Innovative AI Applications in Hematologic Malignancies

A Comprehensive Overview of Current Applications and Future Directions

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Context and Importance

- **Hematologic malignancies:** diverse cancers affecting blood, bone marrow, and lymphatic systems
- Represent ~10% of all new cancer diagnoses worldwide
- **Traditional diagnostic methods:** time-consuming, costly, subject to variability
- AI offers unprecedented opportunities to transform blood cancer management
- Integration of AI represents a fundamental shift in clinical practice

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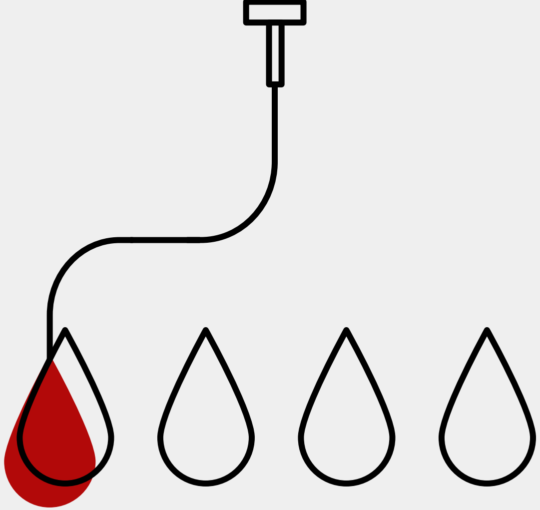
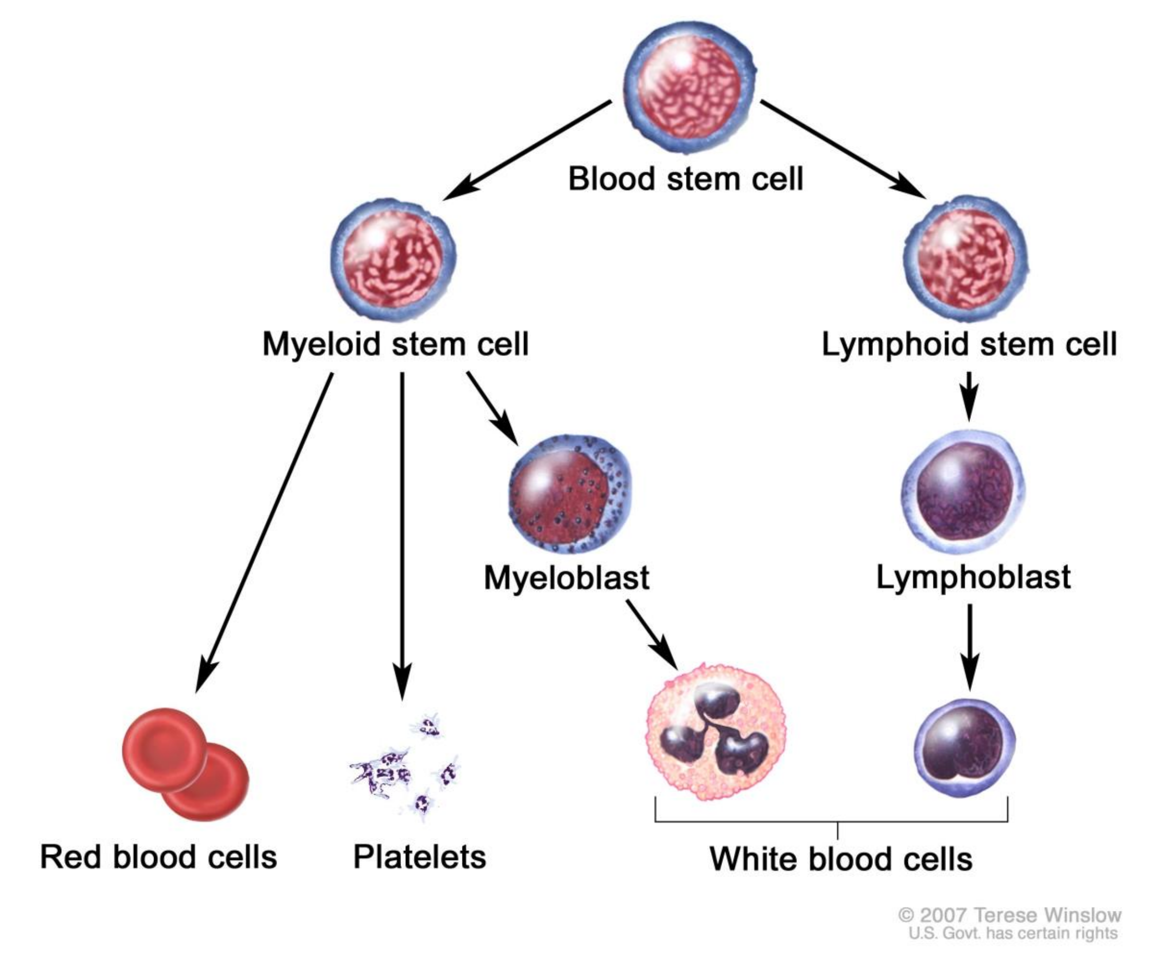


Hematological Malignancies

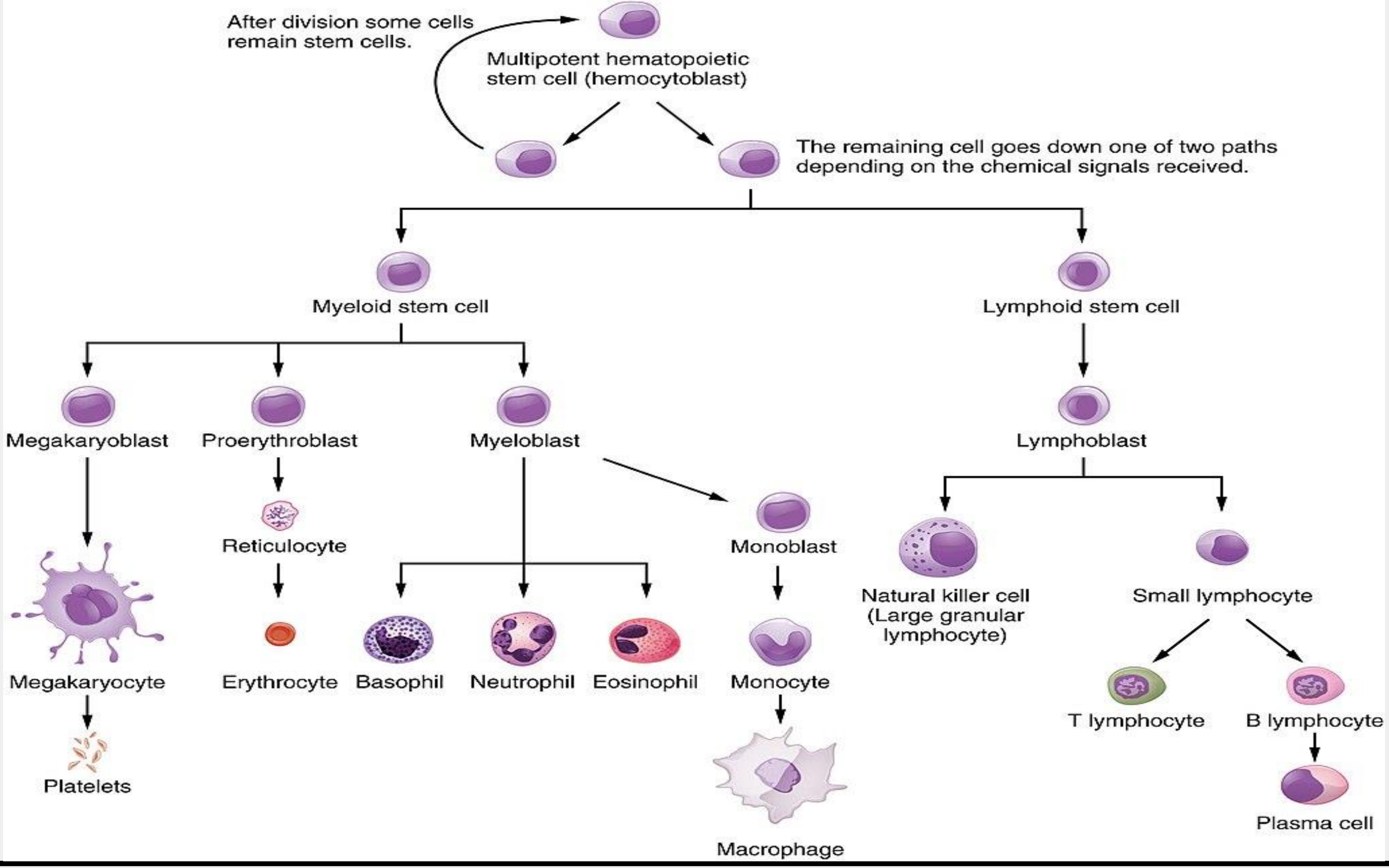
Fundamental concepts of hematology and malignancies

