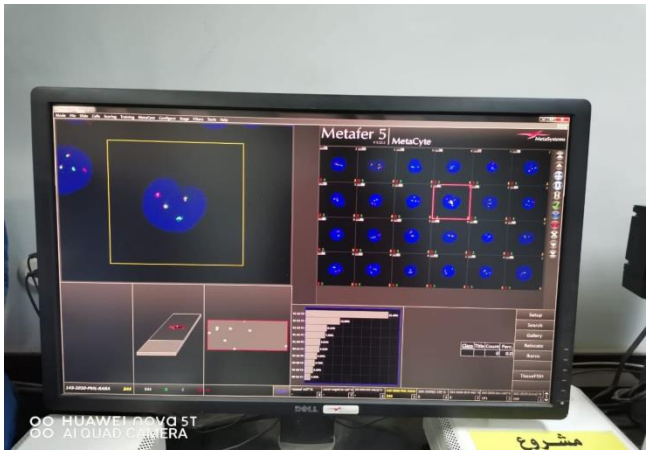
Cytogenetics Laboratory

ABOUT US

- South Egypt Cancer Institute Cytogenetics Laboratory is a pioneer laboratory in the field of cytogenetic testing in South Egypt. Our laboratory is considered the first laboratory in South Egypt that performs cytogenetic testing for hematological neoplasms.
- South Egypt Cancer Institute Cytogenetics laboratory provides a comprehensive genetic testing service for a broad range of clinical conditions, mainly in cancer, and accepts specimens from outpatient facilities. Cytogenetics Laboratory investigates the genome for loss or gain of chromosomal material and structural rearrangements of the chromosomes.



- Our routine oncology service includes chromosomal investigations for hematological neoplasms for detection of chromosomal aberrations using **karyotyping** and **fluorescence in situ hybridization (FISH)**. Detection of these abnormalities is very important for accurate diagnosis and for assisting with clinical management and treatment selection. Cytogenetic markers can monitor the course of disease and provide an early indication of relapse.
- Many research activities and research projects are conducted in our laboratory. The laboratory had a research project from the Science Technology and Development Fund (STDF) (STDF 12457). It was a capacity building project for improvement of Cytogenetics and molecular genetics laboratories in South Egypt Cancer Institute, Assiut University.
- Because the first goal of the laboratory is to provide high-quality services, the laboratory team realized the need to establish and follow a total quality management approach. This quality management approach aims at providing a high-quality service by improving the

quality of services it provides through continuous improvement, and setting standards that ensure the laboratory needs to rise to the best levels and gain ISO 15189 certification.

CLINICAL SERVICES

- South Egypt Cancer Institute Cytogenetics laboratory offers many tests for detection of chromosomal abnormalities in hematological neoplasms using **Fluorescence in Situ Hybridization (FISH) technique**. These tests include:

