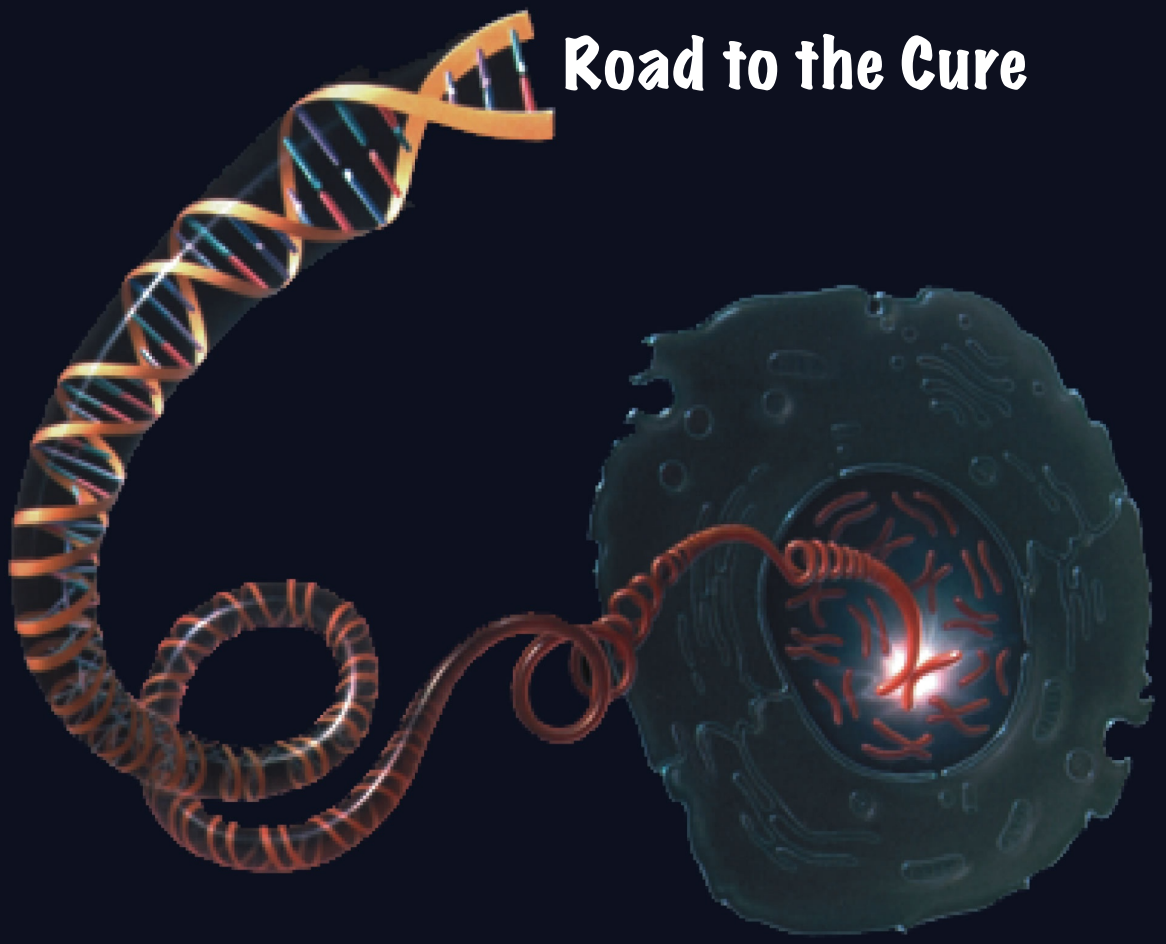
Treatable Genetic Disorders

Road to the Cure



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Genomics & Medicine
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3.10.11

