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PPT Presentation

Signature Role of miRNA in Cell and Therapeutic Value in the Treatment of Acute Myeloid Leukemia(AML)

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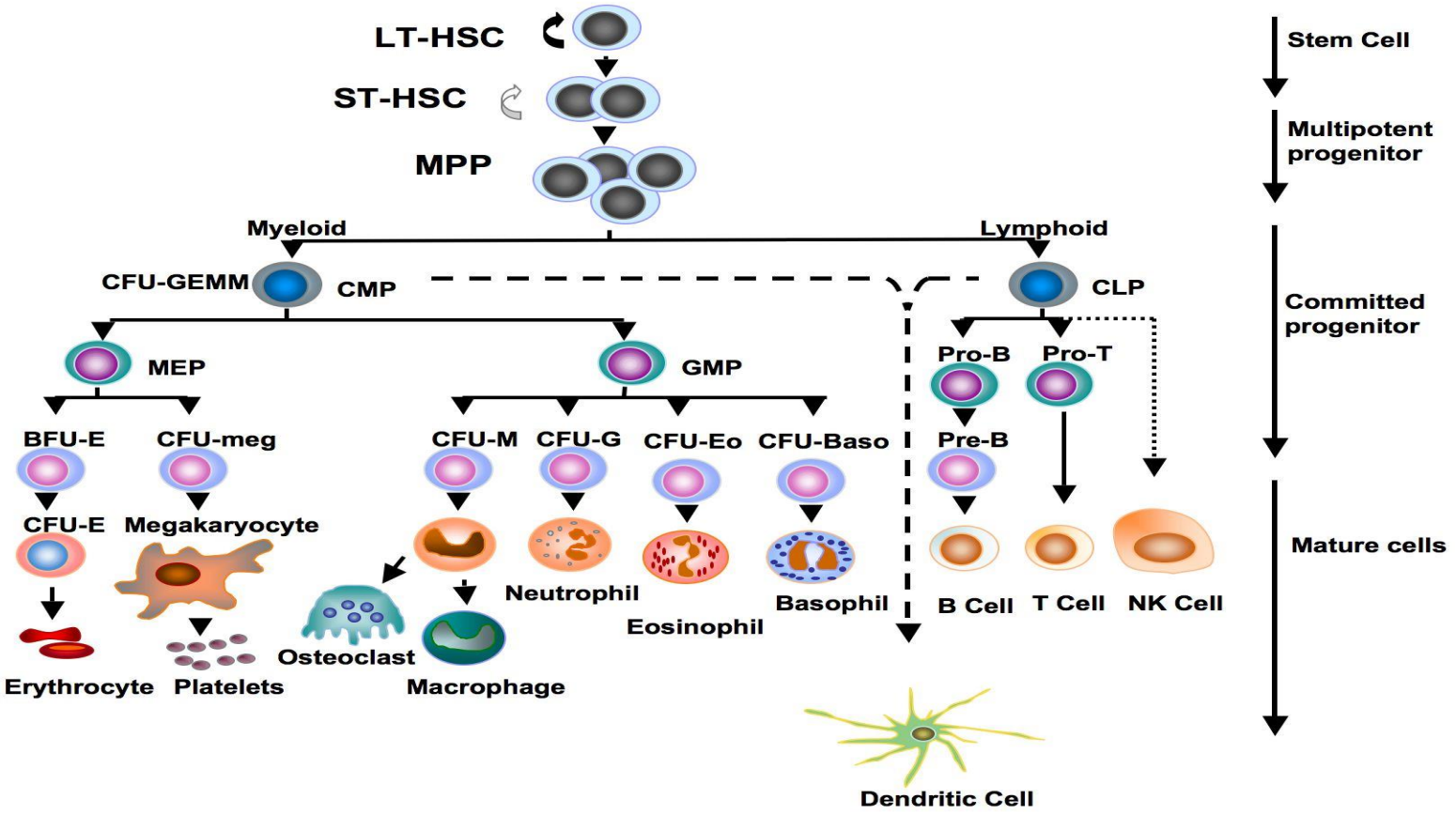
What is Cancer

- Cancer is characterized by the uncontrolled growth and spread of abnormal cells. If the spread remains unchecked, It may spread to other parts of the body.
- It may lead to death.

