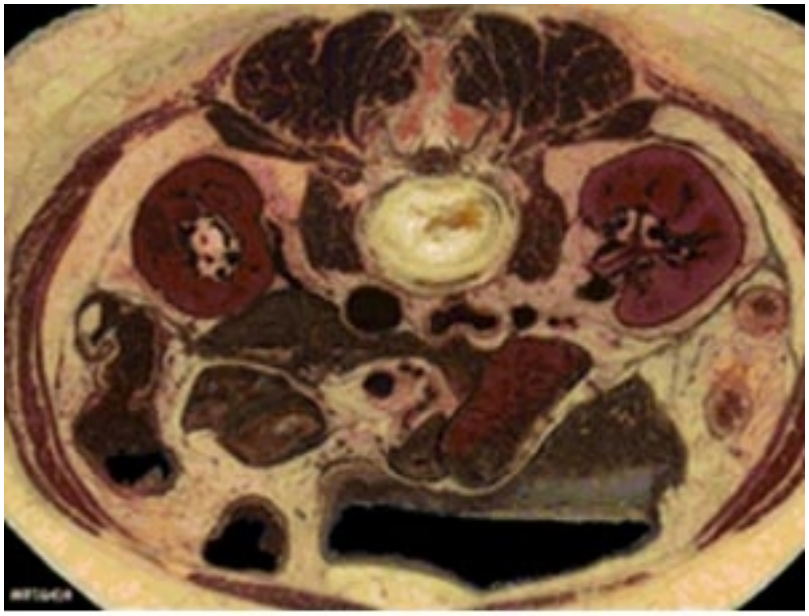
Female-Specific Diseases



Axial view of visible woman. (From the Visible Human Project, National Library of Medicine.)

Biomedical research has demonstrated biological differences between females and males in virtually every organ and system of the body. Research has also revealed the genetic and molecular basis of a number of gender-based differences in health and disease, some of which are related to genotype — XX in the female and XY in the male.

These findings suggest that there are multiple differences in the basic cellular biochemistry of males and females that can affect an individual's health. Many of these differences do not arise from differences in the hormonal regime to which males and females are exposed, but are a direct result of the genetic differences between the two sexes.

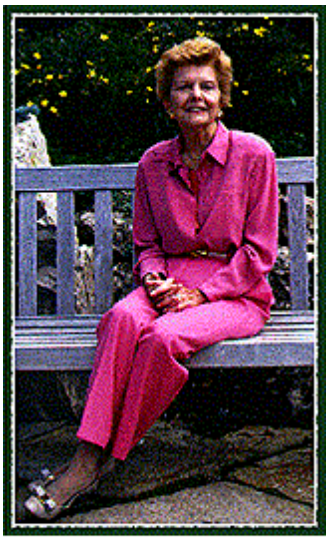
Further studies on the relative roles of the sex chromosome genes is likely to illuminate the reasons for expression of some diseases within and between the sexes. Understanding the bases of these gender-based differences is also important for the development of new approaches to disease prevention, diagnosis, and treatment.

Breast and ovarian cancer

Breast cancer is the second major cause of cancer death in American women, with an estimated 44,190 lives lost (290 men and 43,900 women) in the US in 1997. While ovarian cancer accounts for fewer deaths than breast cancer, it still represents 4% of all female cancers. For some of the cases of both types of cancer, there is also a clear genetic link.

In 1994, two breast cancer susceptibility genes were identified: *BRCA1* on chromosome 17 and *BRCA2* on chromosome 13. When an individual carries a mutation in either *BRCA1* or *BRCA2*, they are at an increased risk of being diagnosed with breast or ovarian cancer at some point in their lives. Until recently, it was not clear what the function of these genes was, until studies on a related protein in yeast revealed their normal role: they participate in repairing radiation-induced breaks in double-stranded DNA. It is though that mutations in *BRCA1* or *BRCA2* might disable this mechanism, leading to more errors in DNA replication and ultimately to cancerous growth.