Hematopoiesis

Hematopoiesis is blood cell production. Your body continually makes new blood cells to replace old blood cells so you have a steady blood supply. Hematopoiesis starts before birth and continues as a cycle throughout life.



National Cancer Institute (NIH)



https://commons.wikimedia.org/

Blood Cell Imbalances

Red Blood Cells

Too Few (Anemia):
Tiredness, weakness
Tissues lack oxygen

Too Many (Erythrocytosis):
Thickens blood
Risk of heart attack or stroke

White Blood Cells

Too Few (Leukopenia):
Higher infection risk

Too Many (Leukocytosis):
Sign of infection
Possible blood disorder or cancer

Platelets

Too Few (Thrombocytopenia):
Bleeding, easy bruising

Too Many (Thrombocytosis):
Risk of blood clots

HAEMATOLOGY

COMPLETE BLOOD COUNT (CBC)

TEST		VALUE	UNIT	REFERENCE
HEMOGLOBIN		15	g/dl	13 - 17
TOTAL LEUKOCYTE COUNT		5,100	cumm	4,800 - 10,800
DIFFERENTIAL LEUCOCYTE COUNT				
NEUTROPHILS		79	%	40 - 80
LYMPHOCYTE	**L**	**18**	**%**	**20 - 40**
EOSINOPHILS		1	%	1 - 6
MONOCYTES	**L**	**1**	**%**	**2 - 10**
BASOPHILS		1	%	< 2
PLATELET COUNT		3.5	lakhs/cumm	1.5 - 4.1
TOTAL RBC COUNT		5	million/cumm	4.5 - 5.5
HEMATOCRIT VALUE, HCT		42	%	40 - 50
MEAN CORPUSCULAR VOLUME, MCV		84.0	fL	83 - 101
MEAN CELL HAEMOGLOBIN, MCH		30.0	Pg	27 - 32
MEAN CELL HAEMOGLOBIN CON, MCHC	**H**	**35.7**	**%**	**31.5 - 34.5**

https://www.labsmartlis.com/cbc-report-format

White Blood Cells

🟠 **Blood cells that are part of the immune system**

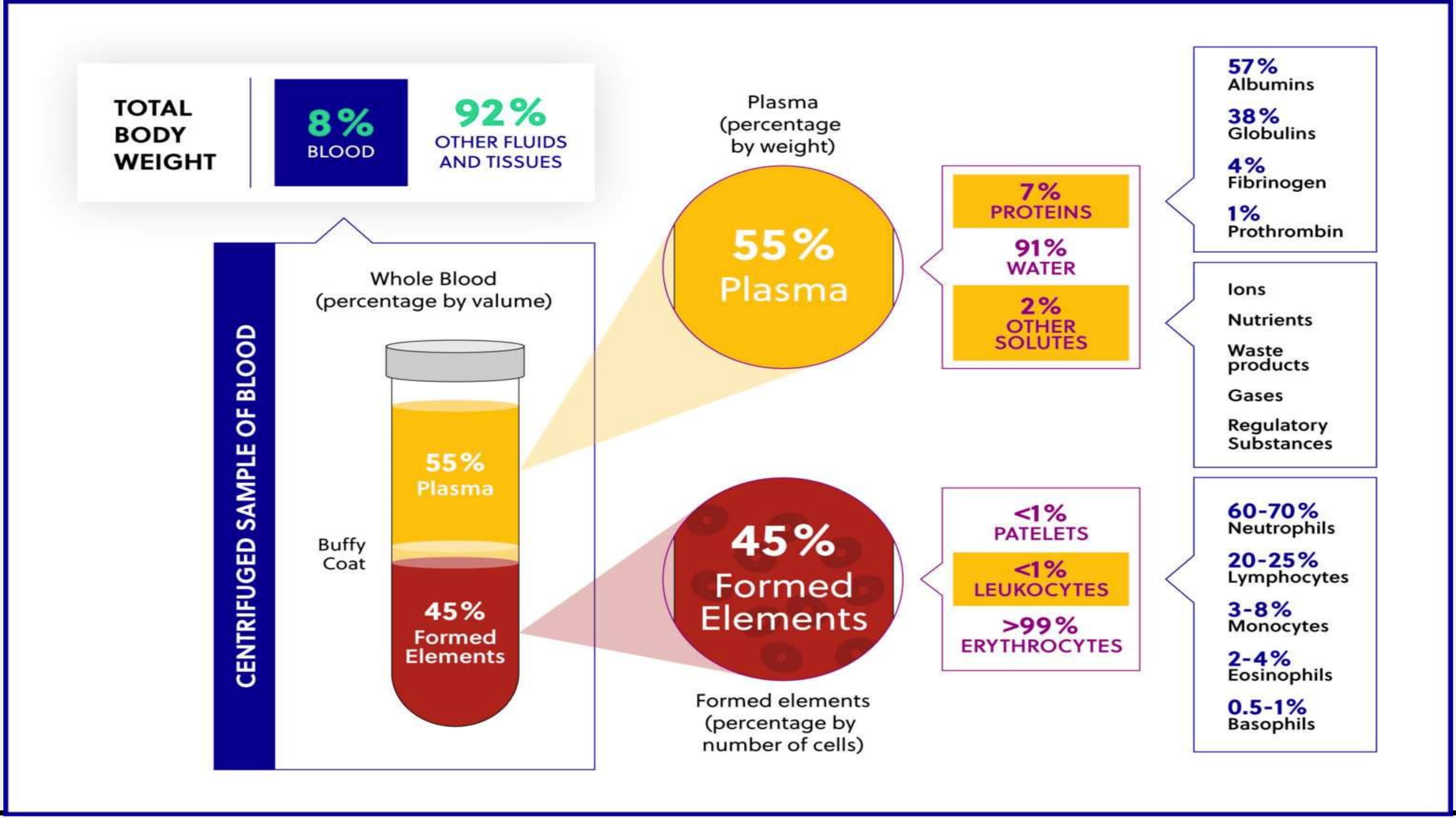
→ *defend* against foreign invaders

🤎 **Nucleated**, unlike:

