Treatable Genetic Disorders
Road to the Cure

Hannah Obasi
Genomics & Medicine
Doug Brutlag
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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
Chronic Myelogenous Leukemia

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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
Treatable Genetic Disorders:

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

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