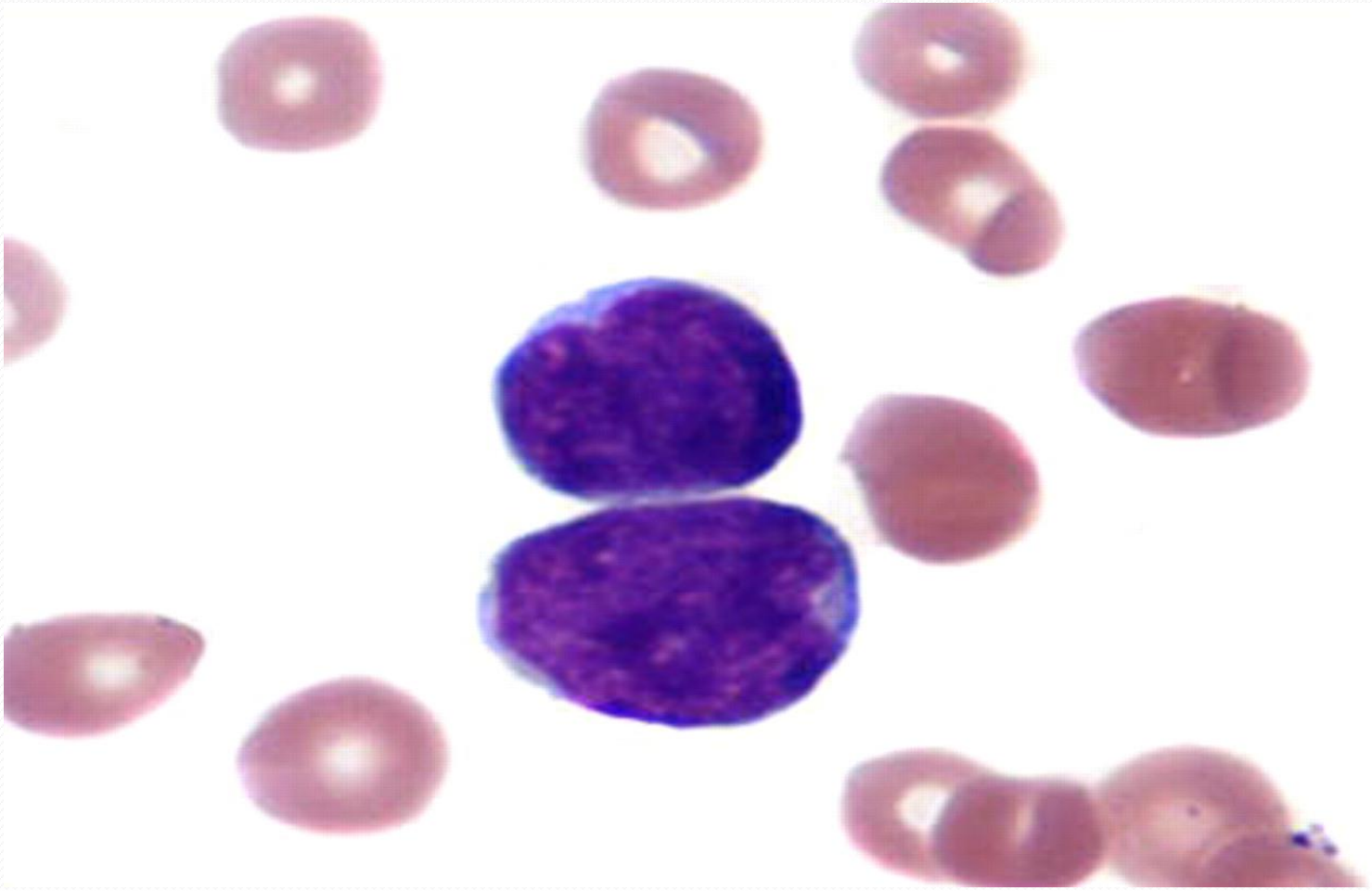
What is Acute Myeloid Leukemia(AML)

- Malignant clonal disorder of immature myeloid progenitor cells characterized by clonal proliferation of abnormal blast cells and impaired production of normal blood cells
- Leukemic blasts may express capabilities for maturation to a variable degree, that lead to morphological heterogeneity

