The Human Genome project is gradually finalizing the last details of the Human DNA sequence. It is only a matter of time before all 23,000 genes and their gene products will have been mapped and characterized. The results of this historic achievement have brought some interesting findings to light. The polymorphic sequence variants (SNP) and copy variants (PCV) in the genome have opened new avenues for analyzing the genome in search of genes involved in complex diseases. The fairly simplistic view we had on the composition and function of genomes has also been altered seriously. A whole series of additional mechanisms that regulate the expression of genes have come to light. In recent years it has indeed been shown that the non-coding sequences of the DNA are not the ‘junk DNA’ they were supposed to be. To give just one example, thousands of miRNAs encoded in introns or in other parts of our DNA, are transcribed and can have dramatic effects on the expression of our genes. Based on this knowledge a new approach for experimental and therapeutic gene silencing (siRNA) has flourished.

In the mean time we are in the middle of the next revolution in our understanding of how our genes are regulated. For years we have known that during maturation of the male and female gametes, a number of regions in the genome receive a sex specific imprint (mainly by methylation). This explained the molecular defects responsible for different neonatal defects, such as Beckwith-Wiedemann syndrome, Prader-Willy en Angelman syndrome and others. Uniparental disomy of particular chromosomes, which occurs more frequently than initially expected, also causes developmental defects because of this differential parental imprinting.

In the mean time, epigenetic regulation of gene expression has come out of the dark and the epigenetic genome is no longer a study object for originals. While not all authors use the same definition of epigenetics, one can identify different modifications which affect the expression of genes in an epigenetic fashion: methylation of DNA; methylation, acetylation, phosphorylation or ubiquitination of histone tails; the use of histone variants; modified local or higher order chromatin structure. All these epigenetic factors have an impact on DNA replication, recombination, repair and gene expression. During development of the embryo and the fetus, tissue and organ specific epigenetic pattern are

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established, which play a role in the tissue-specific
gene expression patterns.

As people grow older, these epigenetic patterns
may change. A nice example is given by studies on
identical twins. The epigenetic patterns in somatic
tissues in these individuals differ significantly later
in life, and these differences are greater in those who
were reared apart and lead to differences in the
expression of many genes and differences in disease
susceptibility. The epigenome is much more suscep-
tible to the effect of external factors than the DNA
sequence. This is nicely illustrated by the Wolbachia
parasite in *drosophila*. This parasite can completely
revert the sexual development of the flies and even
mask lethal mutations. In humans, many diseases
with a genetic predisposition, such as Chon’s dis-
ease, cardiac hypertrophy and diabetes, require an
exogenous trigger (infection, physical stress etc)
before the full blown disease is established.

Nutrigenomics, the study of the interaction
between genes and nutrition, will undoubtedly play
a major role in our understanding of diseases and
their prevention in the future.

Epigenetic changes also play a major role in
malignancy. A profound loss of global 5-methylcy-
tosine genomic content and discrete areas of dense
hypermethylation in promoter sequences of tumor
suppressor genes are well known. In addition, mod-
ifications of histones have been identified and
abnormal chromatin remodeling characterizes
many malignancies. The search for the genes
responsible for these epigenetic changes is ongoing.
The European Epigenome Project Consortium is
systematically analyzing the epigenome of the dif-
ferent chromosomes.

By introducing the Review Series on
Epigenetics, the Journal of Cellular and Molecular
Medicine provides the researchers with an impor-
tant source of up to date information, particularly
for those who have not chosen gene regulation as
their topic of research.

Any new insight into this fascinating and very
complex aspect of genetics can be covered in this
section, provided it takes the reader to the edge of
our present knowledge.

Your contributions, suggestions or comments
are welcomed.

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