→ 🔴 **RBCs** – anucleated

→ 🟣 **Platelets** – not even full cells 😄

🟢 **Derived from multipotent stem cells**


TOTAL BODY WEIGHT
8% BLOOD
92% OTHER FLUIDS AND TISSUES
CENTRIFUGED SAMPLE OF BLOOD
Whole Blood (percentage by valume)
55% Plasma
Buffy Coat
45% Formed Elements
Plasma (percentage by weight)
55% Plasma
7% PROTEINS
91% WATER
2% OTHER SOLUTES
57% Albumins
38% Globulins
4% Fibrinogen
1% Prothrombin
Ions
Nutrients
Waste products
Gases
Regulatory Substances
45% Formed Elements
Formed elements (percentage by number of cells)
<1% PATELETS
<1% LEUKOCYTES
>99% ERYTHROCYTES
60-70% Neutrophils
20-25% Lymphocytes
3-8% Monocytes
2-4% Eosinophils
0.5-1% Basophils

WBC Count & Classification

🧪 **Normal WBC count:** *4,000 – 11,000 cells/μL*

- 🔴 Compared to **RBCs:** *4–5 million/μL!*
- 📍 WBCs make up only **1%** of total blood cell population
- ✨ Critical part of the **"Immune System"**

Clinical Ranges

- 📉 **< 4,000** → *Leukopenia*
- 📈 **> 11,000** → *Leukocytosis*

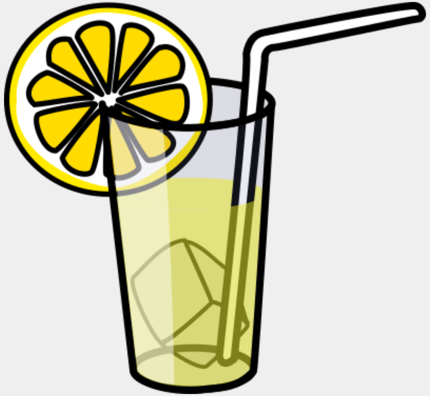
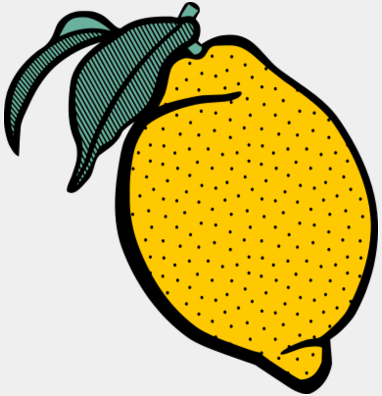
Classification

🧬 **By Structure:**

- **Granulocytes**
- **Agranulocytes**

🧫 **By Cell Lineage:**

- **Myeloid**
- **Lymphoid**

Leukemia	Lymphoma
Blood & bone marrow involvement.	Lymph nodes, MALT, spleen, bone marrow.
	
Some leukemias have a lymphoma component.	Many lymphomas have small leukemia components.

Can you distinguish them under the microscope?

❌ Non, impossible!

✅ You need flow cytometry

Flow cytometry detects "clusters of differentiation" (CD markers)

🔷 Cell Types & Markers

🔶 **Natural Killer (NK) Cells :** CD16, CD56

🔶 **T-Cells**

- **T-helper cells:** CD3, CD4
- **T-cytotoxic cells:** CD3, CD8

🔶 **B-Cells:** MHC II, CD19, CD20

Hematological Malignancies

Leukemia

- ALL
- AML
- CLL
- CML

Lymphomas

- Hodgkin's
- Non-Hodgkin

Myeloma

- Multiple Myeloma

⚠️ Incidence Trends:

- More common in adults than in children
- Males > Females

🧬 ALL (Acute Lymphoblastic Leukemia)

- Most common leukemia overall
- Most common cancer in children

Age Group	Likely Leukemia Type
Newborn – 14 years	**ALL**
40 – 60 years	**AML** or **CML**
Over 60 years	**CLL**

Young patients | Blasts >10%

- Early block in cell maturation
- Cells are immature “**blasts**”

Leukemia

Acute

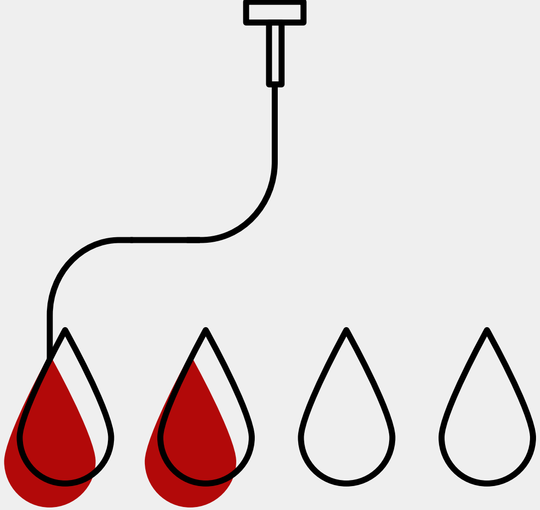
- **ALL** (Acute Lymphoblastic Leukemia)
- **AML** (Acute Myeloid Leukemia)

Chronic

- **CML** (Chronic Myeloid Leukemia)
- **CLL** (Chronic Lymphocytic Leukemia)

Older patients | Blasts <10%

- Late block in maturation
- Cells more mature “**-cytes**”



Overview of AI & its applications in Blood Malignancies

Fundamental concepts of AI in healthcare and blood malignancies

Definition of AI and Its Subsets

Artificial Inteligence simulation of human intelligence in machines

Machine Learning systems that learn from data and improve with experience

Deep Learning neural networks with multiple layers for complex pattern recognition

Natural Language Processing enables interaction between computers and human language

Computer Vision combines image processing with deep learning for visual analysis

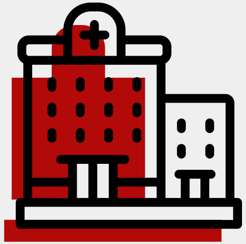
Types of AI Approaches in Healthcare

Supervised Learning	Used for classification and diagnosis
Unsupervised Learning	Identifies patterns and structures
Transfer Learning	Valuable for medical imaging
Reinforcement Learning	Optimizes treatment protocols

