1

Introduction to Hematology

A. TRANSITION GRID

Information concerning Chapter 1, "Introduction;" Chapter 2, "Cellular Homeostasis;" and Chapter 3, "Hematopoiesis" may also be referenced in the following hematology textbooks.

Clinical Laboratory Hematology	Chapter 1	Chapter 2	Chapter 3
McKenzie, 1st edition	Chapter 1	Chapter 2	Chapter 2
Harmening, 5th edition	n/a	n/a	Chapter 1
Rodak, 3rd edition	n/a	Chapter 6	Chapter 7
Turgeon, 4th edition	n/a	Chapter 3	Chapter 4

B. OBJECTIVES

Chapter 1 – Introduction

Levels I and II

1. Compare the reference intervals for hemoglobin, hematocrit, erythrocytes, and leukocytes in infants, children, and adults.

2. Identify the function of erythrocytes, leukocytes, and platelets.

3. Describe the composition of blood.

4. Explain the causes of change in the steady state of blood components.

5. Describe clinical pathway, critical pathway, reflex testing, and disease management and identify the laboratory's role in developing these models.

6. Compare capitated payment, prospective payment, and fee-for-service and describe the impact of capitation on the laboratory.

Chapter 2 – Cellular Homeostasis

Level I

1. Describe the location, morphology, and function of subcellular organelles of a cell.
2. Describe the lipid asymmetry found in the plasma membrane of most hematopoietic cells.
3. Differentiate the parts of the mammalian cell cycle.
4. Define R (restriction point) and its role in cell cycle regulation.
5. Define *apoptosis* and explain its role in normal human physiology.
6. Classify and give examples of the major categories of initiators and inhibitors of apoptosis.
7. List the major events regulated by apoptosis in hematopoiesis.

Level II

1. Explain the significance of SNPs, introns, exons, UTRs, post-translational protein modifications.
2. List the components and explain the function of the Ubiquitin-Proteosome system.
3. Define *cyclins* and *Cdks* and their role in cell cycle regulation; describe the associated Cdk partners and function of cyclins D, E, A, and B.
4. Define *CAK* (Cdk-activating kinase) and the two major classes of CKIs (cyclin-dependent kinase inhibitors) and describe their function.
5. Compare the function of cell-cycle checkpoints in cell-cycle regulation.
6. Describe/illustrate the roles of p53 and pRb in cell-cycle regulation.
7. Propose how abnormalities of cell-cycle regulatory mechanisms can lead to malignancy.
8. Define *caspases* and explain their role in apoptosis.
9. Differentiate the extrinsic and intrinsic pathways of cellular apoptosis.
10. Define and contrast the roles of proapoptotic and antiapoptotic members of the Bcl-2 family of proteins.
11. Describe apoptotic regulatory mechanisms.
12. Give examples of diseases associated with increased apoptosis and inhibited (decreased) apoptosis.
13. Define, and give examples of, epigenetics, oncogenes and tumor suppressor genes and their roles in cell biology.
14. Differentiate using morphologic observations, the processes of necrotic cell death and apoptotic cell death.

Chapter 3 – Hematopoiesis

Level I

1. Describe the basic concepts of cell differentiation and maturation.
2. Compare and contrast the categories of hematopoietic precursor cells: hematopoietic stem cells, hematopoietic progenitor cells, and maturing cells, including proliferation and differentiation potential, morphology, and population size.
3. Describe the hierarchy of hematopoietic precursor cells and the relationships of the various blood cell lineages to each other (including the concept of colony-forming units/CFUs).

4. Discuss the general characteristics of growth factors and identify the major examples of early acting (multilineage), later acting (lineage restricted), and indirect acting growth factors.