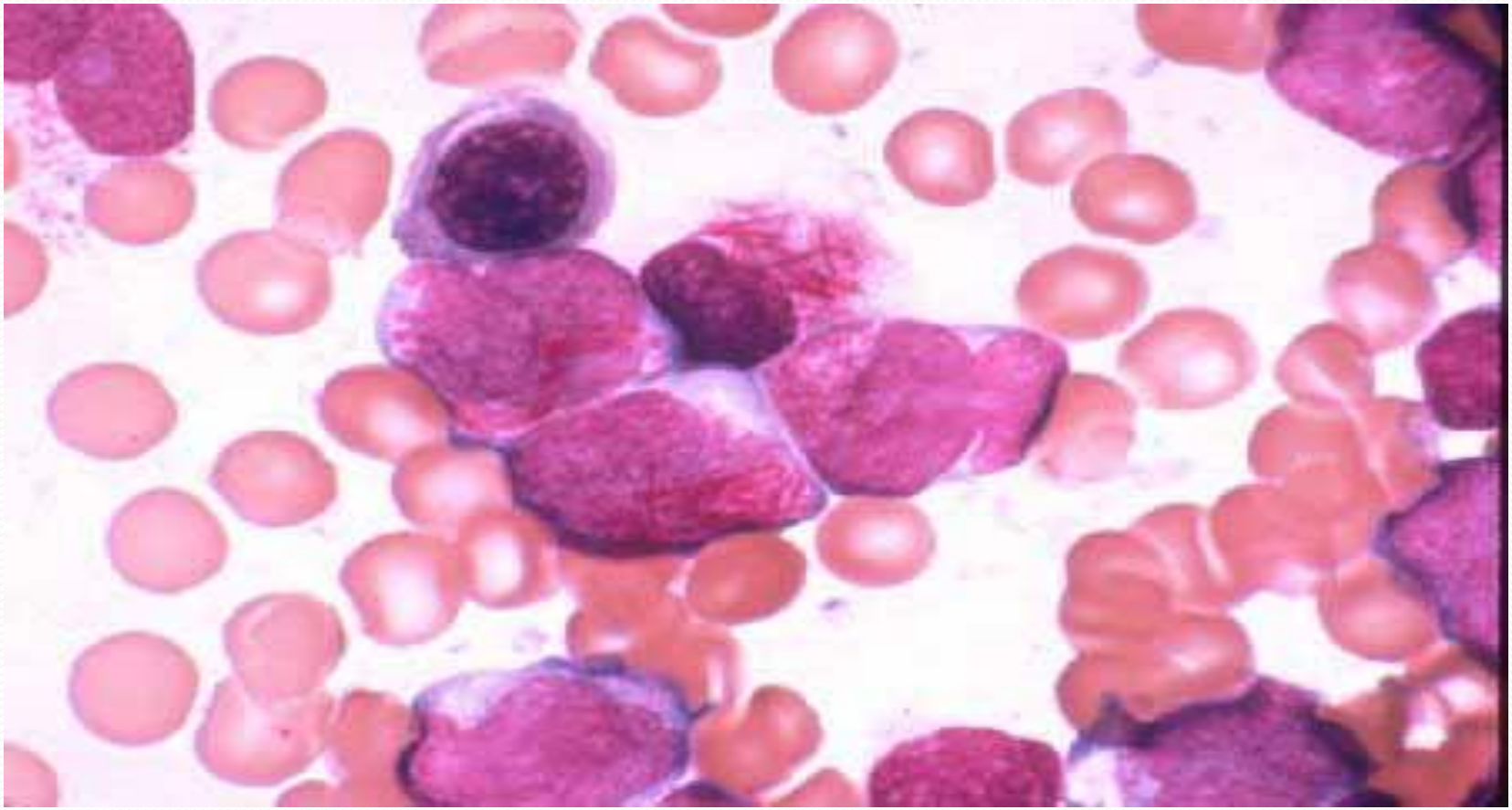
Blood Cell Formation



AML with Minimal Differentiation



Acute Leukemia: Blasts with Auer Rods



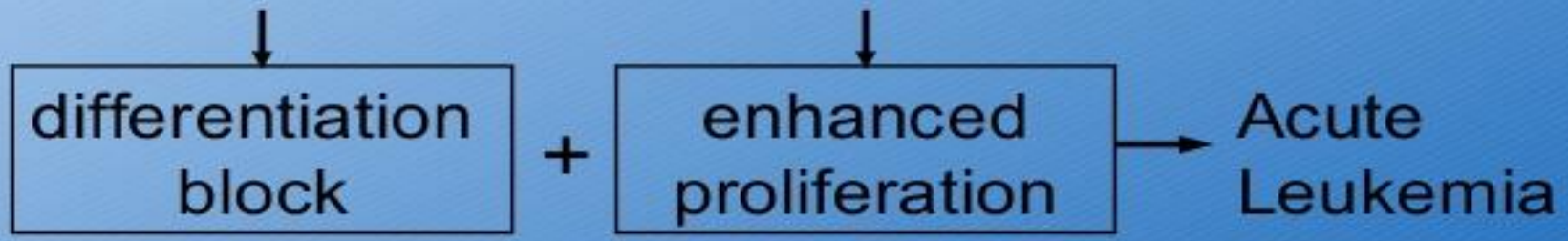
Two-hit model of leukemogenesis

Loss of function of transcription factors needed for differentiation

eg. AML1-ETO
CBFβ-SMMHC
PML-RARα

Gain of function mutations of tyrosine kinases

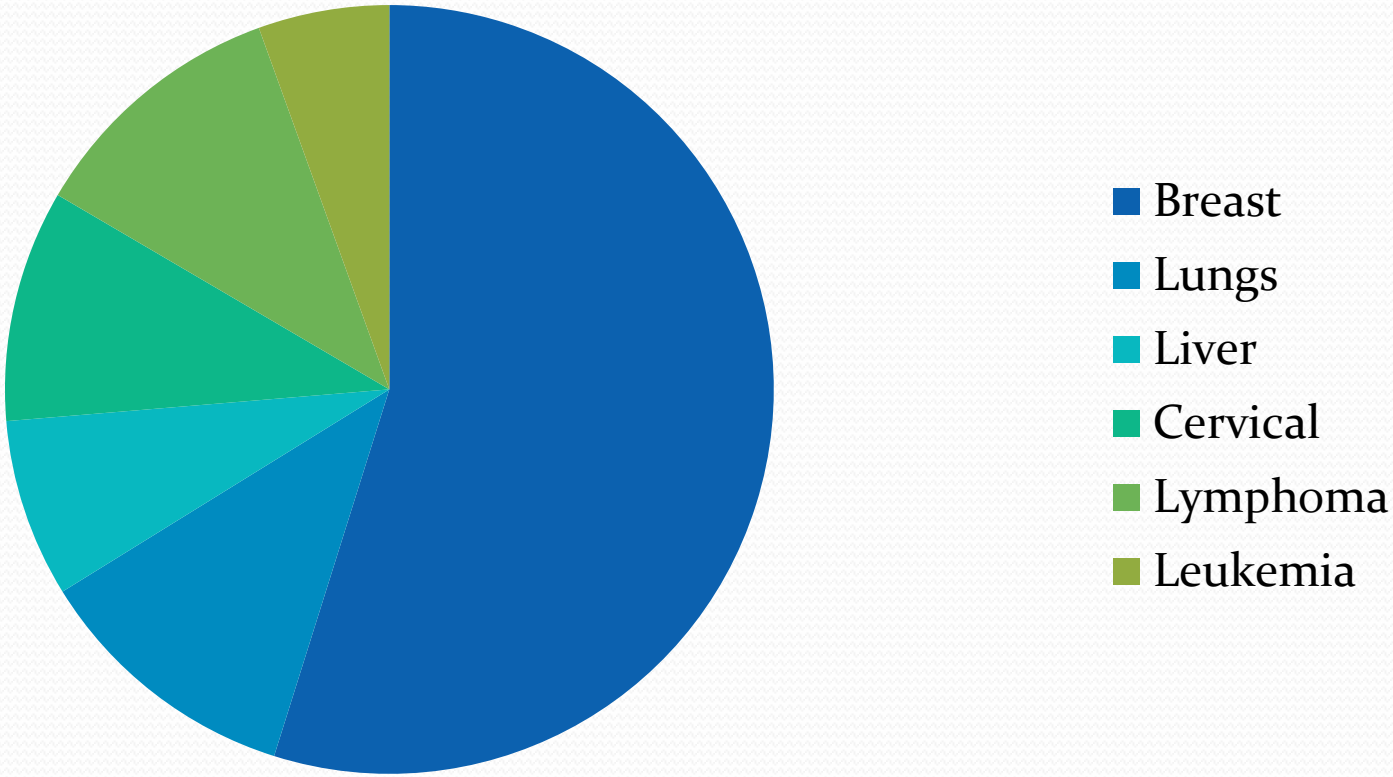
eg. FLT3, c-KIT mutations
N- and K-RAS mutations
BCR-ABL
TEL-PDGFβR



AML Incidence Rate

- The incidence rate of AML in adults is found 80% while in child it is 20% as compared to ALL.
- The incidence rate of 60 years aged people increases up to 10/100000 population.
- The incidence rate of leukemia was found 6.30% at INMOL cancer registry (Pakistan) during 2004–2011 cancer patients
- (Mehmood et al., 2014)

Death Rate Population per 100,000 in Pakistan per Year



Importance of AML

- Approximately every 3 minutes one person in the United States (US) is diagnosed with a blood cancer.
- An estimated combined total of 162,020 people in the US are expected to be diagnosed with blood cancer in 2015.
- Hematological Malignancies (HM) comprise approximately 6.5% of all cancer incidences worldwide in 2012.