Treatment v. Cure

Chronic Myelogenous Leukemia

Acute Promyelocytic Leukemia

Biotinidase Deficiency

Pompe Disease

Chronic Myelogenous Leukemia

Acute Promyelocytic Leukemia

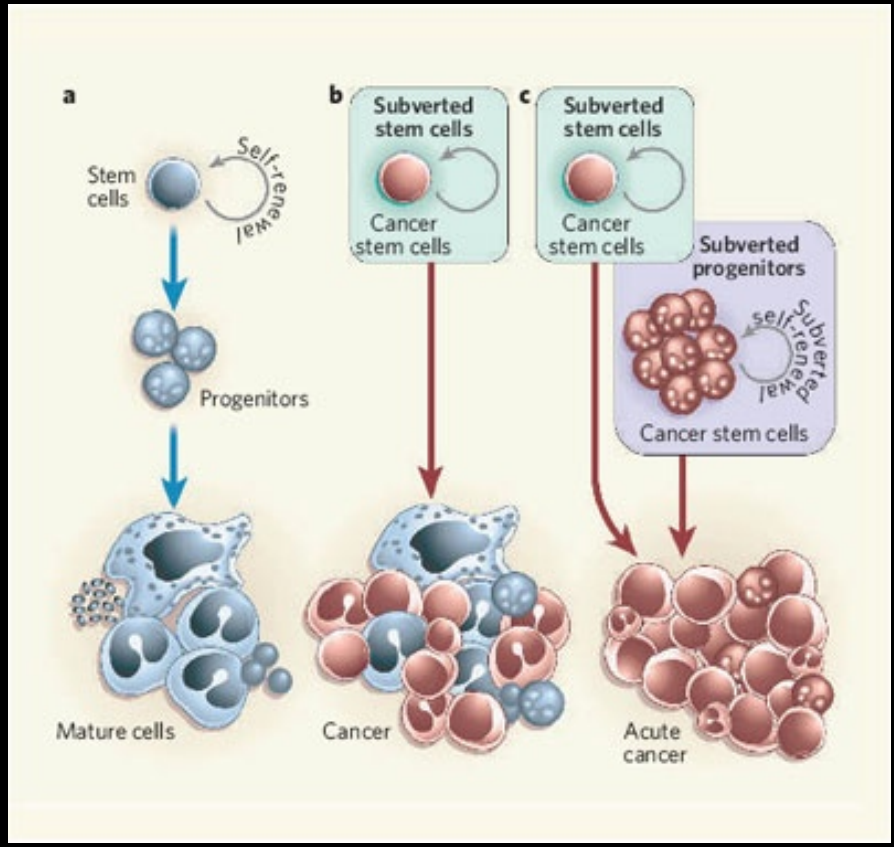
Biotinidase Deficiency

Pompe Disease

Chronic Myelogenous Leukemia

What is it?

- Cancer of blood cells
- Proliferation disorder of pluripotent stem cell
  - Myeloid, erythroid, megakaryocytic, B lymphoid, etc.
- Possibly enlarged spleen and liver



Chronic Myelogenous Leukemia

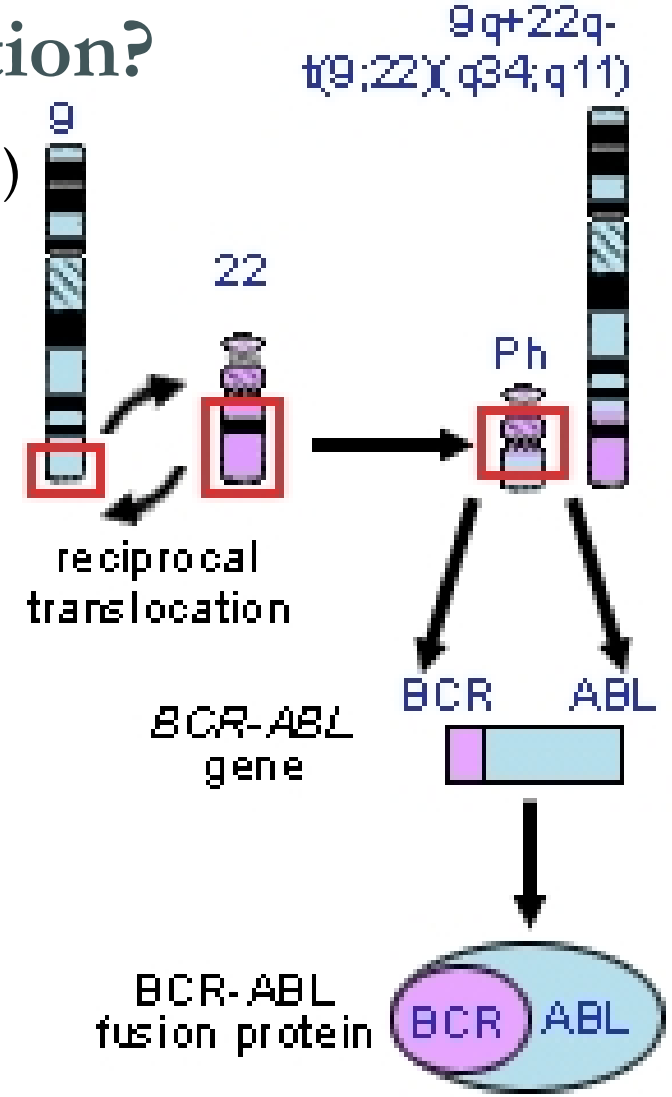
What causes the overproliferation?

