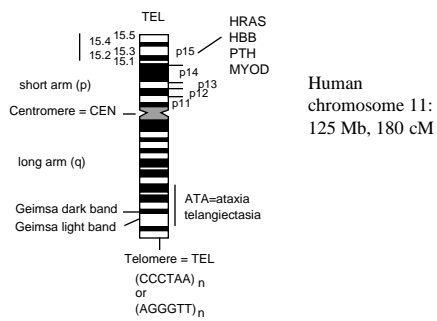


Chromosomes and chromatin

Chromosomes organize and package genes inside cells

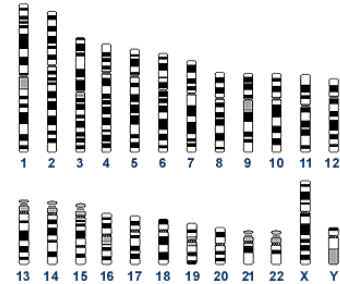
- Bind packaging proteins to DNA to make it more compact.
 - Histones +DNA = chromatin in eukaryotes
 - Virion proteins in viruses
 - HU (?) or other proteins in bacteria
- Loop chromatin and attach it to a matrix in nuclei

Bands and specialized regions of human chromosomes



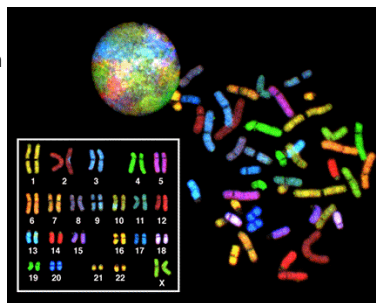
Human chromosomes, ideograms

Mitotic chromosomes are spread and stained with Geimsa. Those that stain are shown in black. G-bands (more A+T rich).



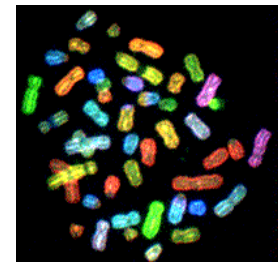
Human chromosomes, spectral karyotype

Reagents specific to each chromosome. Chromosome painting.



Identifying translocations

This photograph shows a complete set of chromosomes from an acute promyelocytic leukemia (APL) patient. A new technique called chromosome painting allows visual distinction between chromosomes and can be used to show the chromosome translocations that frequently occur in human cancers. In the case of APL, chromosome 13 is lost, there is a translocation between chromosomes 7 and 15, translocation between chromosomes 11, 15, 17, and between chromosomes 9 and 18. (Look for chromosomes painted with more than one color.) With thanks to Thomas Ried, National Human Genome Research Institute, NIH, for supplying the picture.



<http://www.ncbi.nlm.nih.gov/disease/>

Distinctive and common features of chromosomes

- Distinctive proteins and DNA sequences have been used to develop chromosome painting reagents.
- Genomic DNA in vertebrates has long (megabase) stretches of G+C rich DNA, and other long stretches of A+T rich DNA
 - Called **isochores**
- Virtually all this DNA is organized into chromatin, which has a common fundamental structure.

Chromatin Structure

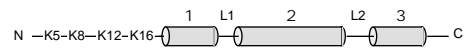
Principal proteins in chromatin are histones

H3 and H4 : Arg rich, mostly conserved sequence
 H2A and H2B : Slightly Lys rich, fairly conserved

H1 : very Lys rich, most variable in sequence between species

Histone structure and function

"Minimal" structure for a core histone, e.g. H4. Others have one additional alpha helix.

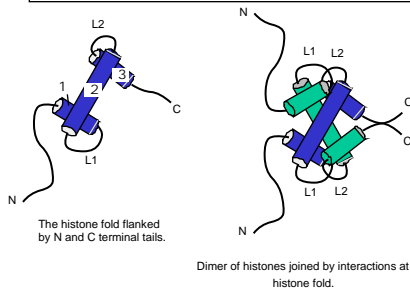


Highly charged N-terminal tail.

Globular, hydrophobic domain for histone-histone interactions and for histone-DNA interactions.

Histone interactions via the histone fold

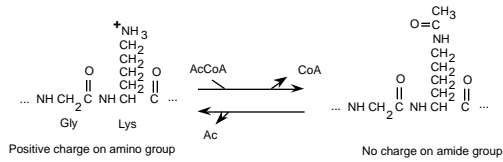
The alpha-helical regions of the core histones mediate dimerization.



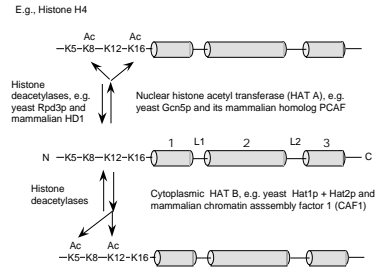
Nucleosomes are the subunits of the chromatin fiber

- Experimental evidence:
 - Beads on a string in EM
 - Micrococcal nuclease digestion

Acetylation and Deacetylation of lysines in proteins



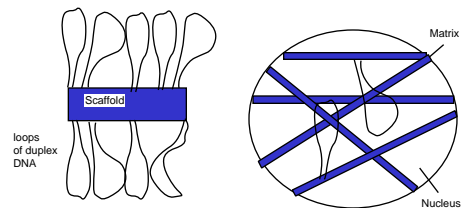
Acetylation and Deacetylation of histones



Effects of histone modifications

- Highly acetylated histones are associated with actively transcribed chromatin
 - Acetylation of histone N-terminal tails may affect the ability of nucleosomes to associate in higher-order structures
 - The acetylated chromatin appears to be more "open", and accessible to transcription factors and polymerases
 - HATs are implicated as co-activators of genes in chromatin, and HDACs are implicated as co-repressors

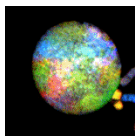
Matrix and scaffold



Mitotic chromosomes, with some DNA released

In interphase chromosomes, at least some DNA is attached to a matrix

Chromosome localization in interphase



In interphase, chromosomes appear to be localized to a sub-region of the nucleus.

Gene activation and location in the nucleus

- Condensed chromatin tends to localize close to the centromeres
 - Pericentromeric heterochromatin
- Movement of genes during activation and silencing
 - High resolution *in situ* hybridization
 - Active genes found away from pericentromeric heterochromatin
 - Silenced genes found associated with pericentromeric heterochromatin