AI Applications in blood Malignancies …

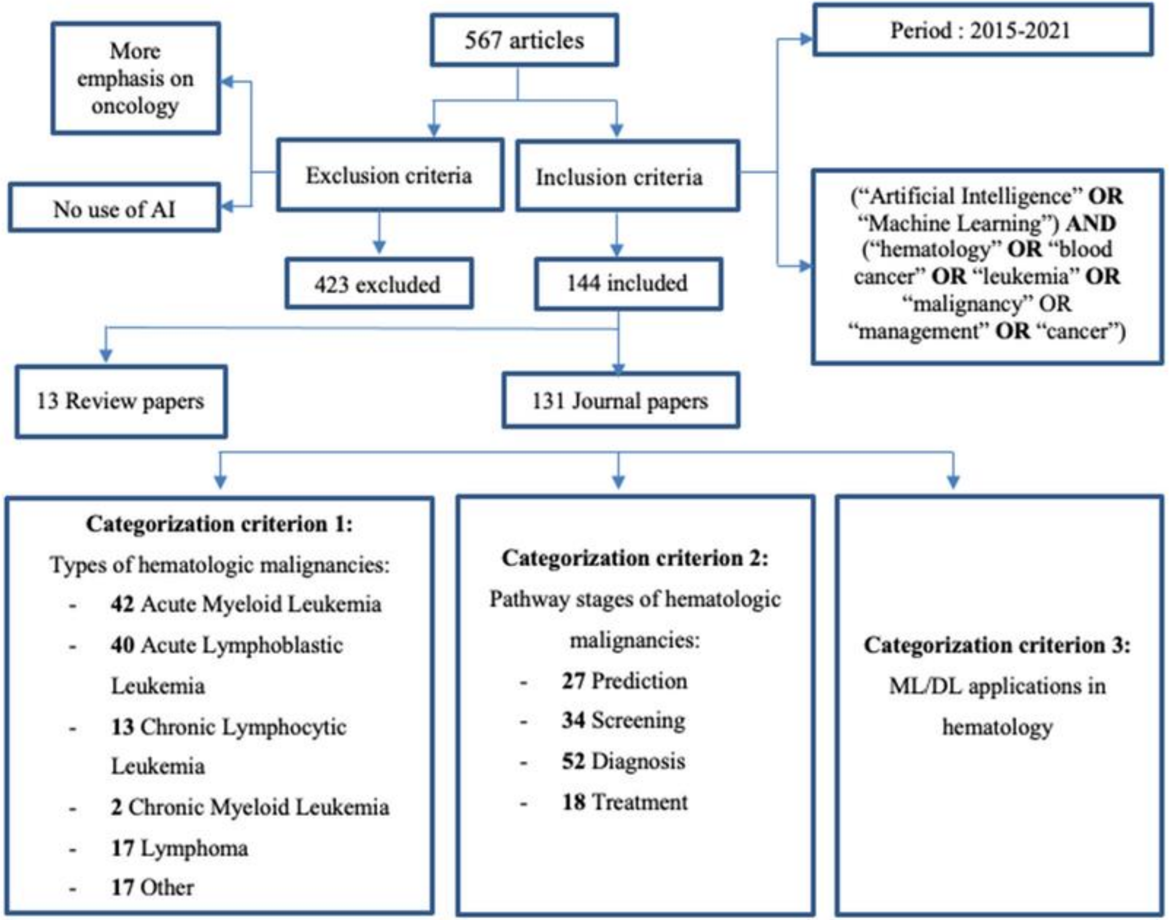
- Diagnostics
- Prognostics
- Treatment

AI Applications in Diagnostics



Lets go...
AI is going to prepare for using in smart hospitals.

Figure 1: Categorization of AI applications in hematologic malignancies by type and pathway stage. Source: El Alaoui et al., 2022



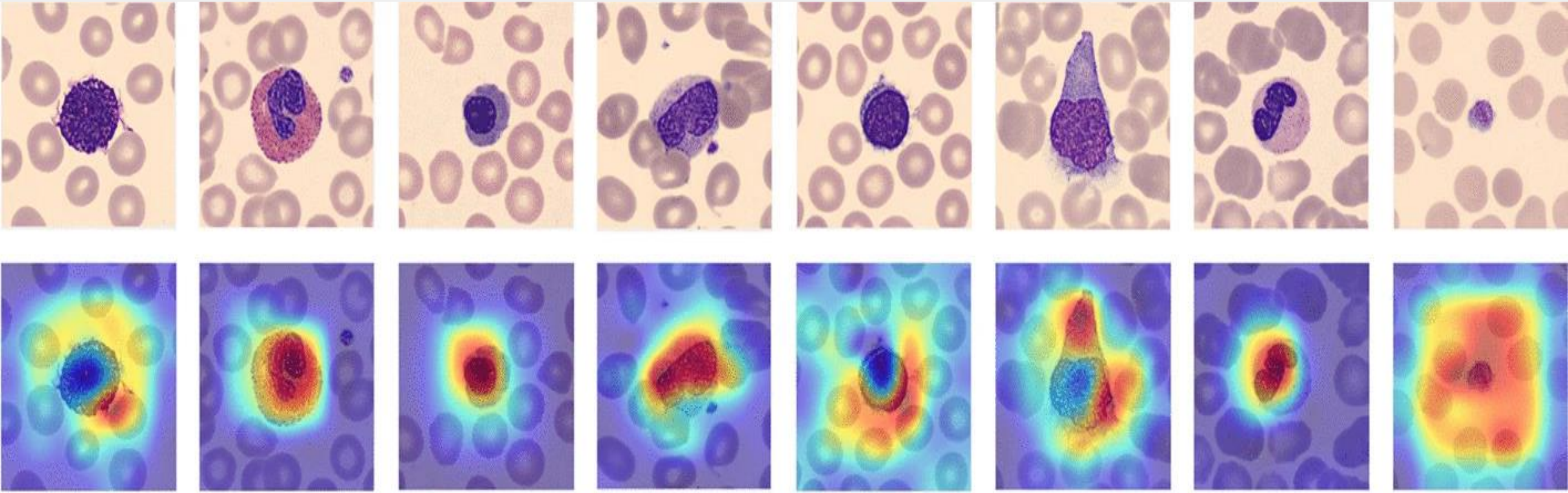
Challenges in Traditional Diagnostic Methods

- Labor-Intensive Processes
- Inter-Observer Variability
- Limited Standardization
- Diagnostic Delays
- Resource Constraints
- Integration Challenges