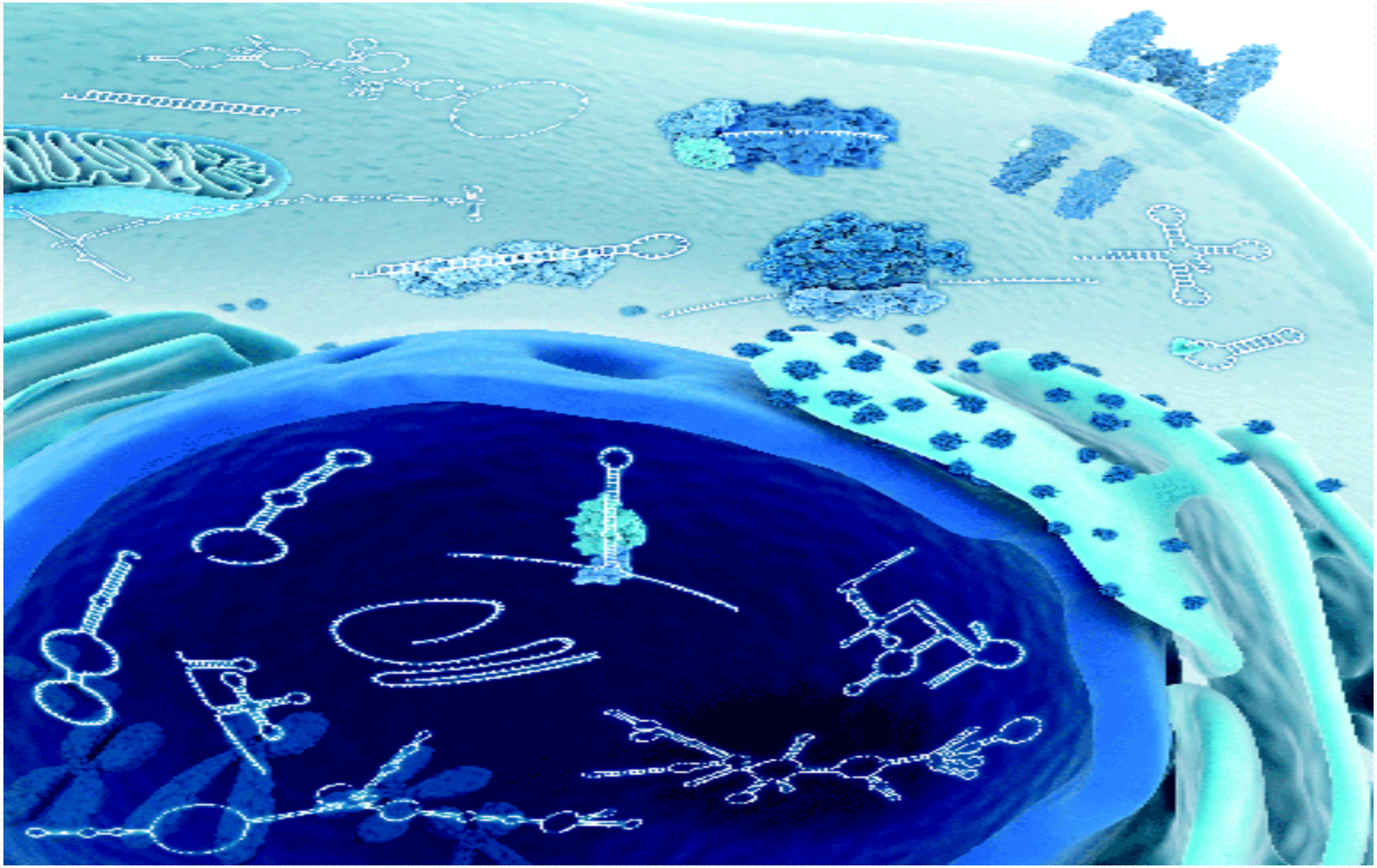
Conti….

- WHO predicts that the number of blood-related cancer cases would increase about 48% in less developed countries by 2030 as compared to 2012.
- It has been estimated that AML incidences are increasing persistently 4.0% per year

What is Micro RNA

- The first micro RNA (abbreviated miRNA) was discovered in the early 1990s.
- miRNA is a small non-coding RNA molecule (containing about 19 to 25 nucleotides) found in plants, animals and some viruses (DNA).
- The human genome encodes more than 1,000 unique mature miRNAs,
- They are controlling approximately 60% of all human genes.
- Any abnormality in miRNA leads to cancer.