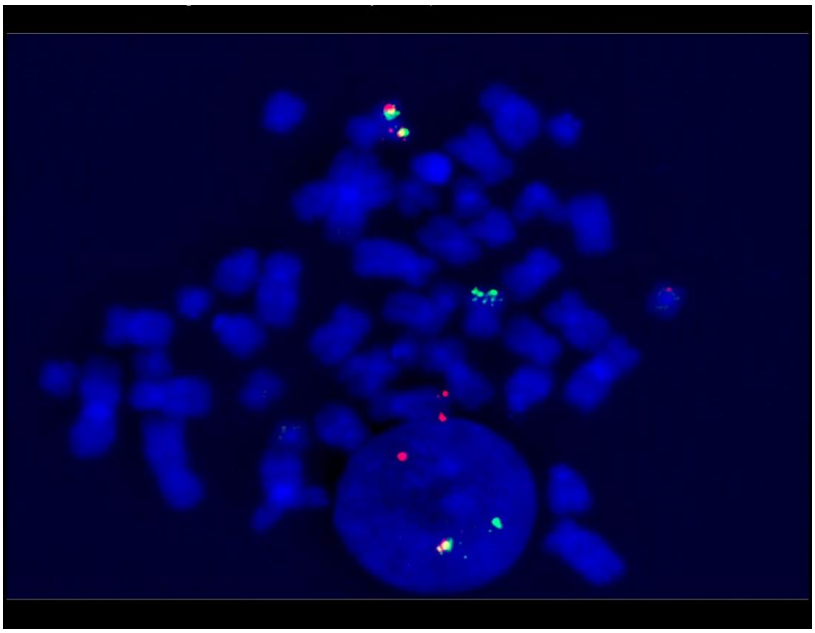
Disease	FISH probe
B-cell Acute Lymphoblastic Leukemia (Pediatric)	• t(12;21) (TEL-AML1 translocation). • 11q23 (KMT2A/MLL) rearrangements. • t(9;22) (BCR-ABL translocation). • 19p13.3 (TCF3 / E2A rearrangement). • CRLF2 rearrangement (BCR-ABL1-like ALL).
B-cell Acute Lymphoblastic Leukemia (Adult)	• 11q23 (KMT2A/MLL) rearrangements. • t(9;22) (BCR-ABL translocation). • CRLF2 rearrangement (BCR-ABL1-like ALL).
Acute Myeloid Leukemia (AML)	• t(8;21) (RUNX1-RUNX1T1) rearrangement. • 11q23 (KMT2A/MLL) rearrangements. • t(9;22) (BCR-ABL translocation). • inv(16) / t(16;16) (CBFB-MYH11) rearrangement. • inv(3)/t(3;3) (EVI1 (MECOM) rearrangement). • 5q deletion (EGR1 deletion). • CEP7 (Monosomy 7 / del(7q)). Acute Promyelocytic leukemia: • t(15;17) (PML-RARA) rearrangement. • 17q (RARA) rearrangement.
Chronic Myeloid Leukemia (CML)	• t(9;22) (BCR-ABL translocation).
Chronic Lymphocytic Leukemia (CLL)	• 11q22 (ATM) deletion. • 13q14 deletion. • 17p13.1 (TP53) deletion.
Myelodysplastic Syndromes (MDS)	• inv(3)/t(3;3) (EVI1 (MECOM) rearrangement). • 5q deletion (EGR1 deletion). • CEP7 (Monosomy 7 / del(7q)). • 17p13.1 (TP53) deletion. • 20q deletion
B-cell Non-Hodgkin Lymphoma	• 14q32 (IGH) rearrangement. • C-MYC rearrangement **(Burkitt leukemia/lymphoma).** • t(11;14) (CCND1-IGH rearrangement) (**Mantle cell lymphoma**). • BCL2 rearrangement. • BCL6 rearrangement.

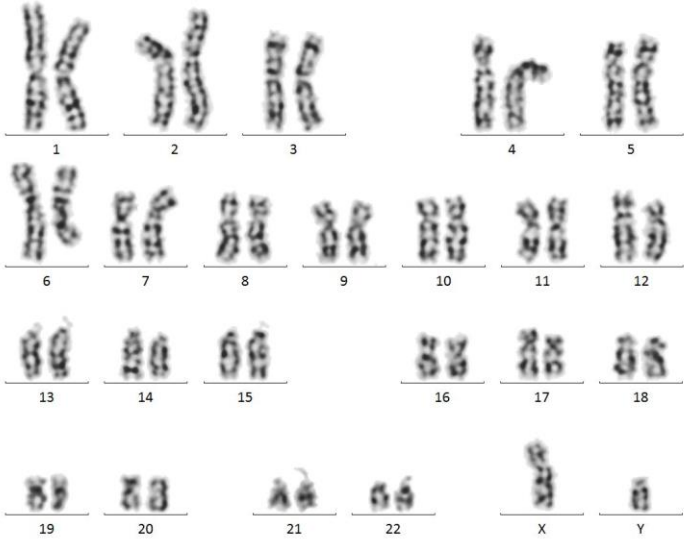
Neuroblastoma	• MYCN amplification.