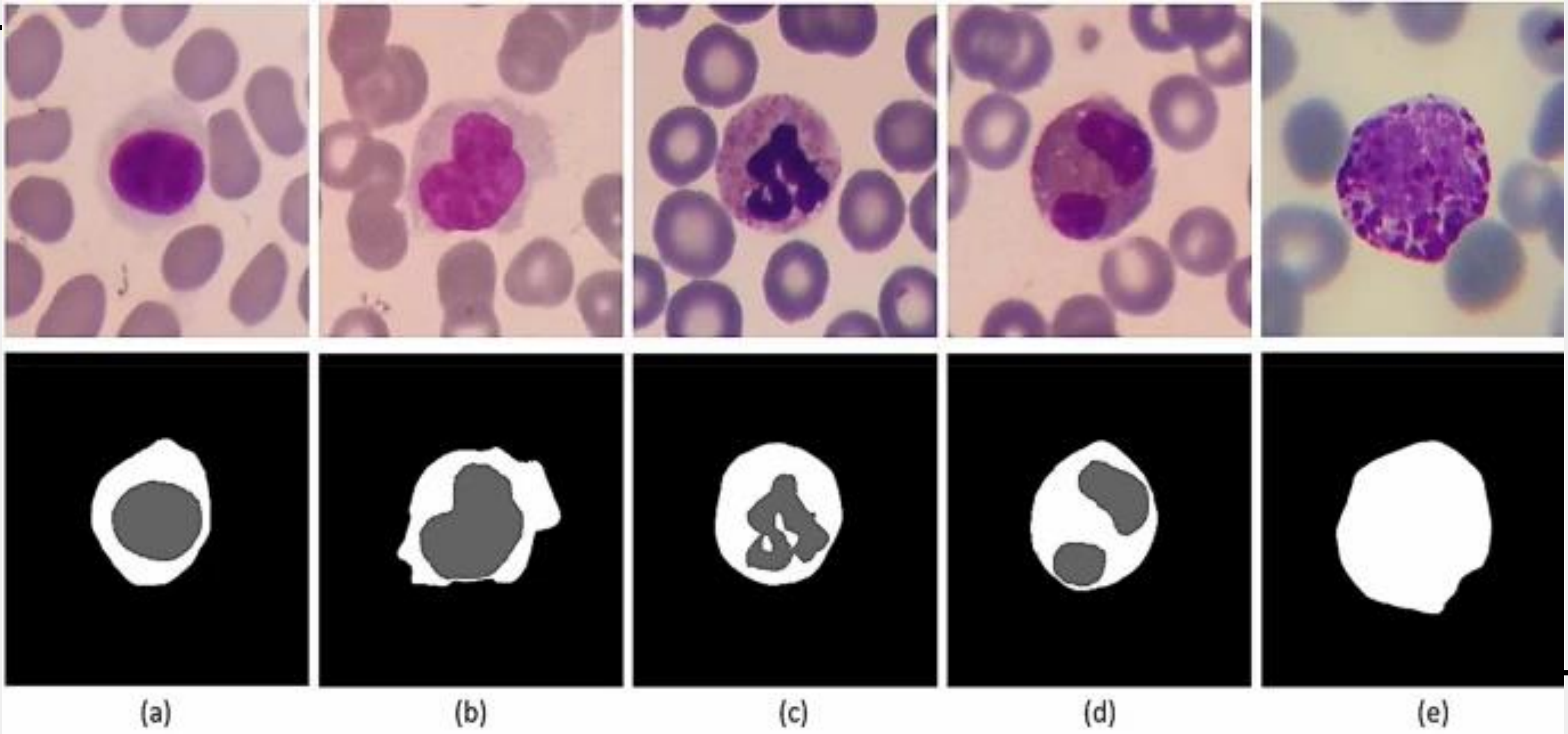
AI Solutions in Diagnostic Methods

Labor-Intensive Processes	Automated Image Analysis
Inter-Observer Variability	Robust algorithms
Limited Standardization	Standardized algorithms
Diagnostic Delays	Real-time analysis
Resource Constraints	Resource optimization
Integration Challenges	Seamless integration

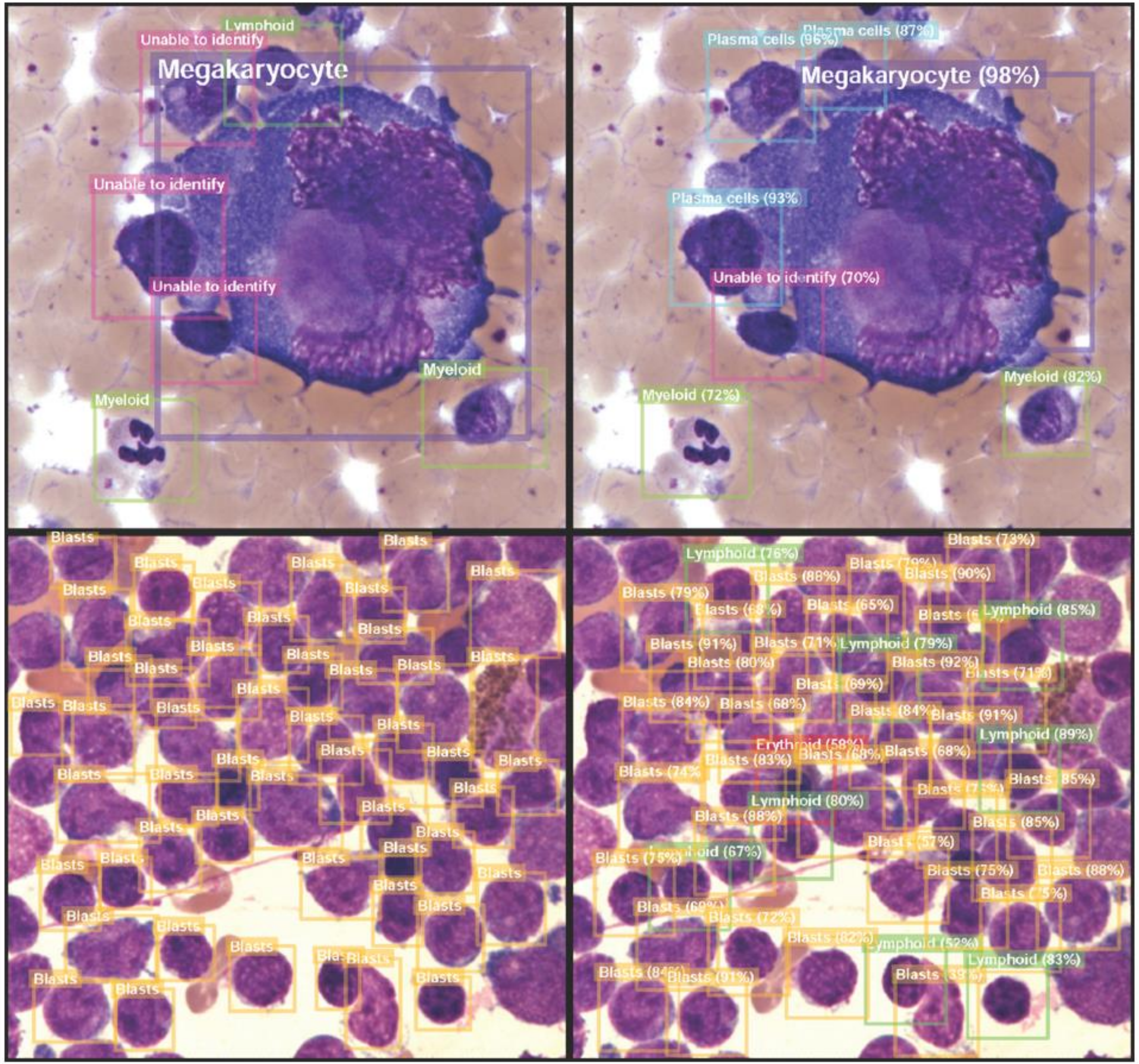
Automated Cell Differentiation



ConcatNeXt: An automated blood cell classification with a new deep convolutional neural network