"Philadelphia" chromosome

Chronic Myelogenous Leukemia

What causes the overproliferation?

- Translocation event (between 9 & 22)
- Fuses BCR and ABL gene
  - Activates tyrosine kinase activity



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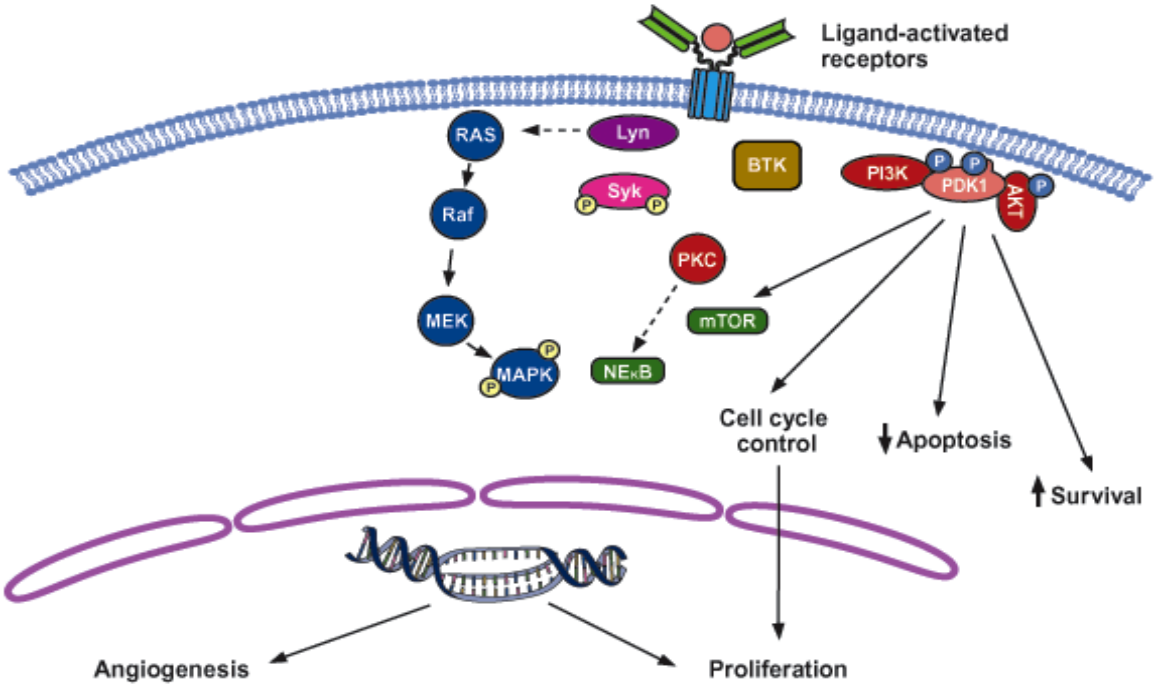


