



CHRONIC MYELOGENOUS LEUKEMIA

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SBS11QHG – 01

PHYSIOLOGY

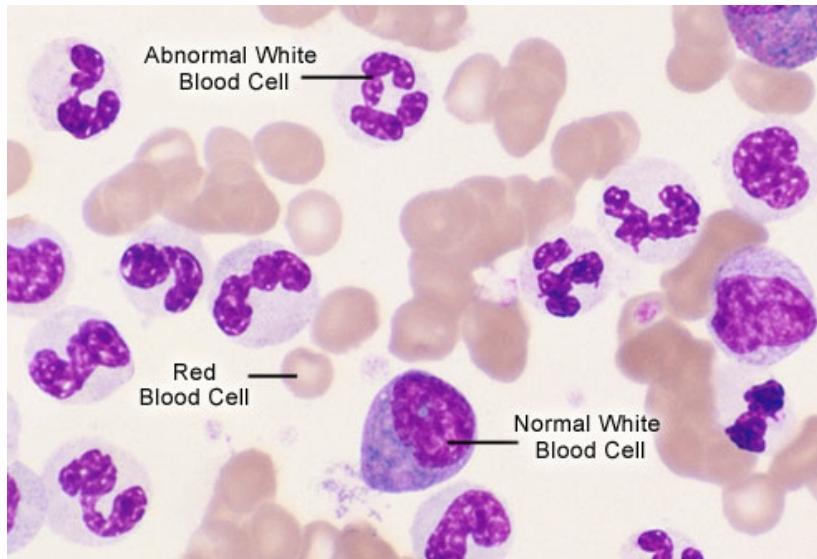


Fig 1



Fig 2

- Also known as Chronic Granulocyte Leukemia
- Common form of Leukemia
- Occurs in bone marrow
 - Over proliferation of white blood cells
- Middle to Late onset
- Causes fatigue, anemia, pain in ribcage area, frequent infections (immune system does not work properly), bone/joint pain, easy bleeding, excessive sweating, weight loss, loss of appetite
- Three phases: Chronic, Progressive, Blast Crisis
- Inheritance pattern: somatic mutation (translocation)