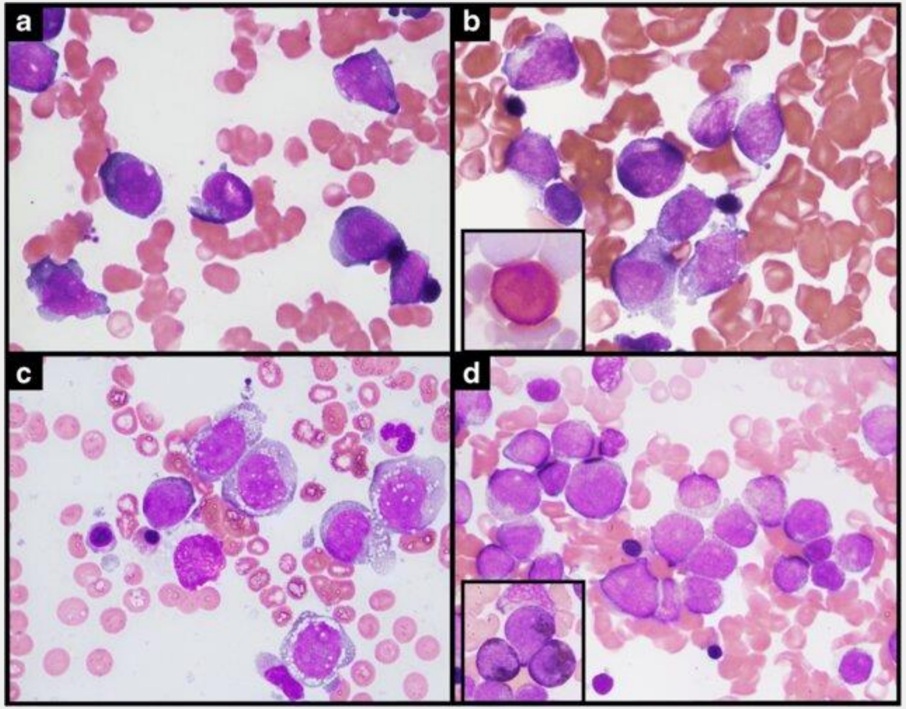


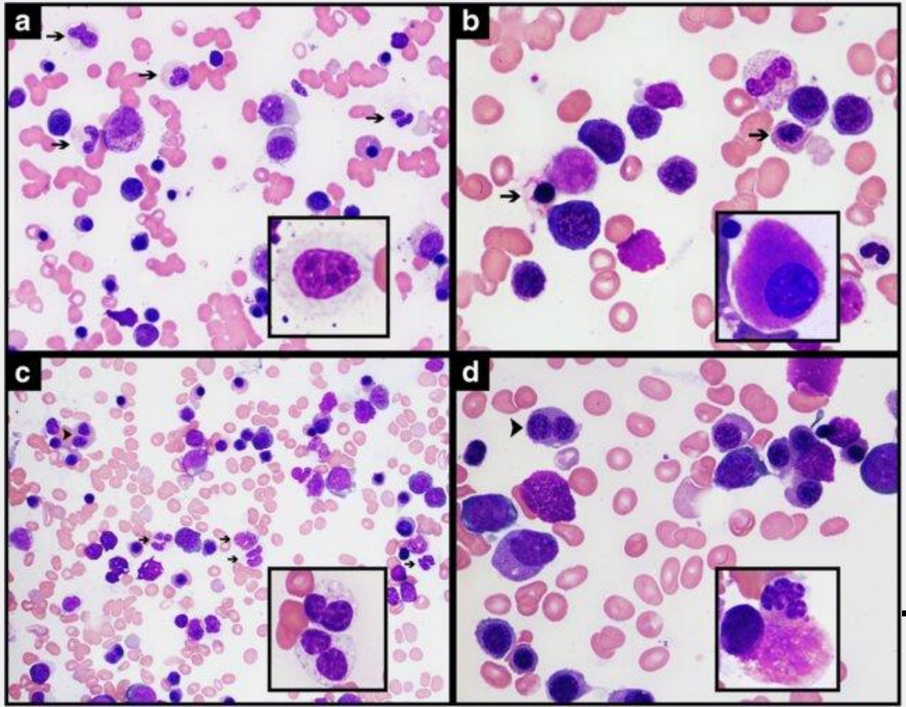
A large dataset of white blood cells containing cell locations and types, along with segmented nuclei and cytoplasm



A large dataset of white blood cells containing cell locations and types, along with segmented nuclei and cytoplasm

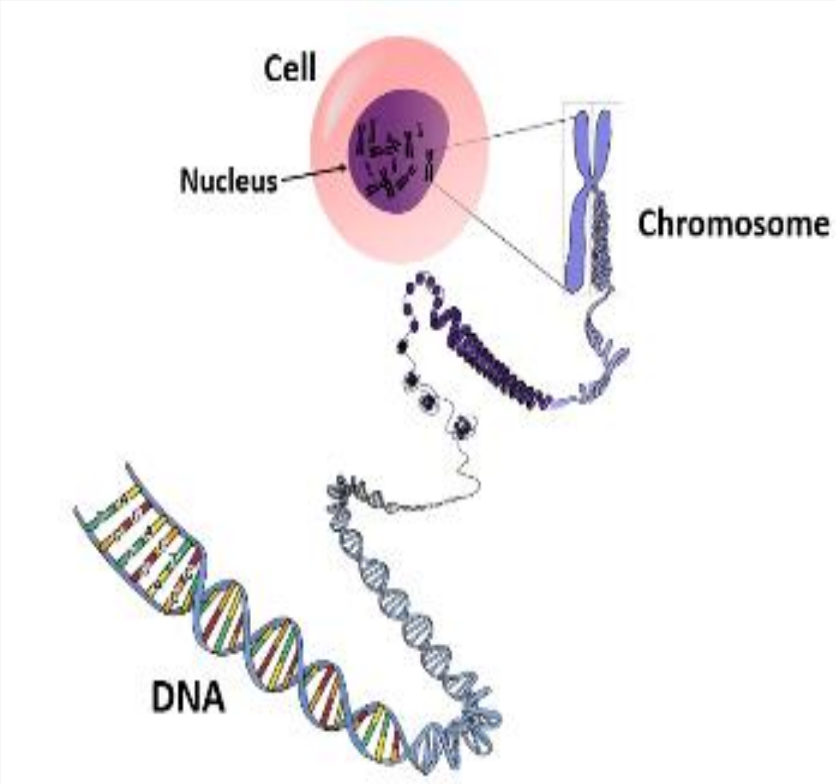
Detection of Malignant Cells



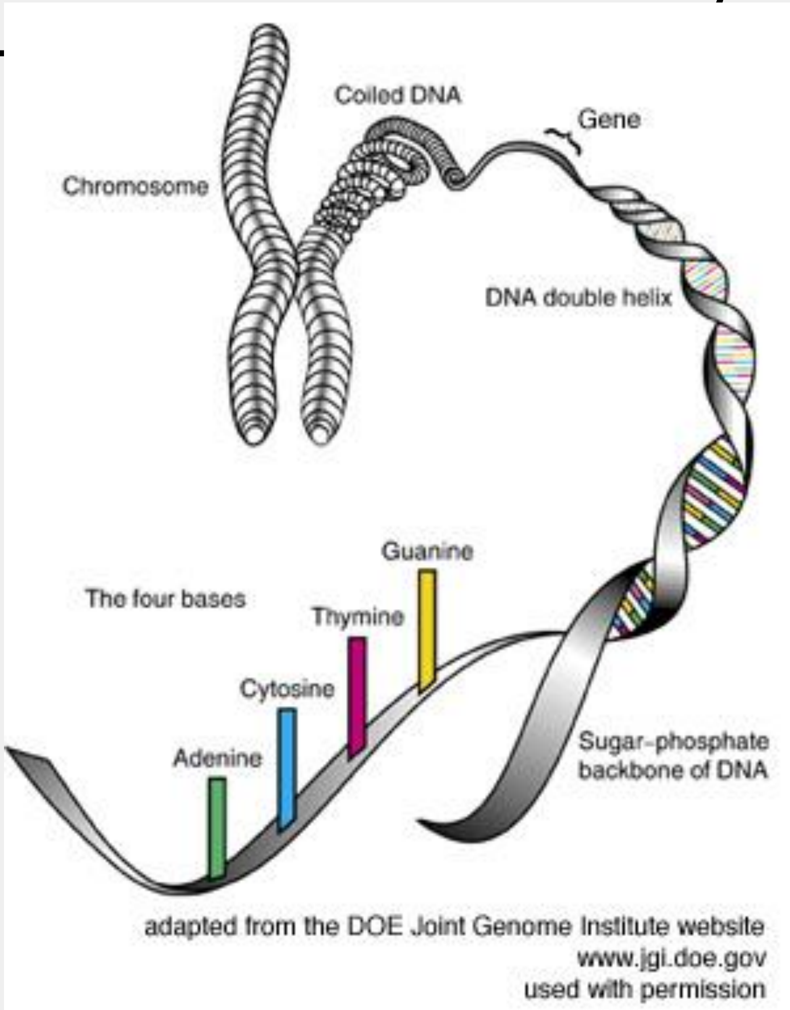


t(11;16)(q23;p13)/*KMT2A-CREBBP* in hematologic malignancies: presumptive evidence of myelodysplasia or therapy-related neoplasm?