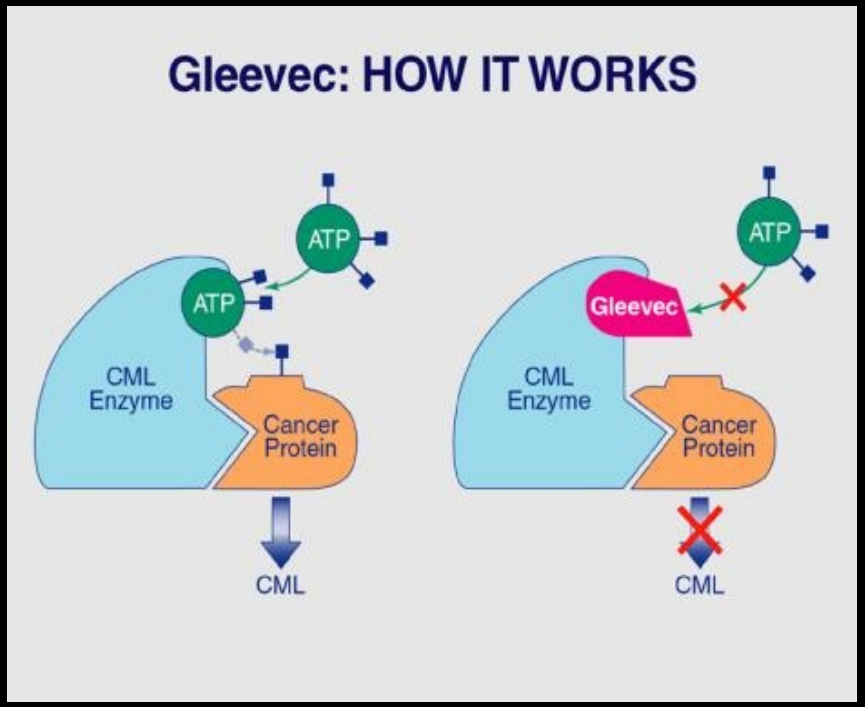
Chronic Myelogenous Leukemia

Diagnosis

- Complete blood count
- Detecting the Philadelphia chromosome
- PCR for the BCR-ABL gene

Treatment

- Imatinib (STI571)
  - Brand name: Gleevec
- Deactivates BCR-ABL protein



Chronic Myelogenous Leukemia

Acute Promyelocytic Leukemia

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Acute Promyelocytic Leukemia

What is it?

- Similar to CML
- Cancer of the blood; bone marrow
- Deficiency of mature cells in myeloid line
- Excess immature cells (promyelocytes)

Symptoms

- Fatigue
- Minor infections
- Hemorrhagic diathesis
- Anemia

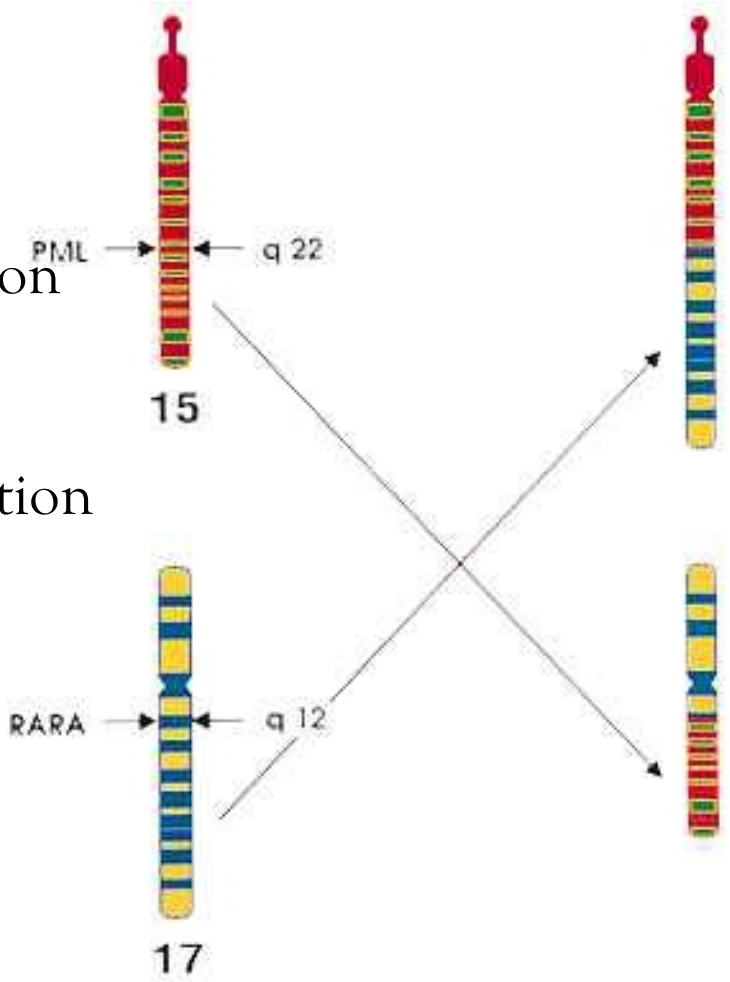
Acute Promyelocytic Leukemia

What causes the overproliferation?