Type of specimen:

- **Bone marrow specimen** collected on **heparin (green-top) vacutainer** is the preferred specimen type.
- Peripheral blood specimen can be used in the following conditions:
  - Acute leukemia (ALL or AML) (new diagnosis): if there are > 20% blasts in PB film.
  - Chronic myeloid leukemia (CML) (new diagnosis).
  - Chronic lymphocytic leukemia (CLL) (new diagnosis).
    - ❖ Transport at room temperature.
    - ❖ If specimen is not transported on the same day, store at 2~8 C overnight and transport on next day.
- Formalin-fixed paraffin embedded blocks: used in cases of neuroblastoma to detect MYCN amplification. Provide 2 slides (3 – 4 μ thickness).

⇒ To send specimens to our laboratory, please use our **request form**





HEMATOLOGICAL NEOPLASMS

Acute Lymphoblastic Leukemia (ALL):

- Acute lymphoblastic leukemia (ALL) is a malignancy of lymphoblasts (precursor T or B cells). There are three morphologic subtypes:

- L1 blasts: are small and uniform with scant cytoplasm and inconspicuous nucleoli.
- L2 blasts: are larger and more heterogeneous with variable amounts of cytoplasm, larger nucleoli, and irregularly shaped nuclei.
- L3 blasts: correspond to Burkitt's lymphoma cells and are medium-sized uniform blasts with basophilic and often vacuolated cytoplasm and prominent nucleoli.

- Because of replacement of normal bone marrow cells by blasts in acute leukemia (ALL or AML), normal blood cell production is decreased and anemia, thrombocytopenia, or neutropenia are usually present and would be fatal without treatment. Acute leukemia can occur in all age groups. In childhood, acute leukemia is usually ALL.

Genetic risk stratification in B-cell ALL:

Favorable risk	Intermediate risk	High risk
Hyperdiploidy (> 50 chromosomes, especially with trisomy 4, 10, 17).	t(5;14) (IL3-IGH).	Hypodiploidy (< 45 chromosomes).
t(12;21) (TEL-AML1).	t(1;19) (TCF3-PBX1)	t(9;22) (BCR-ABL-1).
	Normal karyotype.	KMT2A rearrangement; t(4;11)
	Any other abnormalities not in favorable or unfavorable categories.	B-ALL with iAMP21
		BCR-ABL1-like B-ALL
		Complex abnormalities

Acute Myeloid Leukemia (AML):

- AML is a malignancy of immature bone marrow cells including high numbers of blasts and with subtypes M0 to M7. The subtypes indicate degree or lack of maturation of the cells.

Morphologic subtypes:

- M0 and M1 are characterized by blasts with no or little maturation, including no or little myeloperoxidase reaction, respectively.
- M2 is characterized by some maturation including the presence of promyelocytes or more mature neutrophils. In one form of M2, there is an increase in basophils.
- M3 is characterized by presence of many abnormal promyelocytes and is also referred to as acute promyelocytic leukemia (APL).
- M4 and M5 are characterized by some monocytic differentiation.
- M6 is characterized by some erythroid differentiation and is also referred to as erythroleukemia.
- M7 is characterized by some megakaryocytic differentiation and is also referred to as acute megakaryoblastic leukemia.

Genetic risk stratification in AML (ELN 2022):

Risk Status	Cytogenetic Abnormalities	Molecular Abnormalities
Favorable:	○ Core binding factor AML: AML with t(8;21), AML with inv(16)/t(16;16). ○ Acute promyelocytic leukemia with PML::RARA.	Normal karyotype with: ○ NPM1 mutation without FLT3-ITD mutation. ○ bZIP in-frame mutated CEBPA
Intermediate:	○ AML with t(9;11). ○ Normal karyotype. ○ Other non-defined.	○ Core binding factor AML with KIT mutation. ○ Mutated NPM1 with FLT3-ITD. ○ Wild-type NPM1 with FLT3-ITD (without adverse-risk genetic lesions)
Unfavorable:	○ Complex (> 3 clonal abnormalities). ○ AML with inv(3)/t(3;3) (GATA2::MECOM). ○ t(3q26.2;v)/MECOM(EVI1)-rearranged ○ t(11q23-KMT2A gene) other than t(9;11). ○ AML with t(6;9) (DEK::NUP214). ○ t(8;16)(p11.2;p13.3)/KAT6A::CREBBP ○ AML with t(9;22). ○ Monosomal karyotype. ○ Monosomy 5, del(5q). ○ Monosomy 7, del(7q).	Normal karyotype with: ○ TP53 mutation. ○ Mutated ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1, and/or ZRSR2