Genomic Analysis and Mutation Detection

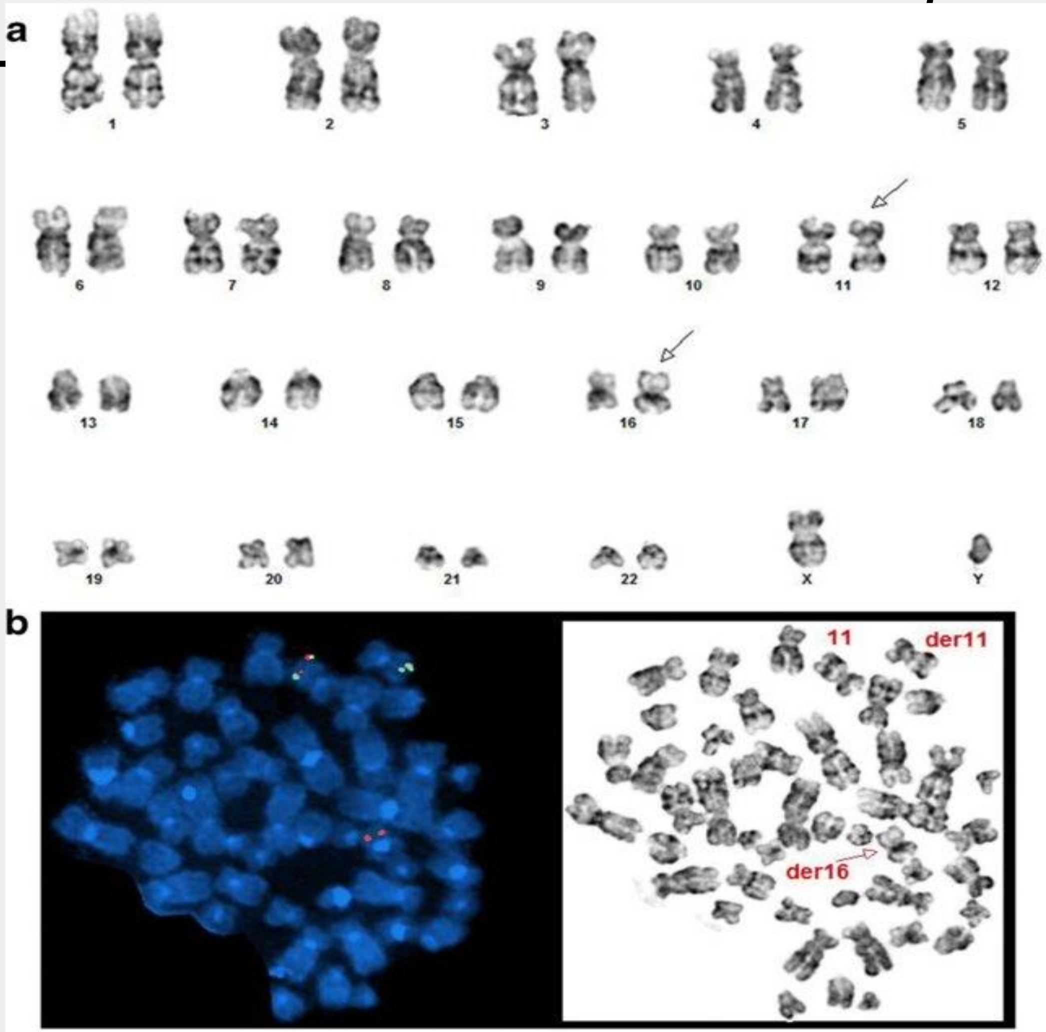


National Center for Biotechnology Information (US).



Chromosomal Abnormality Identification

- Automated karyotyping
- Detection of subtle aberrations
- Integration with FISH and molecular data



National Center for Biotechnology Information (US).

AI Applications in Prognostics

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Predictive Models for Disease Progression

Risk Stratification Algorithms

- Provide dynamic risk assessments that evolve over time

- Create personalized risk profiles beyond conventional categories

Relapse Prediction Models

- blood malignancies outcome prediction incorporating novel parameters

- Early molecular relapse detection before clinical manifestation

Survival Prediction and Complication Detection

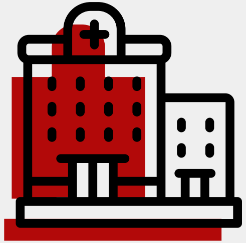
Multi-Modal Data Integration

- Imaging-based prognostication
- Multi-omics integration
- Ensemble approaches for superior accuracy
- Validation across diverse populations

Treatment Complication Prediction

- infection risk prediction
- Chemotherapy toxicity models
- Transplant-related mortality prediction
- Cardiotoxicity risk assessment
- Neurotoxicity prediction for CAR-T therapy

AI Applications in Treatment



Lets go...
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AI-Driven Treatment Selection

Predicting Response to Chemotherapy

- Analysis of patient-specific factors for response prediction
- Identification of resistance patterns
- Combination therapy selection
- Real-time adaptation of treatment recommendations

Determining Optimal Treatment Intensity

- Risk-adapted therapy guidance
- Frailty assessment for elderly patients
- Transplant eligibility prediction

Decision Support and Precision Medicine

Clinical Decision Support

- Comprehensive donor matching
- GVHD risk prediction
- Optimal treatment sequencing
- Clinical trial matching

Multi-Omics Integration

- Genomic-guided therapy
- Transcriptomic analysis
- Proteomic integration
- Metabolomic profiling
- Epigenetic mapping
- Integrative analysis platforms

Transforming Hematologic Oncology with AI

🔬 Diagnosis

- AI enhances precision in detecting blood cancers by automating blast identification, dysplasia detection, and cytogenetic analyses.

📈 Risk Prediction

- AI models identify complex patterns to predict relapse, treatment complications, and survival.

Transforming Hematologic Oncology with AI

💊 Treatment

- Machine learning optimizes chemotherapy selection and intensity based on patient-specific data.

🧩 Overall Impact

- AI bridges diagnostic, prognostic, and therapeutic domains.
- It supports clinical decision-making, improves efficiency, and fosters precision medicine in hematologic malignancies.

Papers Review

Review some beneficial studies on this field

Article | Open access | Published: 07 August 2017

Machine learning applications for prediction of relapse in childhood acute lymphoblastic leukemia

Liyan Pan, Guangjian Liu, Fangqin Lin, Shuling Zhong, Huimin Xia, Xin Sun & Huiying Liang

Scientific Reports **7**, Article number: 7402 (2017) | Cite this article

Objectives or Aims

What problem does it solve?

- Current prognostic models are insufficient for accurately predicting relapse.

Research Question:

- Can machine learning algorithms predict relapse in childhood ALL using clinical variables?

Study Aim:

- To construct and validate a relapse prediction model for childhood ALL based on machine learning techniques applied to clinical data.

Methods

Data Type and Size:

- Clinical data from 336 newly diagnosed ALL children for training.
- An independent test set of 84 patients for validation.

Machine Learning Models Used:

- Random Forest (RF) algorithm was employed to build the prediction model.

Validation Methods:

- Monte Carlo cross-validation nested within 10-fold cross-validation for feature ranking.
- An independent dataset was used to evaluate model performance.

Results

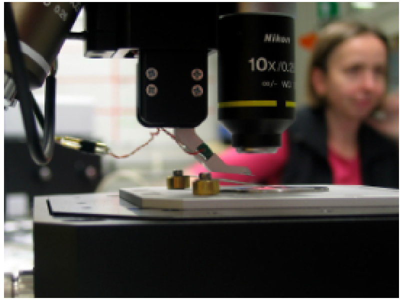
Key Findings:

- The Random Forest model with 14 selected features achieved:
  - **Cross-validation accuracy:** 82.7% ± 3.1%
  - **Independent test set accuracy:** 79.8%
  - **Area Under the Curve (AUC):** 0.902 ± 0.027 (cross-validation), 0.904 (test set)

Significant Predictors:

- Features such as white blood cell count, age at diagnosis, and minimal residual disease levels were among the top predictors.

