

disordered imprinting, as in preeclampsia, which also demonstrates growth restriction in utero. These diseases can only be understood within the context of imprinting as a common mechanism of parental conflict and manipulation of the phenotypic outcome of children.

IMPRINTING AND COGNITION AND BEHAVIOR AFTER BIRTH

Although only approximately 100 human genes are presently known to be subject to parent of origin effects, these prove to have tremendous implications for the development and eventual adult attributes of the human, including its cognitive and behavioral attributes. Imprinting effects, like other genetic expression patterns, need not be only all or none, but also may manifest as earlier age of onset effects or changes in severity.

In Turner's syndrome, a parent of origin effect exists in social and intellectual functioning. The phenotypic female (XO) could have received her only X chromosome from her father (Xp) or her mother (Xm). Xp Turner's women—who received a paternally derived X (the same as every non-Turner's woman)—were shown through surveys to display greater attributes of social intelligence. These data were confirmed by higher performance on tests of verbal IQ and social inhibition when compared to Xm Turner's women. Xm Turner's women—who receive a maternally derived X (which non-Turner's males always receive from their mothers)—performed better than Xp Turner's women on measures of visuospatial function.

Other prominent cognitive and behavioral manifestations of the effects of imprinting are seen in a number of neuropsychological disorders, including autism and schizophrenia, and can help explain such varied phenomenon as motor tic complexity in Tourette syndrome when relevant imprinted genes are maternally inherited (and greater verbal tic complexity when paternally inherited).

SEE ALSO: DNA; Gene Silencing; Turner's Syndrome.

BIBLIOGRAPHY. D.P. Barlow, "Gametic Imprinting in Mammals," *Science* (v.270, 1995); M. Constância, G. Kelsey, and W. Reik, "Resourceful Imprinting," *Nature* (v.432, 2004); A.R. Isles and L.S. Wilkinson, "Imprinted Genes, Cognition and Behavior," *Trends in Cognitive Sciences* (v.4,

2000); R.L. Trivers, "Parental Investment and Sexual Selection," in B. Campbell, ed., *Sexual Selection and the Descent of Man, 1871–1971* (Aldine, 1972).

OMAR SULTAN HAQUE
HARVARD UNIVERSITY

Genomic Library

A genomic library is a collection of genes or DNA sequences created using molecular cloning. These libraries are constructed using clones of bacteria or yeast that contain vectors into which fragments of partially digested DNA have been inserted. These bacteria and yeast are subsequently grown in culture and when these microorganisms replicate their genome, they also replicate the vector genome contained within them, that is, they replicate DNA fragments that had been inserted in vectors producing clones of the original DNA.

This collection of clones, in theory, contains all sequences found in the original source, including the sequence of interest. This sequence of interest is identified using screening methods that are very complex and capable of finding the original clone among 10 million starting clones. Genomic libraries can be constructed using various hosts like plasmids (insert size up to 15 kb), bacteriophage lambdas (insert size up to 20 kb), cosmids (insert size up to 45 kb), YACs and (insert size up to 2,000 kb), and many more. Some important ones are as follows:

CONSTRUCTING GENOMIC LIBRARIES USING PLASMIDS:

This is the process of cloning human DNA fragments by inserting them between two *EcoRI* digested sites of a plasmid cloning vector. After the human DNA fragments are inserted into the plasmid, the plasmids in turn are inserted into bacterial cells. In the end, these host bacterial cells contain their own chromosomal DNA together with plasmid DNA. As these bacteria replicate their chromosomes, they also replicate with them the plasmid cloning vectors. Plasmids are very convenient to work with because they contain one origin of replication, one of more selectable markers (such as a gene that confers resistance to antibiotics),

and one or more restriction sites that can be cut and used for ligation of foreign DNA molecules.

CONSTRUCTING GENOMIC LIBRARIES USING BACTERIOPHAGE VECTORS:

The human genome is partially digested with a restriction enzyme like *Sau3A* in a specific way so that some of the sites are cleaved and others are not. By this way, random cleavage of the sites occurs and a collection of overhanging fragments of length suitable for cloning can be obtained, which are then ligated into bacteriophage lambda “arms” prepared so that the *Sau3A* ends of human DNA fragments can be ligated into the vector. The recombinant lambda chromosomes are then packaged into the infectious bacteriophage, and then the library, containing 1 million or more fragments of genomic DNA, can be stored for the future isolation of many genes. A collection of several hundred thousand phages would represent the entire DNA from the human genome.

CONSTRUCTING GENOMIC LIBRARIES WITH YEAST ARTIFICIAL CHROMOSOMES (YACS):

Large fragments of human DNA (over 500 kb) are generated by partial *EcoRI* digestion of human genomic DNA. Individual vector arms contain telomeres at one end and *EcoRI* compatible overhangs on at the other end. Individual vectors also carry a different selectable marker, and one arm also contains a centromere and selectable markers at each end and a yeast chromosome at the other end. The YACs are transferred into yeast, and the selectable markers are used to select only those yeasts that contain a properly constructed YAC.

ADVANTAGES OF MOLECULAR CLONING

The main task of modern medical genetics is to understand genetic disease in terms of mutations, and to find highly efficient methods of diagnosis and treatment. Medical geneticists, however, are faced by two difficulties when trying to find the basis of genetic disease. The first difficulty is obtaining enough amount of DNA to work with because cells generally have only two copies of a gene and some genes are only transcribed in specific tissues providing very little RNA to work with. The second difficulty is obtaining a purified form of the specific sequence of interest from all other sequences of DNA and mRNA pres-

ent in the cell. To solve these two problems, scientists have come up with various techniques, one of them being molecular cloning. Molecular cloning allows us to obtain large sequences of purified DNA that were, otherwise, impossible to obtain.

SEE ALSO: Clone; Genetic Disorders; Genetic Testing/Counseling; Genetics.

BIBLIOGRAPHY. Robert L. Nussbaum, Roderick R. McInnes, and Huntington F. Willard, *Genetics in Medicine*, 6th, ed., (Thompson & Thompson, 2001); Susan L. Speaker, Elizabeth Hanson, and M. Susan Lindee, *Guide to the Human Genome Project: Technologies, People, and Information* (Chemical Heritage Foundation, 2005).

RAHUL GLADWIN, M.D.

UNIVERSITY OF HEALTH SCIENCES ANTIGUA

Genotype

A genotype is the specific genetic constitution or makeup (genome) of an individual in terms of its DNA. The DNA through the genotype determines the hereditary potentials and also the limitations of an individual person (or indeed that of any organism) from its embryonic formation through to adulthood. For organisms that reproduce sexually, the inherited genotype contains the entire complex set of genes from both parents. This means that after sexual reproduction, it is certain that each individual will have a unique genotype, except for identical twins, triplets, and so forth, who are derived from the same fertilized egg. This contrasts with the phenotype of an individual which involves the physical appearance and constitution of an organism.

For medical research, the genotype is crucial in working out ways of treating diseases in general, separated from the person suffering from the disorder. This has been particularly important in the treatment of cancer, with oncologists and their research teams anxious to work on the fundamental causes of cancer and try to eliminate hereditary factors that might otherwise influence their work. Much of the original research and the development of ideas on genotypes was carried out by the Danish botanist and geneticist Wilhelm Ludvig