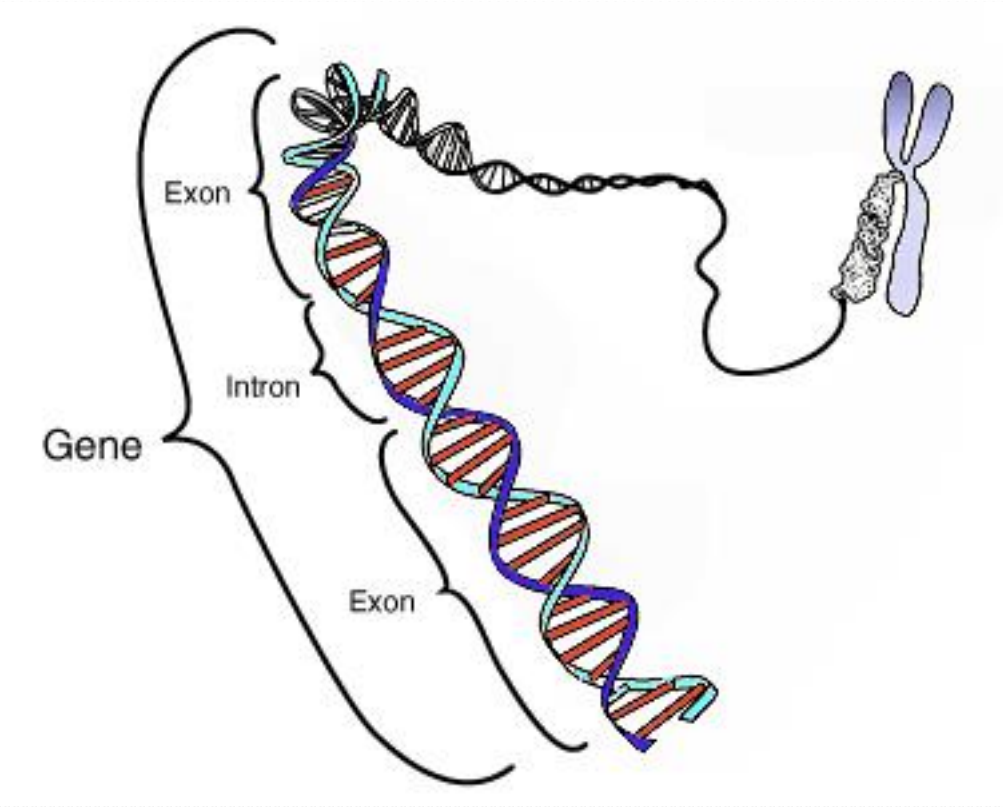
miRNA



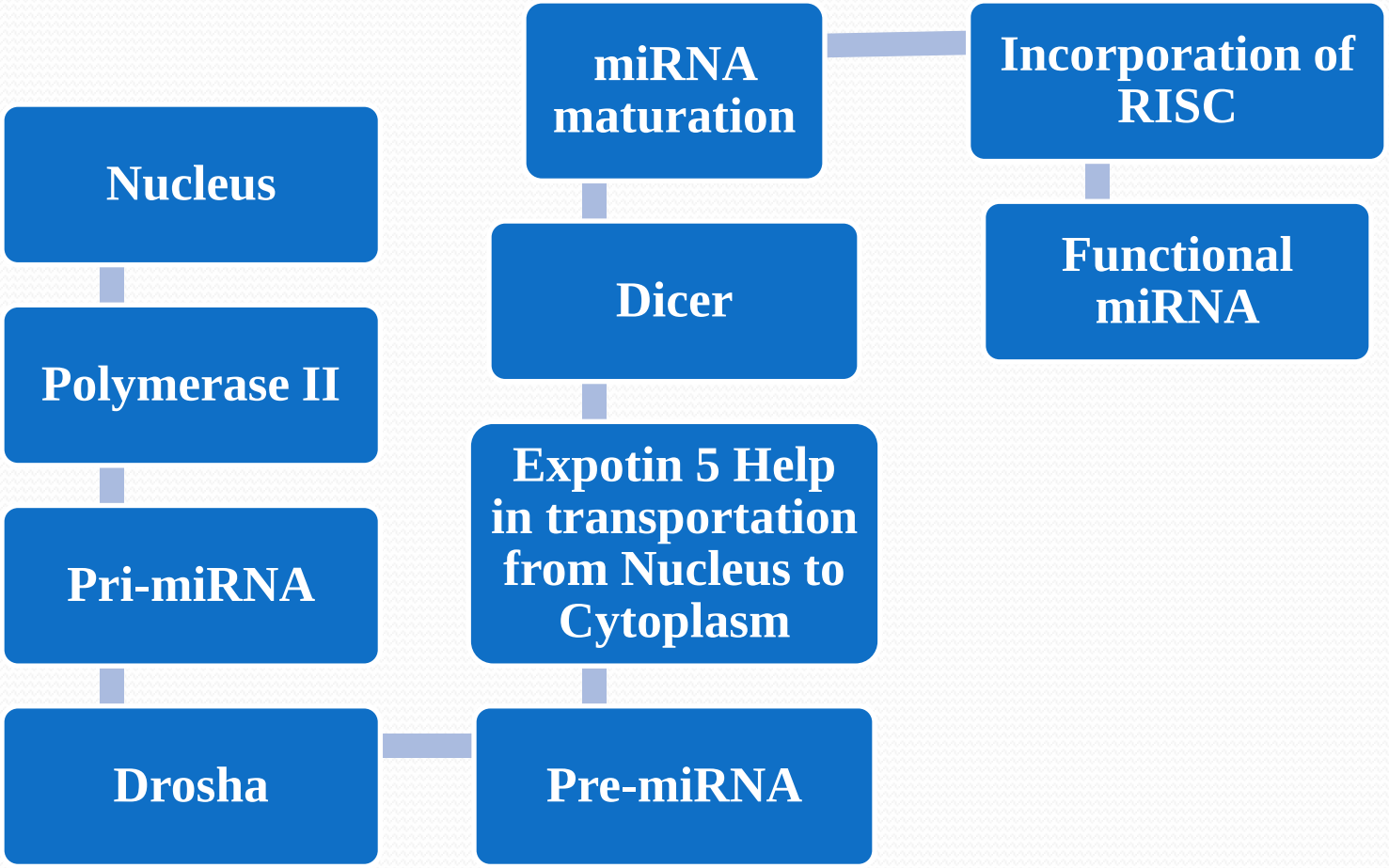
Biogenesis of Micro RNA

- MicroRNAs are produced from either their own genes or from introns.
- As much as 40% of miRNA genes may lie in the introns of protein and non-protein coding genes or even in exons of long nonprotein-coding transcripts.

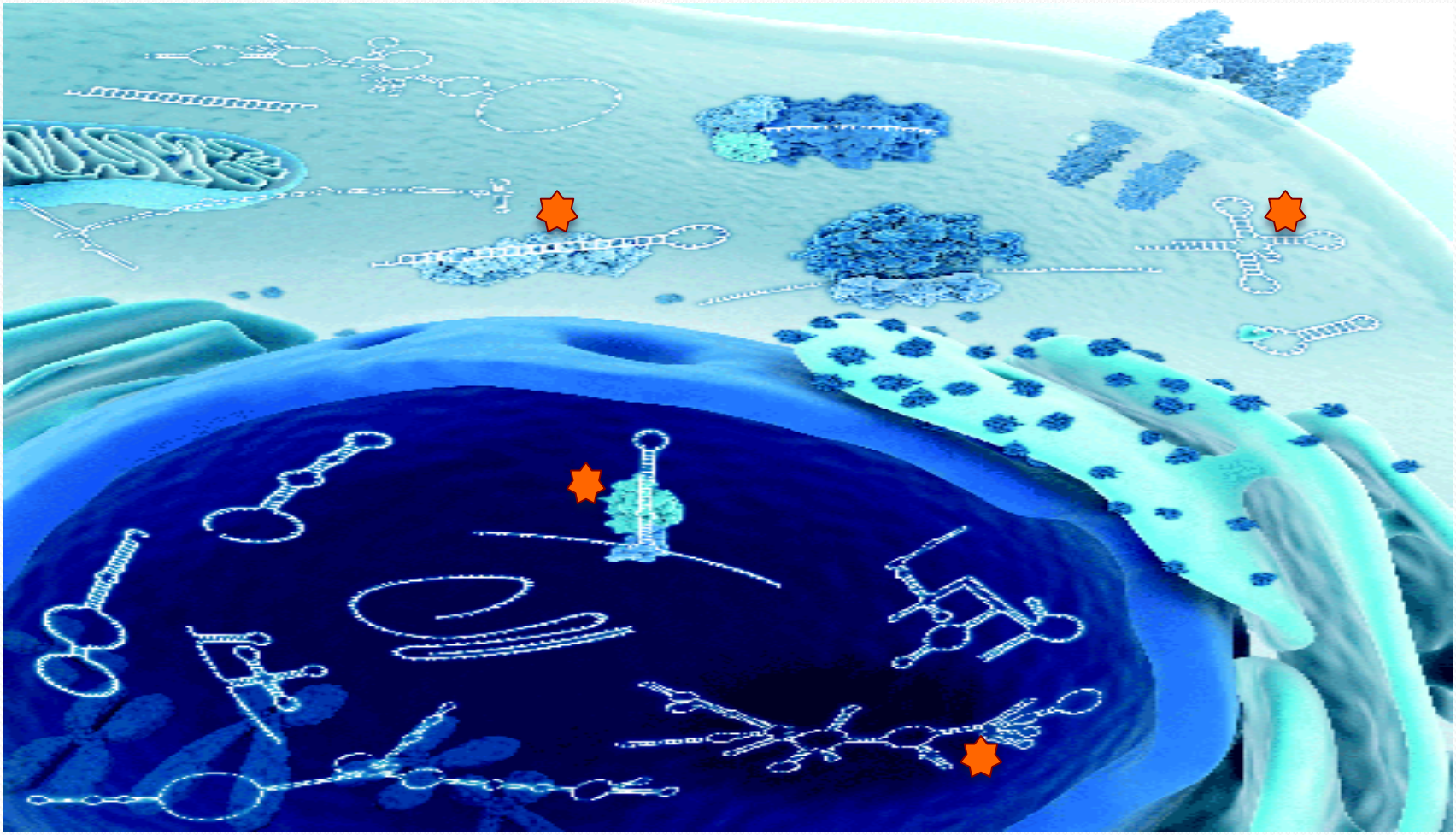
Picture of Interon



Lay out of miRNA Biogenesis



Functional miRNA



miRNA involved in Cell Cycle

Function	Example miRNA
Development/Proliferation	miR-17, miR-18, miR-19, miR-20 miR-92, miR-185 and miR-223 etc.
Differentiation	miR-9, miR-124a and miR-133 etc.
Tumor Suppression	miR15 and miR16 etc.
Apoptosis	miR-21, miR-34, miR-126 and miR-212 etc.