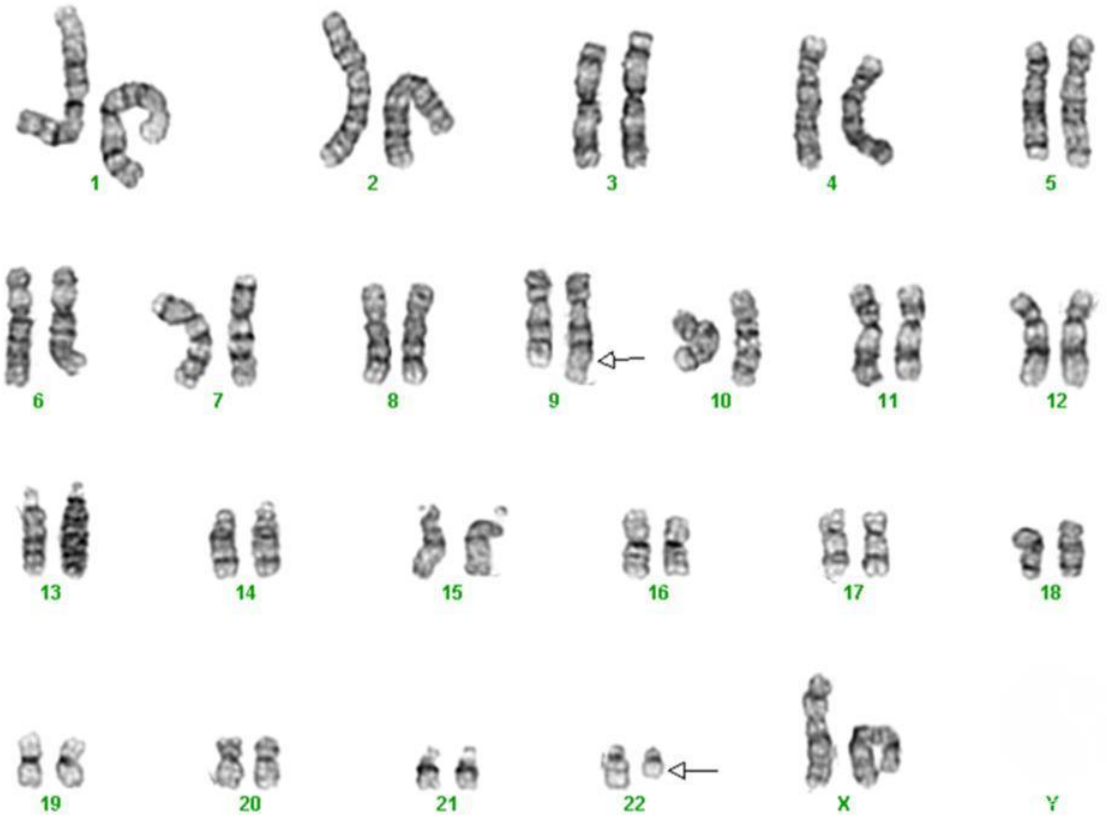
	○ Monosomy 17 / abn(17p)	

Chronic Myeloid Leukemia (CML):

- Chronic Myeloid Leukemia (CML) is a stem cell malignancy affecting all cells of the marrow, including granulocytes, erythroid cells, megakaryocytes, and B lymphoid cells. A high white blood cell count with immature and mature granulocytes is a characteristic feature. Thrombocytosis, anemia, and splenomegaly are often present.
- Initially symptoms may be mild, but without aggressive intervention (bone marrow transplant), the disease ends in terminal acute leukemia (blast crisis or blast transformation) with replacement of marrow by myeloblasts in approximately two-thirds of cases, or lymphoblasts in approximately one-third of cases.
- Transformation from the chronic phase to an accelerated phase may be identified by myelofibrosis, increased basophilia, marked anemia, thrombocytopenia, or karyotypic evolution. CML can be seen at any age but is more common in adults.

