

Fanconi Anemia

Background Info

Symptoms, Genetics, Diagnosis and Treatment

Symptoms -

Congenital Abnormalities - Very heterogeneous

- Hand and arm abnormalities (71%)
- Skeletal anomalies (hips, spine) (71%)
- Skin discoloration (64%)
- Short stature (63%)
- Mental retardation (16%)
- Gastrointestinal difficulties (14%)
- Hearing (11%)
- No abnormalities (30%)



Haematopoietic Abnormalities (next lecture)

- Bone marrow failure
 - aplastic anemia
 - susceptibility to infections

Predisposition to cancer

- leukemia early on
- cancers of rapidly dividing tissues (mouth, esophagus, GI tract, anus)

Fanconi Anemia - Timeline

Often apparent at birth due to congenital abnormalities.

If not, disease usually manifests by age of 12, rare cases, no symptoms before adulthood

73% have overt bone marrow disease by age 10, mean age 7 or 8

Median survival is 7 yrs after development of overt bone marrow disease

Molly Nash

Molly Nash was diagnosed shortly after birth.

She was born with hand abnormalities, hip dislocation, deafness in the left ear, heart and intestinal abnormalities.

Pancytopenia was observed at age 2

Bone marrow failure developed at age 3

Myelodysplasia (pre-leukemia)
developed at age 4



Genetics

Fanconi Anemia is an autosomal recessive disease

Mutations in 11 different genes can lead to Fanconi Anemia

All genes are in a DNA repair pathway

Molecular mechanism by which these mutations lead to FA are not clear

Most commonly mutated genes

FANCA (66%)

100 different mutations

FANCC (12%)

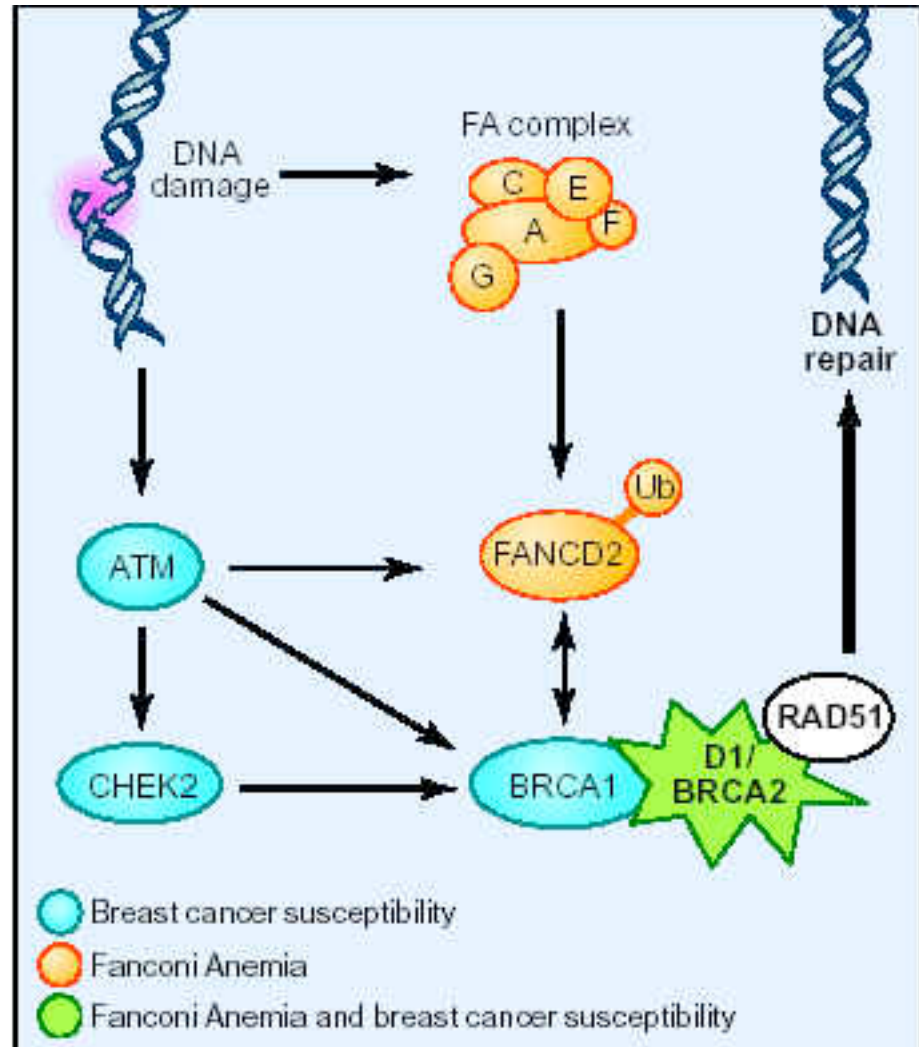
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common in Ashkenazi Jews