Published on 08.04.2020 in Vol 8, No 4 (2020): April



A Hematologist-Level Deep Learning Algorithm (BMSNet) for Assessing the Morphologies of Single Nuclear Balls in Bone Marrow Smears: Algorithm Development

Yi-Ying Wu[1]; Tzu-Chuan Huang[1]; Ren-Hua Ye[1]; Wen-Hui Fang[2]; Shiue-Wei Lai[1]; Ping-Ying Chang[1]; Wei-Nung Liu[1]; Tai-Yu Kuo[1]; Cho-Hao Lee[1]; Wen-Chiuan Tsai[3]; Chin Lin[4, 5]

Objectives or Aims

What problem does it solve?

- The study aims to develop a deep learning model to assist in interpreting bone marrow smears, enhancing diagnostic efficiency and consistency.

Research Question:

- Can a deep learning model match hematologist-level performance in interpreting bone marrow smears?

Study Aim:

- To develop and validate BMSNet, a deep learning model for detecting and classifying hematopoietic cells in bone marrow smears.

Method

Data Type and Size:

- 122 bone marrow smears photographed from January 2016 to December 2018.
- Development cohort: 42 smears with 17,319 annotated cells.
- Validation cohort: 70 smears.
- Competition cohort: 10 smears.

AI/ML Models Used:

- BMSNet: A convolutional neural network based on YOLO v3 architecture for detecting and classifying single cells.

Results

Key Findings:

- BMSNet achieved an average precision of 67.4% for bounding box prediction.
- **In detecting >5% blasts in the validation cohort:**
  - BMSNet AUC: 0.948
  - Hematologists AUC: 0.929
  - Pathologists AUC: 0.985
- **In detecting >20% blasts:**
  - BMSNet AUC: 0.942
  - Hematologists AUC: 0.981
  - Pathologists AUC: 0.980

Article | Open access | Published: 16 March 2020

Artificial Intelligence based Models for Screening of Hematologic Malignancies using Cell Population Data

Shabbir Syed-Abdul, Rianda-Putra Firdani, Hee-Jung Chung, Mohy Uddin, Mina Hur, Jae Hyeon Park, Hyung Woo Kim, Anton Gradišek & Erik Dovgan

Scientific Reports **10**, Article number: 4583 (2020) | Cite this article

Objectives or Aims

What problem does it solve?

- Traditional diagnostic methods can be time-consuming and may lack sensitivity.
- The study explores the use of AI to enhance screening processes, aiming for quicker and more accurate detection of blood cancers.

Research Question:

- Can machine learning algorithms effectively screen for hematologic malignancies using Cell Population Data (CPD)?

Study Aim:

- To develop and evaluate AI-based models that utilize CPD for the screening of hematologic malignancies, potentially improving diagnostic accuracy and efficiency.

Methods

Data Type and Size:

- Utilized CPD from routine Complete Blood Count (CBC) tests.
- Total of 882 cases: 457 with hematologic malignancies and 425 without.

AI/ML Models Used:

- Seven machine learning algorithms were tested:
  - Stochastic Gradient Descent (SGD) --- Support Vector Machine (SVM)
  - Random Forest (RF) --- Decision Tree (DT)
  - Linear Model --- Logistic Regression
  - Artificial Neural Network (ANN)

Results

Key Findings:

- The Artificial Neural Network (ANN) model outperformed other algorithms.
- ANN achieved:
  - Accuracy: 82.8%
  - Precision: 82.8%
  - Recall: 84.9%
  - Area Under the Curve (AUC): 93.5% ± 2.6

Utilizing CPD, which is readily available from routine blood tests, can facilitate early detection without additional testing.

ELSEVIER

Leukemia Research

Volume 109, October 2021, 106639

A machine learning approach to predicting risk of myelodysplastic syndrome

Ashwath Radhachandran [1], Anurag Garikipati, Zohora Iqbal [1],
Anna Siefkas, Gina Barnes, Jana Hoffman, Qingqing Mao, Ritankar Das

Objectives or Aims

What problem does it solve?

- MDS is often underdiagnosed and recognized late.
- This study presents a machine learning model that uses routine EHR data to predict MDS one year before clinical diagnosis.

Research Question:

- Can we accurately predict the risk of developing MDS using non-specialized, routinely collected EHR data?

Aim of the Study:

- Develop and validate a machine learning algorithm (MLA) to predict MDS risk without needing bone marrow data or genetic testing.
- Enable early detection and potential timely intervention for high-risk patients.

Methods

Dataset:

- Retrospective cohort of **790,470 patients**, aged 45+, across 700+ US healthcare sites (2007–2020).
- **Data includes:**
  - Demographics (age, sex)
  - Vital signs (HR, BP, SpO_2, temp, etc.)
  - Lab values (CBC, metabolic panel, etc.)
  - Diagnosis codes (ICD-9/10)

Models Used:

- XGBoost , Logistic Regression (LR) , Artificial Neural Network (ANN)

Results

Temporal validation:

- Train set: 2007–2017.
- Test set: 2018–2020.

Limitation :

- Retrospective design (potential EHR biases).
- Generalizability to non-U.S. populations untested.

Model	AUROC (±SD)	Sensitivity	Specificity
XGBoost	**0.87**	79%	80%
Logistic Regression	0.838	75%	77%
ANN	0.832	74%	76%

Open Access Article

An Efficient Multi-Level Convolutional Neural Network Approach for White Blood Cells Classification

by César Cheuque [1], Marvin Querales [2], Roberto León [1], Rodrigo Salas [3,4] and Romina Torres [1,4,*]

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[2] Escuela de Tecnología Médica, Universidad de Valparaíso, Viña del Mar 2540064, Chile

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[4] Instituto Milenio Intelligent Healthcare Engineering, Valparaíso 2362905, Chile

[*] Author to whom correspondence should be addressed.

Diagnostics **2022**, *12*(2), 248; **https://doi.org/10.3390/diagnostics12020248**

Submission received: 30 November 2021 / Revised: 17 December 2021 / Accepted: 28 December 2021 / Published: 20 January 2022

Objectives or Aims

Research Question:

- Can a multi-level convolutional neural network (CNN) effectively classify different types of white blood cells in peripheral blood smear images?

Study Aim:

- To develop and evaluate a two-stage hybrid multi-level CNN model that classifies WBCs into four categories: lymphocytes, monocytes, neutrophils, and eosinophils.

What problem does it solve?

- The study addresses the need for an automated, efficient, and accurate method to classify WBCs, reducing reliance on manual processes and improving diagnostic consistency.

Methods

Data Type and Size:

- Peripheral blood smear images containing various WBCs.

AI/ML Models Used:

- A two-stage hybrid model:
    - **Stage 1:** Faster R-CNN for detecting regions of interest and separating mononuclear from polymorphonuclear cells.
    - **Stage 2:** Two parallel CNNs with MobileNet architecture for subclass classification.

Results

Model Performance :

- Accuracy: 96.5%.
- Precision: 96.2%.
- Recall: 96.0%.
- F1-Score: 96.1%.

Key Findings:

- The proposed model achieved high classification accuracy across all four WBC types.
- Demonstrated improved performance over traditional single-level classification models.

Conclusion

Discuss important topics and current challenges in this field

- Technical Infrastructure Requirements
- Clinician Adoption Barriers
- Cost-Effectiveness Considerations

Integration Challenges

Areas Needing Further Investigation

- Rare hematologic malignancies
- Pediatric applications
- Treatment sequencing optimization
- Enhanced MRD detection
- Explainable AI for clinical adoption

Summary of Key Points

- AI is enhancing diagnostic precision in hematologic malignancies
- Prognostic models are becoming more sophisticated and accurate
- Treatment personalization is advancing through AI applications
- Implementation is progressing despite remaining challenges
- Ethical considerations are paramount for responsible development
- The future holds promising technologies and approaches

Questions & Discussion

Thank you for your attention!

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Urmia University of Medical Sciences

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