Inheritance Patterns of BREast CANcer
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**Discovery**

- Mary-Claire King began her search for the hereditary gene of cancer in 1974.
- A genetic analysis on 23 extended families that had 146 cases of breast cancer was performed.
- Diagnosis at a young age and frequently affected males pointed to inheritance rather than sporadic accumulation.
- Multiple statistical methods were performed to test likelihood of linkage.
- Logarithms, a model of inheritance, and pedigrees were formed.
- These statistics led to a linkage at D17S74, a marker on chromosome 17.
- The breast cancer gene (BRCA) is the first inheritable cancer gene to be found.

**Structure and Function**

- BRCA plays a role in transcriptional regulation, cell cycle checkpoints, tumor suppression, and DNA repair.
- The gene consists of a RING domain, an exon and coiled region, and a BRCT domain.
- The RING attaches to ubiquitin which regulates the cell cycle growth and DNA synthesis.
- The exon and coiled region code for and transport proteins to help repair damaged DNA.
- The BRCT domain is a phosphoprotein binding area for tumor suppressors to attach to and regulate the cell cycle.
- All areas of BRCA work with multiple other proteins to ensure DNA repair, correct cell cycle steps, and tumor suppression.

**Mutations**

- Mutations could be caused by an insertion, premature stop codon, a deletion, and more.
- When the coiled region contains a mutation, homologous recombination (HR) malfunctions and regenerates damaged DNA.
- If the RING domain contains a mutation, the tumor suppressor function of ubiquitin fails to stop tumor growth.
- Mutations in the BRCT domain affect tumor suppression.
- When binding sites are damaged in the exon and coiling region, BRCA is unable to send help to repair damaged DNA.

**Inheritance**

- More than 1700 inheritable mutations of BRCA have been found.
- One in eight women will get breast cancer before 85.
- Women with a BRCA mutation have a 72 percent chance of getting breast cancer.
- BRCA mutations make you susceptible to ovarian, pancreatic, skin, and colon cancer.
- The inheritance of BRCA is autosomal dominant and often infect one or more individual in a generation.
- BRCA is a germline mutation that is inheritable and is passed from parents to offspring in either a sperm or egg cell.

**Figure 1:** A timeline of the search for the genetic underpinnings of early onset familial breast cancer.

**Figure 2:** Structure of BRCA gene.

**Figure 3:** 3D structure of BRCA.

**Figure 4:** Pedigree of families 1-7 of Mary King's study.

**References**