5. Differentiate between paracrine, autocrine, and juxtacrine regulation.

6. List examples of negative regulators of hematopoiesis.

7. Define *hematopoietic microenvironment.*

Level II

1. Identify the phenotypic characteristics differentiating the hematopoietic stem cells and progenitor cells.

2. Identify the key cytokines required for lineage-specific regulation.

3. Describe the structure and role of growth factor receptors.

4. Summarize the concept of signal transduction pathways.

5. Discuss the roles of transcription factors in the regulation of hematopoiesis and differentiation.

6. Outline current clinical uses of cytokines.

7. Describe the cellular and extracellular components of the hematopoietic microenvironment.

8. Discuss the proposed mechanisms used to regulate hematopoietic stem/progenitor cell proliferation/differentiation.

Note: *Statements in parts C, D, & E identified with asterisks suggest Level II competencies*

C. ACTIVE LEARNING SUGGESTED ACTIVITIES

*{Background information on each suggested activity is provided in the **Introduction/Teaching Tips** section at the beginning of this Instructor's Resource Manual.}*

1. **Clear the Mud**   At the end of class, pass out index cards to all students and ask each of them to write down any topic, current or past, that is still unclear. Have students place their respective index cards into a container on the instructor's desk. As students leaves, they should randomly pick an index card from the container, research the topic, and prepare an answer or explanation to the "muddy point" written on the card. The instructor may choose to ask a few students to present their explanation during the next class period.

2. **Diagrams**
   a. Using the information provided in Chapter 2, have the learners create their own explicit diagram of the:
      • Cell structure
      • Stages of the cell cycle
      • **Hematopoietic precursor cell model

3. **Group Discussion**
   a. Create a group discussion on the topic of the Medical Ethics concerning stem cell transplants.

4. **Mystery Box**
   a. Create a Mystery Box with the different blood components and corresponding reference ranges. Be sure to include at least
      • Leukocytes
      • Erythrocytes

- Thrombocytes
- Plasma
- Whole blood
- $4.5 - 11.0 \times 10^9/L$
- $4.5 - 5.5 \times 10^{12}/L$
- $150 - 450 \times 10^9/L$
- 55 percent of blood volume
- 5 – 6 liters in adults
- And so on

5. **One-Minute Paragraph**   Have learners submit a one minute paragraph on the:
   a. Composition of blood
   b. **Abnormal tissue homeostasis and cancer

6. **Short Story**   Have the learners, individually or as a group, write:
   a. The story of "The Life and Development of a Cell"
   b. A "Murder Mystery" of a Cell

7. **Think-Pair-Share**
   a. **Discuss the value and need for "clinical" and "critical" pathways.
   b. **Discuss Necrosis versus Apoptosis.

8. **Thumbs Up/Thumbs Down**   Remember to get immediate feedback on any topic during the class period, call for a quick "Thumbs Up or Thumbs Down." Ask students to indicate if they comprehend the information presented by showing either a thumbs up, indicating they understand the information, or thumbs down, meaning more explanation or clarification is needed.

D. LABORATORY ACTIVITIES

1. **Perform WBC and RBC counts on each learner in the class, and create a "class reference range" for WBC and RBC. You might want to have students read the section "Reference Interval Determination" in Chapter 41 if you include this activity.

E. PRACTICE QUESTIONS

1. List the components of whole blood and state the reference range for each. [Taxonomy 1]

2. **Explain why "reflex testing protocols" are designed. [Taxonomy 1].

3. A patient experiencing a viral infection is likely to demonstrate an increase in which of the following? [Taxonomy 1]
   a. Erythrocytes
   b. Hematocrit
   c. Leukocytes
   d. Thrombocytes

4. Patient Aaron had an RBC count of $4.0 \times 10^{12}/L$. Explain why a hospital in Alabama might consider this value "normal," whereas a facility in Utah may recognize Aaron's RBC as "below" normal. [Taxonomy 2]

5. **In the text *Clinical Laboratory Hematology,* differentiate "precursor cells" from "maturing cells." [Taxonomy 2]