Acute Promyelocytic Leukemia

What causes the overproliferation?

- Translocation event (between 15 and 17)
- PML/RARa fusion gene
  - PML: growth suppressor transcription factor
  - RARa: retinoic acid receptor alpha
    - Regulates myeloid differentiation



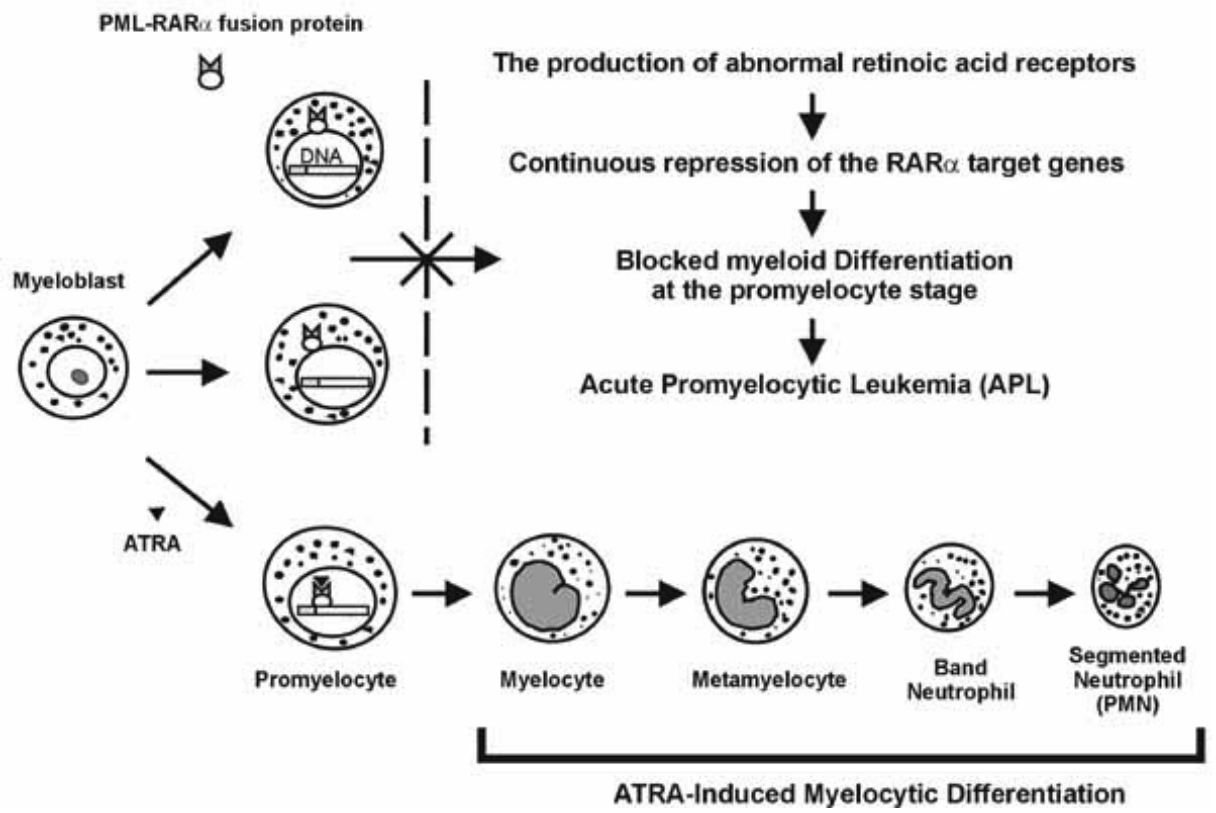
Acute Promyelocytic Leukemia

Diagnosis

- Complete blood cell count
- Chromosome phenotype
- Test for PML/RARa gene

Treatment

Acute Promyelocytic Leukemia



Treatment

- ATRA: all-trans retinoic acid
  - Malignant cells → phenotypically mature myeloid cells

Chronic Myelogenous Leukemia

Acute Promyelocytic Leukemia

Biotinidase Deficiency

Pompe Disease

Biotinidase Deficiency

What is it?