1 in 89 carries

common in Japanese

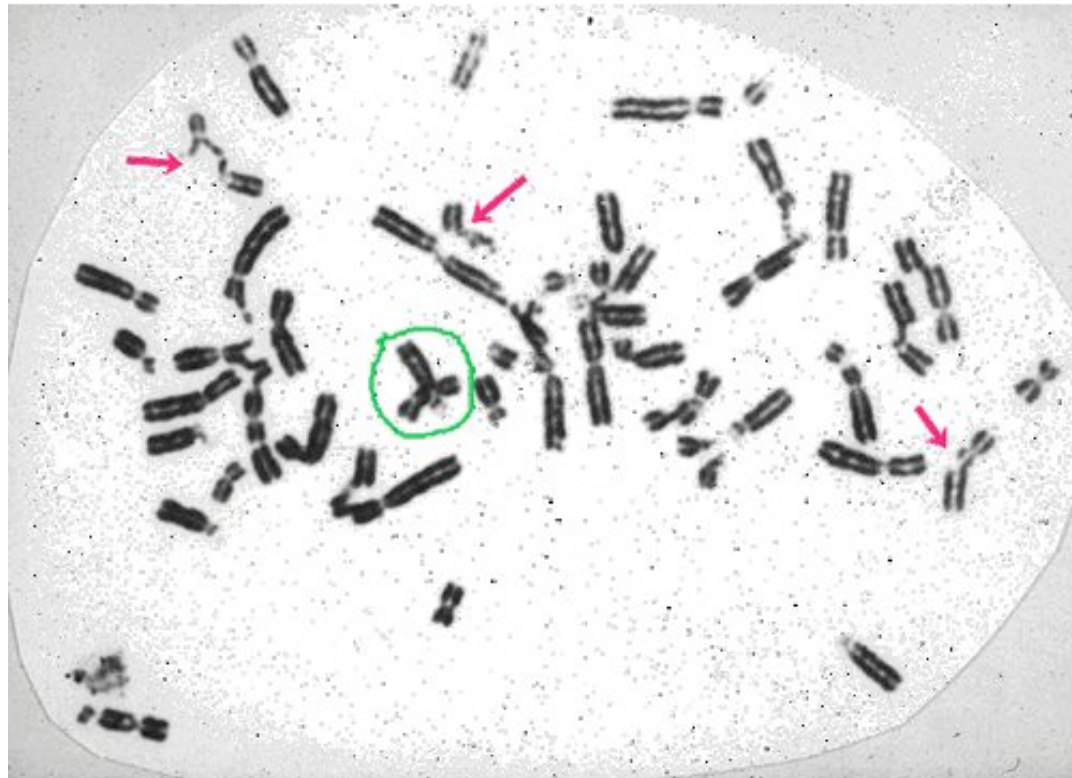
FANCG (12%)



Diagnosis

FA is diagnosed by a chromosome breakage test

Lymphocytes are cultured in the presence of mitomycin C and observed for excess chromosome breakage



Treatment

Bone Marrow Transplant (BMT)

Cells from the patient's bone marrow are replaced by someone else's cells.

Cells from a donor's bone marrow or umbilical cord blood can serve as a source for the transplant.

The 2 year survival rate following BMT in FA patients is variable

60 - 85% with a matched sibling donor

20 - 40% with a donor from a bank.

Molly Nash

Umbilical cord blood from her matched brother served as the source for donor cells.

With a bone marrow transplant Molly Nash is doing well.

She attends school, dances, plays soccer

She no longer has anemia, and is no longer at risk for leukemia (her new bone marrow cells do not have the mutation)

However, she still needs treatment for intestinal and spinal abnormalities and she is at risk for various cancers later in life.