6. Analyze each set of results and answer the following questions. [Taxonomy 2]

A.	*B.*	*C.*
WBC = 18.6×10^9/L	WBC = 0.6×10^9/L	WBC = 6.5×10^9/L
RBC = 3.50×10^{12}/L	RBC = 2.12×10^{12}/L	RBC = 4.79×10^{12}/L
Hgb = 10.2 g/dL	Hgb = 7.5 g/dL	Hgb = 16.4 g/dL
Hct = 31.1%	Hct = 24.3%	Hct = 49.6%
Plt = 202×10^9/L	Plt = 89×10^9/L	Plt = 543×10^9/L

   Which set of results demonstrates a
   a. Leukocytosis
   b. Erythrocytopenia
   c. Thrombocytopenia
   d. Critically decreased H & H
   e. Leukopenia
   f. Thrombocytosis

7. **Compare and contrast a "fee-for-service" reimbursement system to a "capitated payment" plan. [Taxonomy 3]

8. Compare and contrast the processes of cell "self-renewal" versus "cell differentiation." [Taxonomy 3]

9. Evaluate the following patient results and conclude which body function (mechanism) will be adversely affected. Explain why. [Taxonomy 3]

   WBC = 0.8×10^9/L
   RBC = 2.5×10^{12}/L
   Hgb = 8.2 g/dL
   Hct = 25.1%
   Plt = 222×10^9/L

10. A 26-year-old male, Type I diabetes mellitus patient is seen in the emergency department. The patient's blood chemistry results confirm the need for renal dialysis. Explain the etiology for this patient's hematology results. [Taxonomy 3]

    WBC = 11.8×10^9/L
    RBC = 3.2×10^{12}/L
    Hgb = 9.5 g/dL
    Hct = 27.6%
    Plt = 321×10^9/L

Introduction to Hematology—Level I

Figure out what words the clues represent. Then find the words in the grid. Words can go horizontally, vertically, and diagonally in all eight directions.

```
V  H  E  H  N  J  N  H  D  T  R  F  N  E  M  M
N  L  P  S  C  T  D  T  S  S  S  Z  T  X  E  S
O  Y  Y  R  E  Y  L  T  E  E  M  Y  S  N  M  I
I  H  R  G  Y  D  E  N  N  H  C  N  U  M  B  S
T  R  E  C  Y  M  E  I  K  O  B  K  E  M  R  O
A  P  V  M  C  G  K  P  B  L  N  L  L  N  A  T
R  R  H  E  O  O  G  M  A  Q  B  N  C  M  N  P
E  Z  L  C  T  S  O  S  W  I  X  T  U  M  E  O
F  L  N  Y  L  R  T  P  Q  R  D  L  N  H  W  P
I  O  C  T  H  E  M  A  T  O  L  O  G  Y  T  A
L  Q  T  T  X  P  L  Z  S  X  Q  L  C  W  M  M
O  K  K  Y  Z  T  V  R  D  I  X  Y  V  W  F  L
R  D  G  G  G  L  V  T  N  P  S  M  R  W  Y  V
P  Q  L  F  E  U  C  H  R  O  M  A  T  I  N  D
R  N  N  R  M  K  C  N  A  L  B  U  M  I  N  C
L  S  I  S  E  I  O  P  O  T  A  M  E  H  M  W
```

- cell division—repeated reproduction
- another term for hematopoietic growth factor
- study of formed cellular blood elements
- process of forming a blood clot
- outer boundary of a cell
- the earliest morphologically recognizable cell of each blood cell lineage
- the process of blood cell formation
- how a blood cell passes through vessel walls
- part of cell that contains the genetic material
- genes that induce tumor formation
- main constituent of plasma
- programmed cell death
- platelet
- lightly stained portions of chromatin
- undifferentiated, pleuripotential hematopoietic cell (2 words)