- Autosomal recessive
- Absence of biotinidase

Function of biotinidase

Biotinidase Deficiency

What is it?

- Autosomal recessive
- Absence of biotinidase

Function of biotinidase

- Biotin cycling
- Carboxylase enzyme co-activation

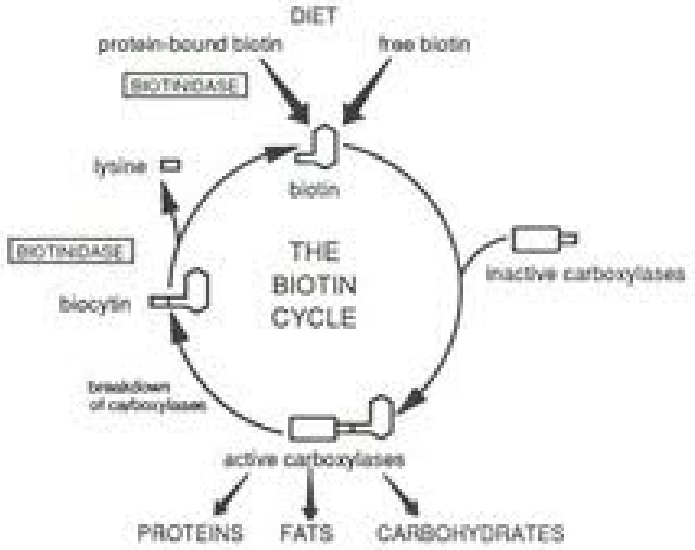
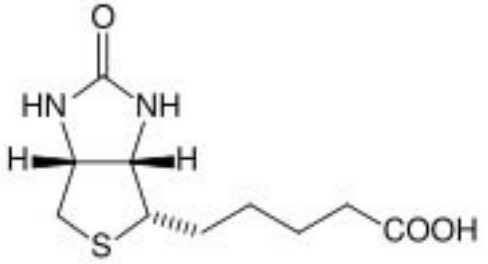


Figure 2: The biotin cycle

Deficiency symptoms

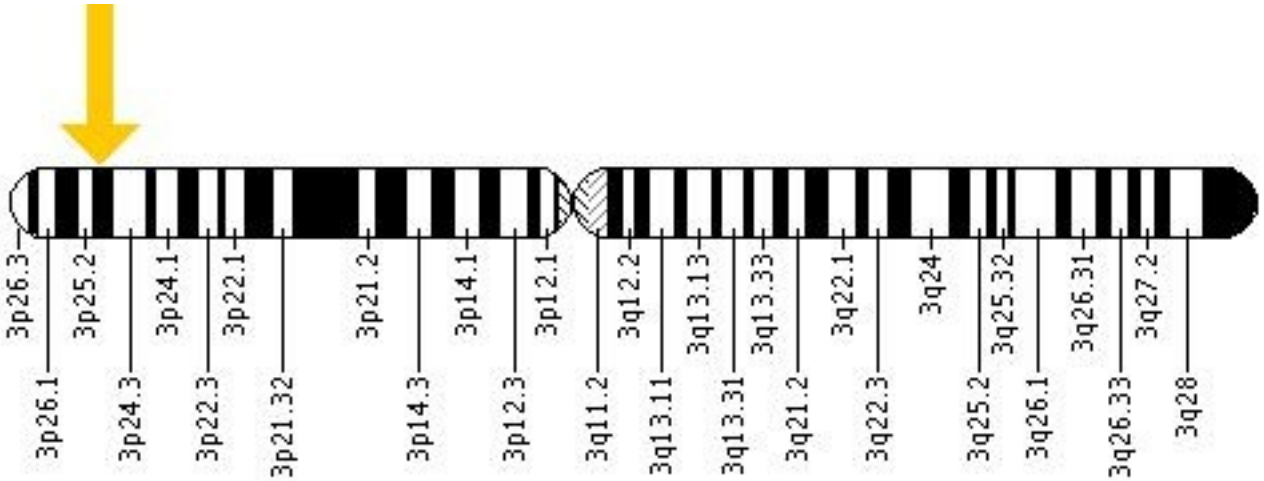
- infantile or early childhood encephalopathy,
- seizure disorder
- dermatitis
- alopecia
- neural deafness
- optic atrophy



Biotinidase Deficiency

What causes the deficiency?

