-leukemia, GVL, effect), and reconstituting immunity. Unfortunately, they mediate Graft-vs.-Host Disease (GVHD), an attack on recipient tissues. Transplants from immediately available donors, such as family members who are fully mismatched for one HLA haplotype, has recently been achieved by our group through transplantation of high numbers of T cell-depleted hematopoietic stem cells.



These grafts result in the rapid generation of natural killer (NK) cells. NK cells are negatively regulated by major histocompatibility complex (MHC) class I-specific inhibitory receptors. In humans, receptors termed killer Ig-like receptors (KIRs) recognize groups of HLA class I alleles. In any given individual's NK repertoire there are cells which express a single KIR and are blocked only by a specific class I allele group. Missing expression of the KIR ligand on mismatched allogeneic cells can therefore trigger NK cell alloreactivity. We have recently observed that the most impressive influence associated with a KIR ligand mismatch in the GvH direction, is a dramatically reduced risk of relapse in acute myeloid leukemia (AML) patients.