Introduction to Hematology—Level I

```
V H E H N J N H D T R F N E M M
N L P S C T D T S S S Z T X E S
O Y Y R E Y L T E E M Y S N M I
I H R G Y D E N N H C N U M B S
T R E C Y M E I K O B K E M R O
A P V M C G K P B L N L L N A T
R R H E O O G M A Q B N C M N P
E Z L C T S O S W I X T U M E O
F L N Y L R T P Q R D L N H W P
I O C T H E M A T O L O G Y T A
L Q T T X P L Z S X Q L C W M M
O K K Y Z T V R D I X Y V W F L
R D G G G L V T N P S M R W Y V
P Q L F E U C H R O M A T I N D
R N N R M K C N A L B U M I N C
L S I S E I O P O T A M E H M W
```
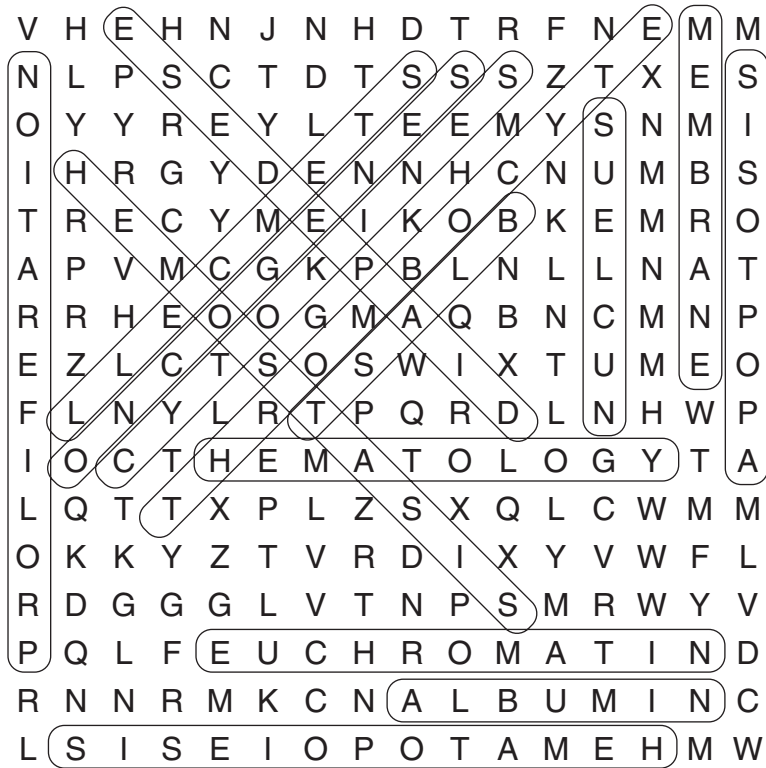
- cell division—repeated reproduction (proliferation)
- another term for hematopoietic growth factor (cytokines)
- study of formed cellular blood elements (hematology)
- process of forming a blood clot (hemostasis)
- outer boundary of a cell (membrane)
- the earliest morphologically recognizable cell of each blood cell lineage (blast)
- the process of blood cell formation (hematopoiesis)
- how a blood cell passes through vessel walls (diapedese)
- part of cell that contains the genetic material (nucleus)
- genes that induce tumor formation (oncogenes)
- main constituent of plasma (albumin)
- programmed cell death (apoptosis)
- platelet (thrombocyte)
- lightly stained portions of chromatin (euchromatin)
- undifferentiated, pleuripotential hematopoietic cell (2 words) (stem cell)