So far, the best opportunity to reduce mortality is through early detection (general screening of the population for *BRCA1* and *BRCA2* is not yet recommended). However, new strategies to find anti-cancer drugs are constantly being developed. The latest, called "synthetic lethal screening" looks for new drug targets in organisms such as yeast and fruit flies. In the same way that studies in yeast recently helped to identify the functions of BRCA1 and BRCA2, it is thought that drugs that work in more primative organisms will also be applicable to humans.



"While we all work toward a cure, education, research and increased access to treatment remain our best allies in the fight against breast cancer."

Betty Ford, former breast cancer patient and now an activist on behalf of expanded breast cancer research and education.

Important Links

Gene sequence

Genome view see gene locations

LocusLink [www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=breast%20cancer&ORG=Hs&V=0] collection of gene-related information

BLink [www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=6552299&org=1] related sequences in different organisms

The literature

Research articles online full text

Books online books section

OMIM catalog of human genes and disorders

Websites

CancerNet [cancernet.nci.nih.gov/] from the National Cancer Institute, NIH

Oncolink [oncolink.upenn.edu/] comprehensive cancer information from the University of Pennsylvania

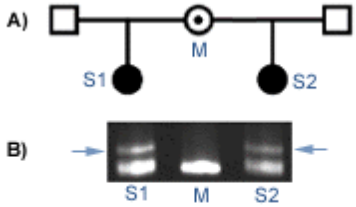
GeneClinics [www.geneclinics.org/profiles/brca1/index.html] a medical genetics resource

Rett syndrome

Rett syndrome (RTT) is a progressive neurodevelopmental disorder that almost exclusively affects females. It has an incidence of about 1 in 10,000 births, making it one of the most common causes of profound mental retardation in girls. Individuals with RTT develop normally until the age of 6 to 18 months, when they begin to lose purposeful use of their hands and speech. Affected individuals also show reduced muscle tone, wringing hand movements, autistic-like behavior and seizures.

A gene which causes RTT, *MeCP2*, has been found on the long arm of chromosome X (Xq28). Normally, females have two X chromosomes and males have an X and a Y. Since males do not have an additional copy of X to offset a defect, most X-linked diseases affect males. Then, why are males not affected by RTT? One possible explanation is that the absence of a functional copy of *MeCP2* is lethal to the male fetus before birth. Researchers have shown this to be the case in a mouse model. Another question is why females are affected by RTT, even though one of their X chromosomes is normal. This is likely due to X inactivation, a normal process whereby one X chromosome is randomly inactivated in every cell. This partial deficiency - where the normal copy of *MeCP2* is active in some cells and inactive in others - allows girls with RTT to survive and develop normally during early infancy.

MeCP2 is believed to code for a protein which controls gene expression in the cell. Although it is not clear what the mechanism is, partial loss of this protein may lead to over expression of certain genes, leading to the RTT phenotype. With the discovery of *MeCP2*, investigators hope to develop a test for RTT which will allow for early diagnosis, prenatal detection and, ultimately, presymptomatic therapy.



A) Pedigree of half-sisters (S1 and S2) with Rett syndrome and their carrier mother (M). **B)** Conformation-sensitive gel electrophoresis (CSGE) showing the same extra band (arrows) in the DNA of both half-sisters, not present in their mother (M). It is likely that the mother, who is normal, transmitted the disease to her daughters through a germline mutation present in her ovum, but not in the other cells of her body. [Adapted from Amir, R.E. et al. (1999) *Nature Genetics* 23, 185 –188., with permission.]

Important Links

Gene sequence

Genome view see gene locations

LocusLink [www.ncbi.nlm.nih.gov/LocusLink/list.cgi?Q=rett&ORG=Hs&V=0] collection of gene-related information

BLink [www.ncbi.nlm.nih.gov/sutils/blink.cgi?pid=4826830&org=1] related sequences in different organisms

The literature

Research articles online full text

Books online books section

OMIM [www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=312750] catalog of human genes and disorders

Websites

Information Sheet [www.ninds.nih.gov/health_and_medical/disorders/rett_doc.htm] from the National Institute of Neurological Disorders and Stroke, NIH

International Rett Syndrome Association [www.rettsyndrome.org/] support and information for families