MOLECULAR CAUSE

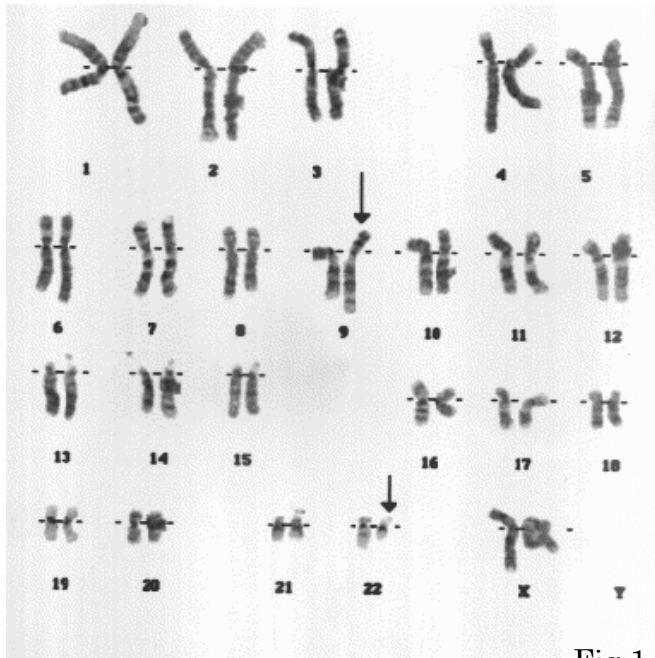


Fig 1

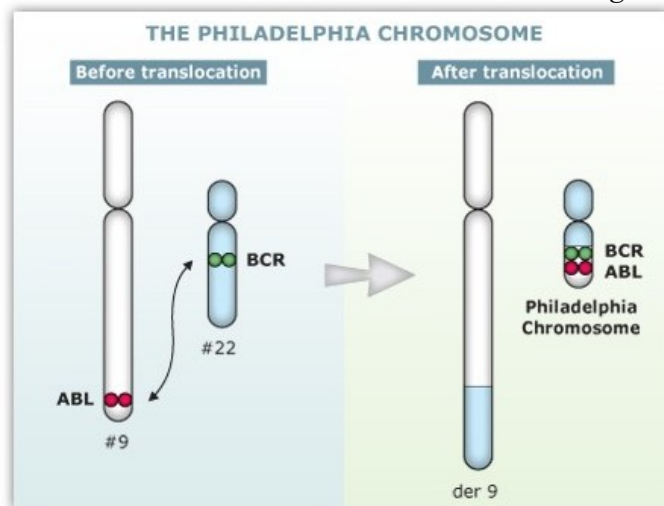


Fig 2

- Genetic Pattern: Somatic Mutation
- Two genes not serving proper function:
 - ABL = Proto-oncogene on Chromosome 9
 - BCR = Breakpoint cluster region gene on 22
 - BCR-ABL fusion gene formed when ABL translocates onto 22 (Philadelphia chromosome)
- Fusion gene codes for BCR-ABL protein
 - Causes cascade reactions in cell cytoplasm
 - Granulocytes prematurely become white blood cells
- Cells rapidly divide and begin to form a tumor in the bone marrow
 - Don't die when they're supposed to
 - Get in the way with other blood cells' functions

TREATMENTS/RISKS AND LIMITS

- Tyrosine Kinase Inhibitors block ATP binding sites to prevent the BCR-ABL protein from causing cascade reactions/Cells can become immune over time
- Chemotherapy: Kill rapidly dividing cells
 - Systemic: inject substance into muscle or bloodstream/ May not attack the proper target
 - Direct: target one specific area
 - Disadvantage: Many side effects
- Chemo with Stem Cell Transplant
 - Store stem cells → Return to patient after chemo
 - Disadvantages: Patients cannot have used other treatments, failure rate is high
- Splenectomy: Partially or completely remove spleen
 - May cause infection, hemorrhage, platelet abnormalities
- Interferon: insert immune system substance in order to stop growth of cancer cells/ Many side-effects



PROPOSED CURE/LIMITS

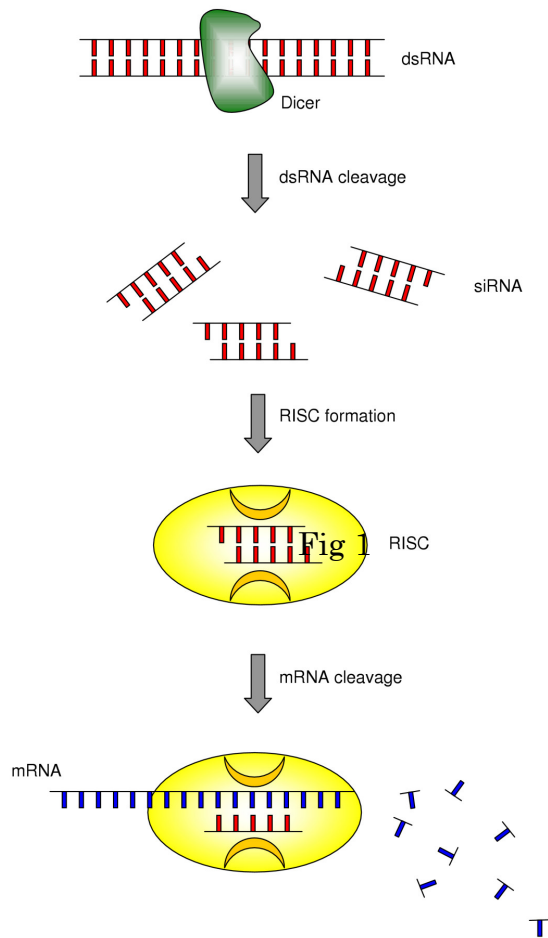


Fig 1

- Deal with the lesion and treat symptoms
- Sequence the BCR-ABL gene
- RNA interference system:
 - siRNA and miRNA cut and bind to Argonaute proteins forming RISC (RNA induced silencing complex)
 - RISC binds to mRNA, based on complementarity, and degrades it
 - Through Argonaute2-catalyzed endonucleolytic cleavage or deadenylation
- RNAi makes it so mRNA is not fully functional and is not able to translate to the BCR-ABL fusion protein
- Combine with blood transfusion to replenish patient with healthy blood and cells
- Limits: Hard to target specific cells, RNAi is generally experimental right now

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