Introduction to Hematology—Level I
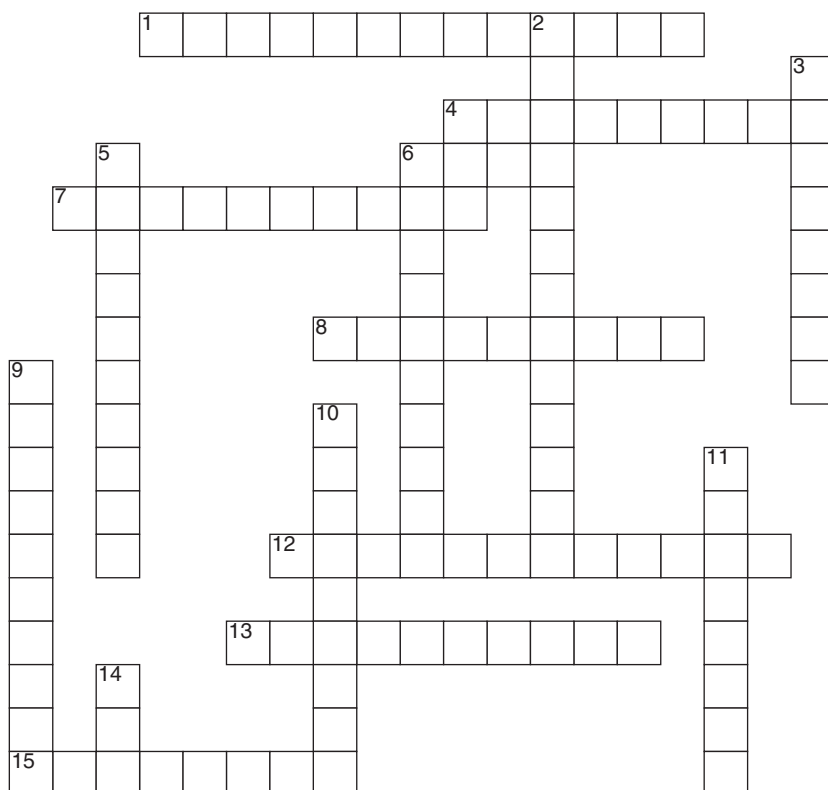
ACROSS

1 Growth and development of lymphoid cells
4 Stage during which microtubular spindles align during mitosis
7 Cells that defend against foreign antigens
8 Where the metabolic activities of the cell takes place
12 Alternate copies (alleles) of a gene
13 Type of cell that differentiates into mature, functional cells
15 Cell murder

DOWN

2 Outside of cell
3 Study of the entire genome of an organism
5 Arrest of bleeding
6 Study of the formed cellular blood elements
9 Vital protein inside erythrocytes
10 Organelles that assemble amino acids into protein
11 Group of proteins responsible for apoptotic cell death
14 Complete blood count (abrv)

Introduction to Hematology—Level I

```
                    L Y M P H O P O I E S I S
                                    X                       G
                              M E T A P H A S E             E
              H             H           R                   N
          L E U K O C Y T E S           A                   O
              M             M           C                   M
              O             A           E                   I
              S           C Y T O P L A S M                 C
      H       T             O           L                   S
      E       A       R     L           U
      M       S       I     O           L             C
      O       I       B     G           A             A
      G       S     P O L Y M O R P H I S M           A
      L               S                       P
      O           P R O G E N I T O R         A
      B       C     M                         S
      I       B     E                         E
      N E C R O S I S                         S
```
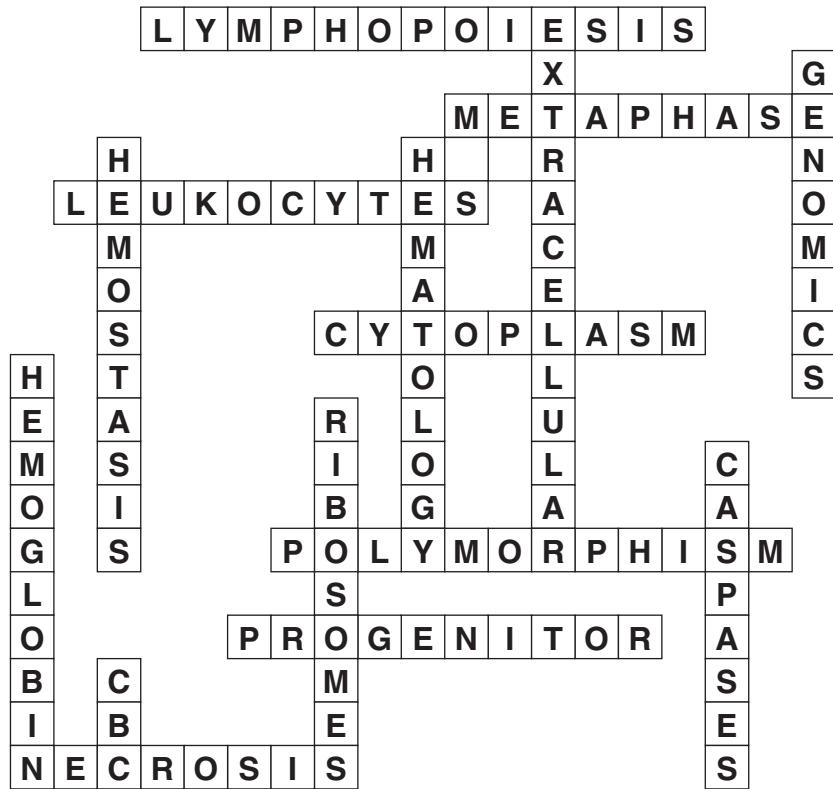
Introduction to Hematology—Level II