- BTD gene mutation



Biotinidase Deficiency

Diagnosis

- Measure biotinidase enzyme activity
- Test BTD gene

Treatment

- Biotin therapy
  - Children: 5 – 10 mg/day

Chronic Myelogenous Leukemia

Acute Promyelocytic Leukemia

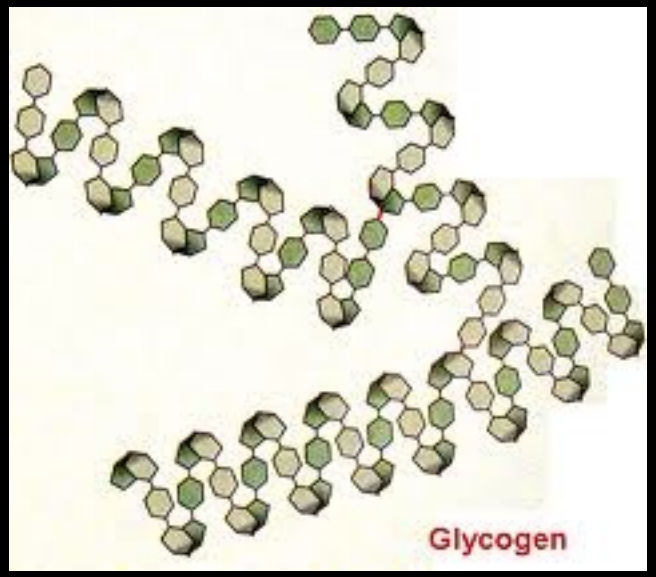
Biotinidase Deficiency

Pompe Disease

Pompe Disease

What is it?

- Glycogen storage disease type II
- Acid maltase deficiency
- Buildup of glycogen in cells
  - Impairs cell function
- Autosomal recessive



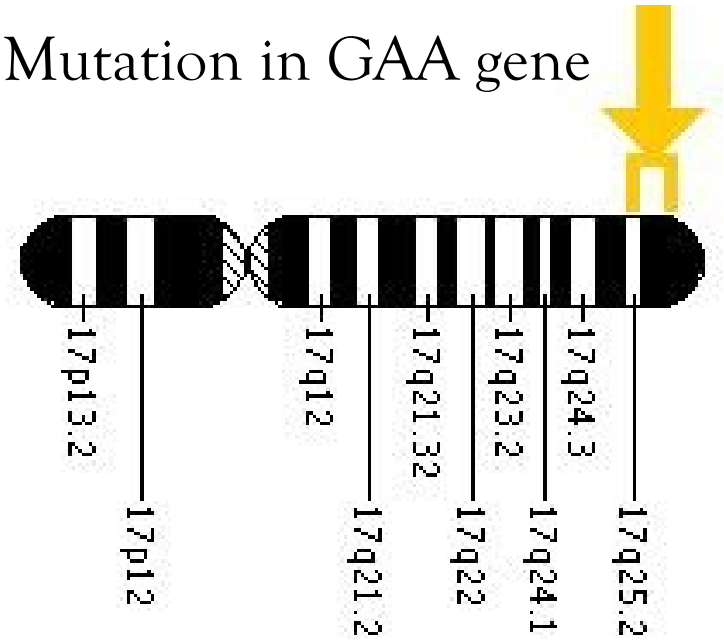
Symptoms

- Classic infantile-onset
  - Muscle weakness
  - Cardiomegaly
  - Feeding difficulties
  - Respiratory distress
  - Hearing loss
- Non-classic infantile-onset
  - Motor delays
  - Ventilatory failure → death

Pompe Disease

What causes the disease?

- Mutation in GAA gene



Pompe Disease

Diagnosis

- Measure alpha-glucosidase (GAA) enzyme activity
- Test GAA gene

Treatment

- enzyme replacement therapy (ERT) with Myozyme® or Lumizyme®

last note

Treatment v. Cure

- Gene Therapy
- Stem Cell Research

References

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