Cytogenetic abnormalities in CML:

t(9;22) (BCR-ABL)	Philadelphia chromosome; primary abnormality
+8	Secondary change
+der(22)t(9;22)	Extra Philadelphia chromosome; secondary change
i(17q)	Isochromosome 17q; secondary change

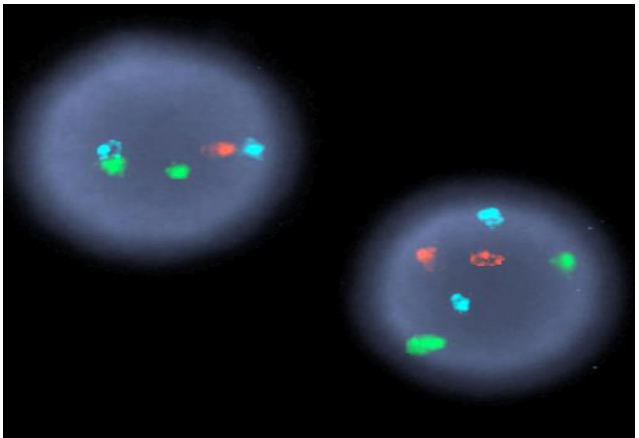


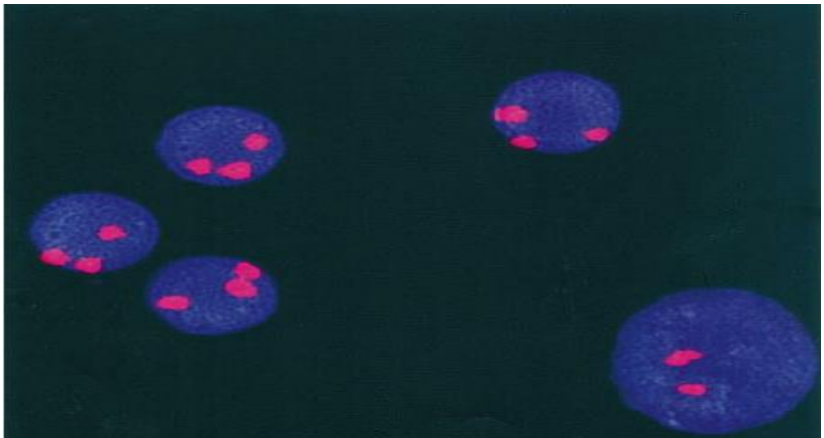
Chronic Lymphocytic Leukemia (CLL):

- Chronic lymphocytic leukemia (CLL) is an indolent malignancy of small lymphocytes (nearly always B cells) with blood and bone marrow involvement. The leukemia cells also infiltrate lymph nodes (producing a picture indistinguishable from small lymphocytic lymphoma), the spleen, and other organs. CLL occurs in older age groups.

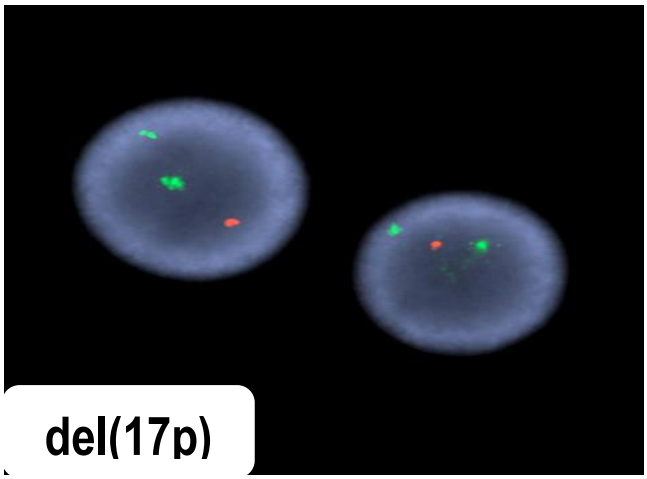
Cytogenetic abnormalities in CLL:

Cytogenetic Abnormality	Risk Category
13q14 deletion (Most common abnormality)	Favorable risk
Trisomy 12	Intermediate risk
11q23 (ATM) deletion	Unfavorable risk
17p (TP53) deletion	Unfavorable risk





del(13q) Trisomy 12

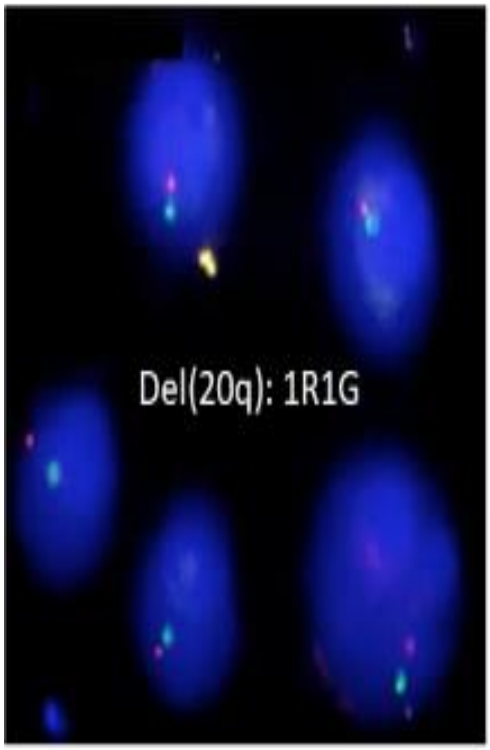


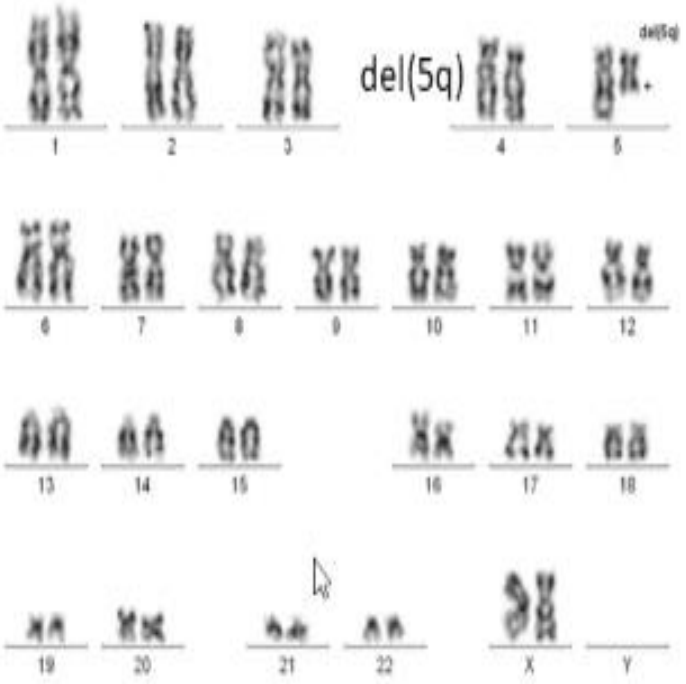
Myelodysplastic Syndromes (MDS):

- Myelodysplastic syndromes (MDS) are disorders of bone marrow characterized by hypercellularity, dysplastic (abnormal) maturation, and often an excess number of blasts. Anemia and often neutropenia and thrombocytopenia are present. A high percentage of cases progress to acute leukemia (usually AML), and for this reason, MDS has been called preleukemia. MDS may be primary or secondary (therapy-related). MDS is more common in older adults but can be seen at any age.

Cytogenetic abnormalities in MDS:

Gain or loss of chromosomal material (relatively common):	
Monosomy 5 or del (5q)	Trisomy 6
Monosomy 7 or del (7q)	Trisomy 8
del (9q)	del (11q)
del 12 or unbalanced translocation of chromosome 12	Monosomy 13 or del (13q)
Monosomy 17, i(17q)	Monosomy 20 or del (20q)
Trisomy 21, Monosomy 21	-Y
Other translocations and inversions (relatively common):	
t(3;3)(q21;q26), inv3 (q21;q26), t(3;21)(q26;q22) and other 3q21 and 3q26 translocations	
t(1;7)(p11;p11)	t(2;11)(p21;q23)
t(6;9)(p23;q34)	t(11;16)(q23;p13)





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