Figure out what words the clues represent. Then find the words in the grid. Words can go horizontally, vertically, and diagonally in all eight directions.

```
L  X  Z  B  K  R  D  L  N  S  D  I  P  I  L
S  N  E  F  Q  L  I  H  Q  T  R  T  E  G  C
S  C  B  L  Z  N  F  N  S  L  N  N  E  A  T
E  W  F  T  F  X  F  V  R  C  E  M  S  F  N
N  G  B  W  K  E  E  R  N  G  G  P  A  T  T
I  C  B  L  R  C  R  N  O  W  A  B  H  A  I
K  L  B  V  V  T  E  C  P  S  W  B  P  D  R
O  X  R  M  H  N  N  W  E  W  L  O  O  Q  C
T  P  R  M  I  O  T  S  W  T  P  H  R  K  O
Y  M  C  L  I  Y  I  K  B  T  C  T  P  N  T
C  T  C  T  Q  G  A  P  O  E  P  O  Y  N  A
F  Y  N  N  K  F  T  S  N  D  M  K  L  J  M
C  A  B  C  A  P  I  T  A  T  E  D  N  T  E
K  L  L  M  H  S  O  F  H  H  J  T  T  K  H
N  X  N  F  X  T  N  L  T  Y  F  M  B  L  J
```
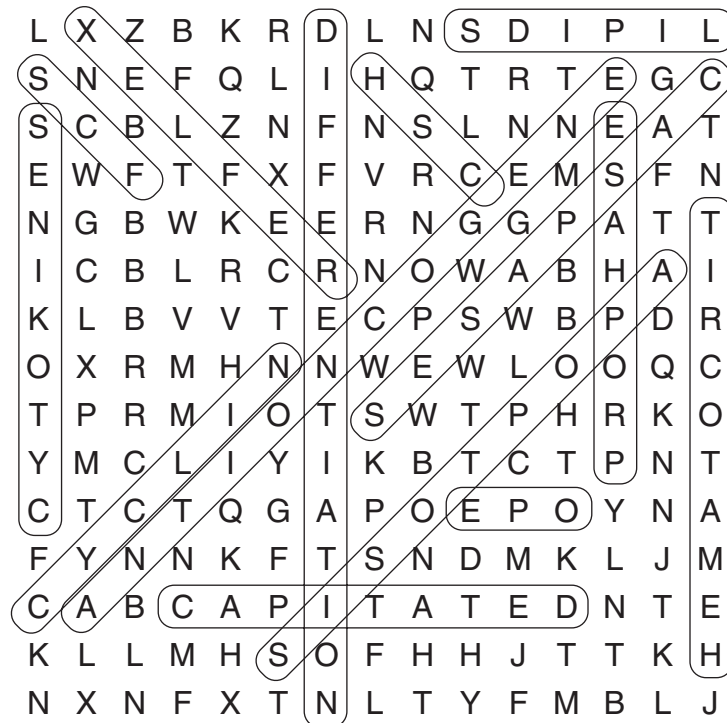
- stage in mitosis where cells condense their chromosomes
- tumor suppressor gene
- payment plan whereby the provider is reimbursed a fixed amount for a service
- growth factor that promotes proliferation and differentiation of progenitor cells (abrv)
- process for generating diverse cell populations
- programmed cell death
- cell membranes are composed of proteins and _____
- packed red cell volume
- testing done based on results of screening tests
- regulatory subunit of Cdks
- proteins that direct apoptosis
- hematopoietic growth factors
- hematopoietic growth factor for erythroid cells (abrv)
- precursor of all hematopoietic cells (abrv)