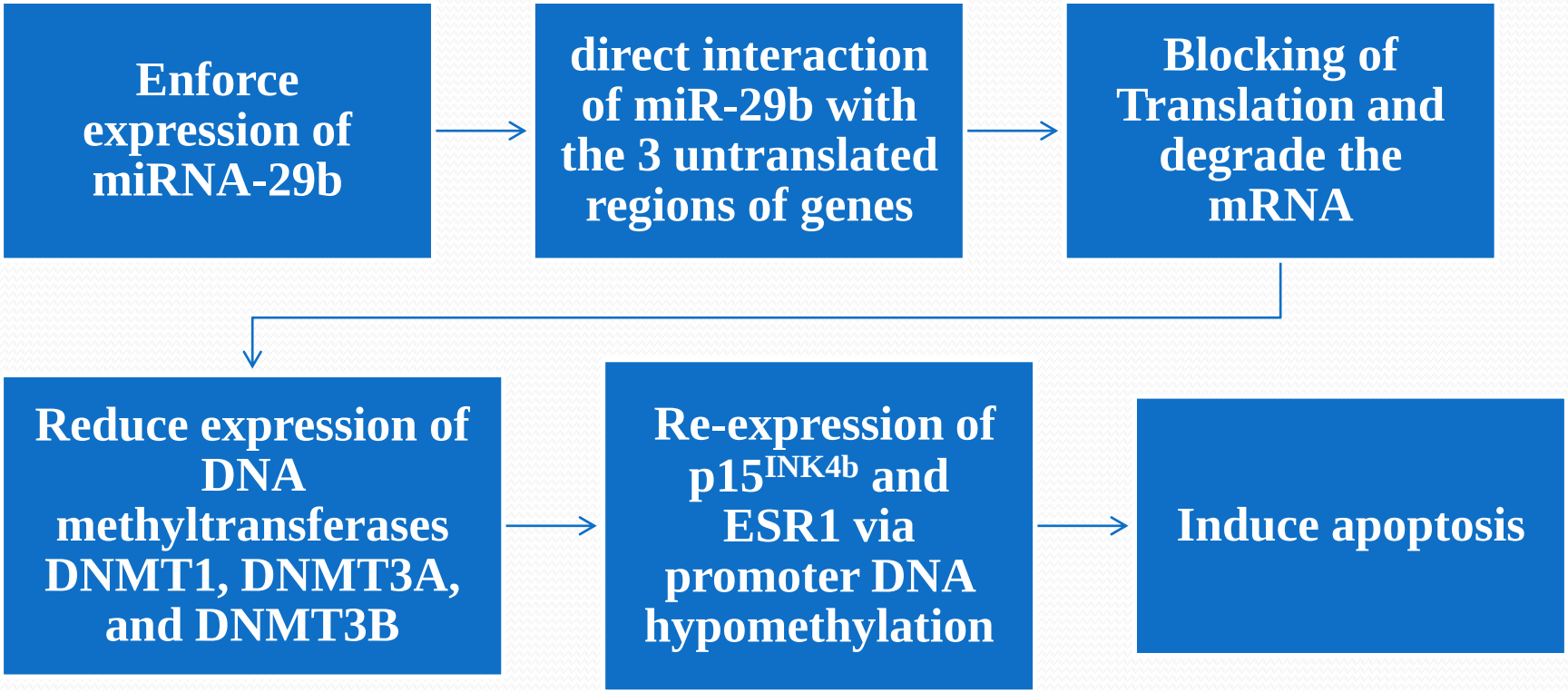
Pathways of Gene Silencing

- Cleavage of the mRNA strand into two pieces
- Destabilization of the mRNA through shortening of its poly(A) tail.
- Less efficient translation of the mRNA into proteins by ribosomes.
- The miRNA are also helpful in gene silencing in AML.

miRNA and Targets in Gene Silencing in AML

miRNA	Targeting Genes
miR-26	*MYC, EZH2, E2F7 and PTEN*
miR-29	*DNMT3A, DNMT3B, SP1 and MCL1.*
miR-125	*CBFB, ABTB1, BAK1, PTPN18 and PTPN7.*
miR-223	*E2F1, NFI-A and FBXW7.*

Mode of Gene Silencing of miRNA-29b in AML




THANKS!