

Chronic Myelogenous Leukemia (CML)

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Genomics & Medicine

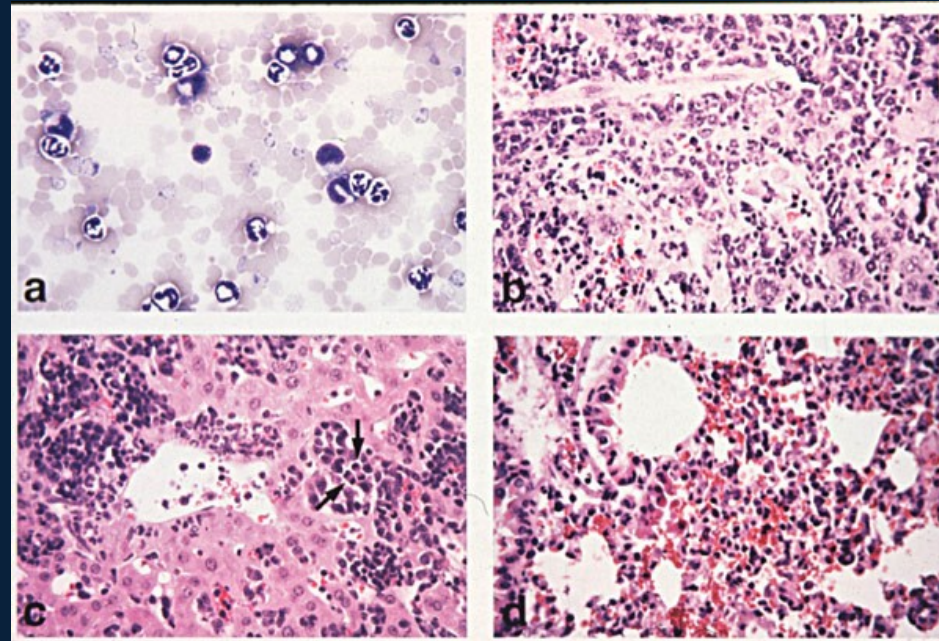
September 28, 2010

Disease and Classical Symptoms

- CML is a cancer of white blood cells.
- Characterized by the malignant, unregulated growth of myeloid cells in bone marrow and the collection of these cells in the blood
- Symptoms: bruising around body, excessive sweating, pain in abdomen due to enlarged spleen, weight loss, fatigue
- Median survival is 5 years

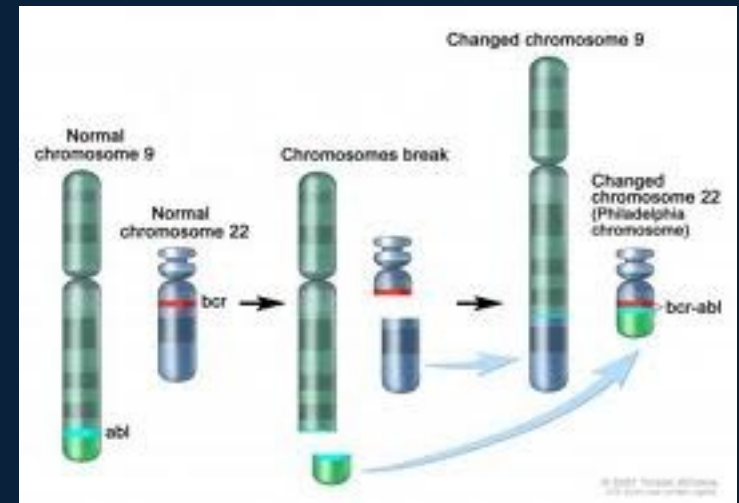
Classical Treatments

- Tyrosine Kinase Inhibitors (TKIs)- most commonly used, oral medications
 - Gleevec
- Stem Cell Transplantation- only potential cure
- Interferon- daily injection, strengthen immune system
- Chemotherapy- not as effective



Genetic Origin

- Acquired translocation, not hereditary
- Translocation between chromosomes 9 and 22- Ph chromosome
 - Sub-bands 22q11.21 and 9q34.1
- Results in a mutated gene called BCR-ABL (breakpoint cluster region and Ableson leukemia virus)



Genetics ctd.

- BCR-ABL codes for a fusion protein that has Tyrosine Kinase Activity.
 - Activates signal transduction pathways, which lead to uncontrolled cell growth and turns off apoptosis.
 - This allows white blood cells to grow uncontrollably, and eventually prevent the functions of red blood cells, platelets, normal white blood cells, etc.

Diagnostic Method

- Molecular testing is primary diagnostic.
- RT-PCR test- primers that identify fusion transcripts from the translocation of the two chromosomes. Based on distances of the fused genes from each other, CML can be diagnosed.

What Genetic Knowledge Provides Us

- Better Diagnostics:
 - Genetic testing for fusion protein
- Better Treatments:
 - TKIs