Introduction to Hematology—Level II

```
L  X  Z  B  K  R  D  L  N  S  D  I  P  I  L
S  N  E  F  Q  L  I  H  Q  T  R  T  E  G  C
S  C  B  L  Z  N  F  N  S  L  N  N  E  A  T
E  W  F  T  F  X  F  V  R  C  E  M  S  F  N
N  G  B  W  K  E  E  R  N  G  G  P  A  T  T
I  C  B  L  R  C  R  N  O  W  A  B  H  A  I
K  L  B  V  V  T  E  C  P  S  W  B  P  D  R
O  X  R  M  H  N  N  W  E  W  L  O  O  Q  C
T  P  R  M  I  O  T  S  W  T  P  H  R  K  O
Y  M  C  L  I  Y  I  K  B  T  C  T  P  N  T
C  T  C  T  Q  G  A  P  O  E  P  O  Y  N  A
F  Y  N  K  F  T  S  N  D  M  K  L  J  M
C  A  B  C  A  P  I  T  A  T  E  D  N  T  E
K  L  L  M  H  S  O  F  H  H  J  T  T  K  H
N  X  N  F  X  T  N  L  T  Y  F  M  B  L  J
```

- stage in mitosis where cells condense their chromosomes (prophase)
- tumor suppressor gene (antioncogene)
- payment plan whereby the provider is reimbursed a fixed amount for a service (capitated)
- growth factor that promotes proliferation and differentiation of progenitor cells (abrv) (scf)
- process for generating diverse cell populations (differentiation)
- programmed cell death (apoptosis)
- cell membranes are composed of proteins and _____ (lipids)
- packed red cell volume (hematocrit)
- testing done based on results of screening tests (reflex)
- regulatory subunit of Cdks (cyclin)
- proteins that direct apoptosis (caspases)
- hematopoietic growth factors (cytokines)
- hematopoietic growth factor for erythroid cells (abrv) (epo)
- precursor of all hematopoietic cells (abrv) (hsc)

Introduction to Hematology—Level II
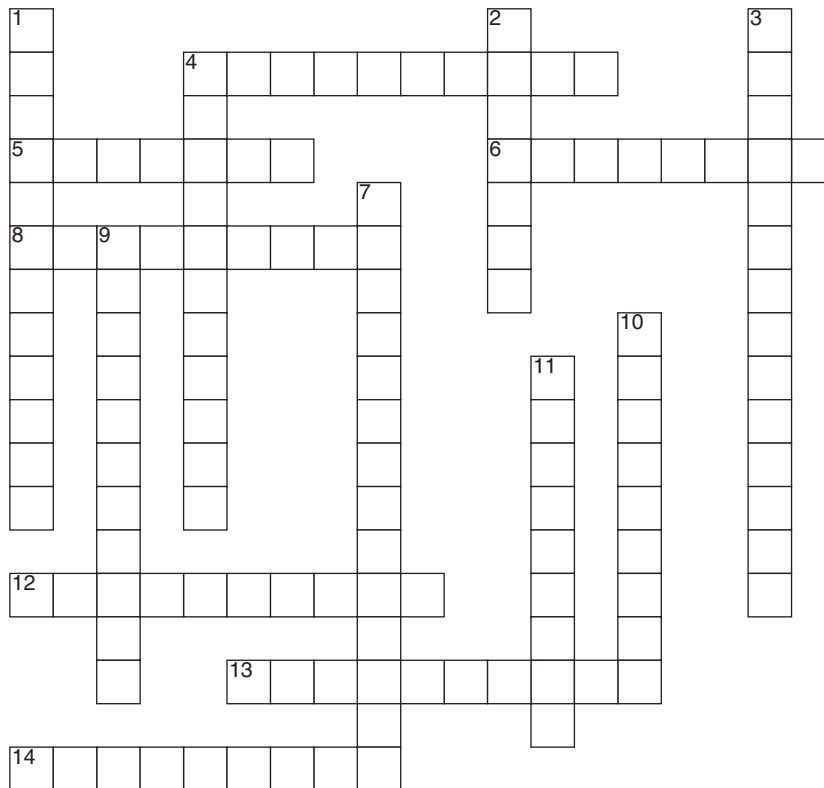
ACROSS

4 Type of cells that differentiate into mature, functional cells

5 Multiprogenitor cell capable of differentiating into leukocytes, erythrocytes, and megakaryocytes (2 abrv)

6 Gene that can transform cells into malignant cells

8 Physical manifestation of an individual's genotype

12 Describes a cell that has exited the cell cycle—nonproliferative state

13 Specialized type of paracrine signaling—cytokine is not secreted by the cell that produced it

14 Thrombocytes

DOWN

1 Lineage specific marker for erythrocytes

2 Cells of the bone marrow that include adipocytes, endothelial cells, and fibroblasts

3 Process of producing granulocytes

4 Describes characteristic in which growth factors act on more than one cell type

7 Platelets are derived from _____

9 "On top of genetics"

10 Fat cell

11 Small polypeptide that tags molecules for destruction

Introduction to Hematology—Level II

```
Col:    1  2  3  4  5  6  7  8  9 10 11 12 13 14 15 16 17 18 19 20
R1      G  .  .  .  .  .  .  .  .  .  .  S  .  .  .  .  .  .  .  G
R2      .  .  .  .  P  R  O  G  E  N  I  T  O  R  .  .  .  .  .  R
R3      .  .  .  .  L  .  .  .  .  .  .  R  .  .  .  .  .  .  .  A
R4      C  F  U  G  E  M  M  .  .  .  .  O  N  C  O  G  E  N  E  N
R5      O  .  .  .  I  .  .  .  M  .  .  M  .  .  .  .  .  .  .  U
R6      P  H  E  N  O  T  Y  P  E  .  .  A  .  .  .  .  .  .  .  L
R7      H  .  P  .  T  .  .  .  G  .  .  L  .  .  .  .  .  .  .  O
R8      O  .  I  .  R  .  .  .  A  .  .  .  .  .  A  .  .  .  .  P
R9      R  .  G  .  O  .  .  .  K  .  .  .  U  .  D  .  .  .  .  O
R10     I  .  E  .  P  .  .  .  A  .  .  .  B  .  I  .  .  .  .  I
R11     N  .  N  .  I  .  .  .  R  .  .  .  I  .  P  .  .  .  .  E
R12     A  .  E  .  C  .  .  .  Y  .  .  .  Q  .  O  .  .  .  .  S
R13     .  .  T  .  .  .  .  .  O  .  .  .  U  .  C  .  .  .  .  I
R14     Q  U  I  E  S  C  E  N  C  E  .  .  I  .  Y  .  .  .  .  S
R15     .  .  C  .  .  .  .  .  Y  .  .  .  T  .  T  .  .  .  .  .
R16     .  .  S  .  .  J  U  X  T  A  C  R  I  N  E  .  .  .  .  .
R17     .  .  .  .  .  .  .  .  E  .  .  .  N  .  .  .  .  .  .  .
R18     P  L  A  T  E  L  E  T  S  .  .  .  .  .  .  .  .  .  .  .
```

Words in the puzzle:

Across:
- PROGENITOR
- CFUGEMM
- ONCOGENE
- PHENOTYPE
- QUIESCENCE
- JUXTACRINE
- PLATELETS

Down:
- GLYCOPHORINA
- STROMAL
- GRANULOPOIESIS
- PLEIOTROPIC
- EPIGENETICS
- MEGAKARYOCYTE
- UBIQUITIN
- ADIPOCYTE