## 7.013 Recitation 19 -2013

**Summary from Lectures #33-35:**

HIV is a retrovirus that infects the $T_H$ cells of our immune system. HIV gets into our $T_H$ cells by docking onto a protein called CD4 that our $T_H$ cells have on their surface. Our $T_H$ cells have CD4 on their surfaces because CD4 helps $T_H$ cells recognize the MHC class II molecules on the surface of macrophages, which is the job of a $T_H$ cell. However the HIV virus has evolved to have a glycoprotein on its surface that binds to CD4, thus targeting HIV to $T_H$ cells. This glycoprotein also has the ability to fuse the lipid bilayer of HIV to the cell membrane of our $T_H$ cells, thus dumping the contents of the HIV virus into our $T_H$ cells. The HIV virus harms our $T_H$ cells, thereby depleting our immune system and therefore our ability to fight the virus. HIV also mutates very quickly due to it having a reverse transcriptase that is highly mutagenic. This allows the HIV to be constantly changing the amino acid makeup and the shape of its viral proteins so that our immune system cannot gain immunity to the HIV.

**SCNT:** This is the regulation of transcription that is not dependent upon the DNA sequence. Epigenetics depends upon chromatin, and the chromatin is influenced by methylation of DNA. Methylation of DNA inhibits transcription, and the pattern of methylation of DNA varies depending on cell type and cell age. The embryo produced via somatic cell nuclear transfer (SCNT) will have the methylation pattern that is normal for the cell that donated the nucleus, but this pattern is not the normal embryonic pattern, and clones produced by SCNT are usually abnormal.

**Microarrays**: Not all cancers respond equally well to all treatments, so knowing the specific type or subtype of cancer is important to successful treatment. Some cancers can be identified by using histological tools, but other are best characterized by determining the gene expression profile. A DNA microarray is a multiplex technology that allows comparison of cells based upon the expression of many different genes. A DNA microarray consists of an arrayed series of thousands of microscopic spots of DNA, each spot representing a gene. When a DNA microarray is probed with mRNA isolated from cells, individual mRNA molecules will hybridize to the appropriate DNA spot. If a gene is highly expressed, more mRNA will be made from that gene, so more mRNA will hybridize to the corresponding DNA spot, and the signal from that spot will be greater.

**Environmental toxins:** Although there are approximately 200,000 FDA approved compounds only few have been tested for toxicity. One such compound is Bisphenol A, which is a present in plastics and can mimic the effect of estrogen a steroid hormone. Exposure to this compound has been shown to suppress fertility, cause cancer and also heart disorders in multiple species. This clearly demonstrates the importance of testing compounds for their potential toxicity.

**Human genome project:** Part 1 of this project has been completed and we now know there are 20,000 genes in our genome. We also know the protein coding regions of the gene. The 2$^{nd}$ part of Human genome project marks the era of new genetics and is an attempt to find out the disease genes alleles (approximately 70,000 caused by the changes in the human genome), describe all possible RNAs ($2X10^6$ approximately), identify different proteins, protein modifications, DNA-protein and protein –protein interactions. This is enormous information and requires advanced information processing and data storage programs and rapid and cheaper technology for

sequencing.As an outcome of new genetics we now know that our genome is really changeable i.e. big chunks of chromosomes flanked by direct repeats (50-150 bp long/ hot spots) can either be deleted or duplicated by unequal crossing over. This can help us better understand diseases like cancer, autism, schizophrenia etc.

**Organ repair and replacement:** There are about 1 million people who need organ transplant or repair. This problem is being dealt with in different ways some of which are described below.

**Artificial organs:** Here there is really no biological material. A good example is the foldable polyacrobate hydrogel lens, which is being used during cataract surgery. Limb replacement (uses artificial limbs made of titanium alloys) is also very successful. However, they come with a drawback since they are never connected to the neurons and can therefore not be controlled by the brain.**Bionic organs:** These are combination of synthetic and natural organs. A good example is the formation of 3D- micropatterned scaffold of hepatocytes, which make the liver. **Xenografts:** This represents other species i.e. pigs as donor for organ transplant. This has been a big failure because of hyper acute rejection of the organs by the recipient. One major issue with xenografts is the concern that other species may have viruses for which the humans have no immunity. These viruses may have devastating effect on organ recipients.

**Prions (Optional lecture, not a part of the final exam):** These are the infective proteinaceous particles. The diseases caused by prions are caused by the defective proteins. The defects arise not from the mutations in the genes that express these proteins, but from errors in the folding of these proteins into the proper three dimensional conformation. The protein with the altered conformation then seems to induce a change in the conformation of the normal protein counterpart so that it also becomes abnormal. The altered proteins have profound effects on its function in the cell. There is a long period of several years between the onset of the disease and the manifestations of the disease symptoms. Prions unlike the bacteria, viruses or nucleic acids cannot be altered or killed through UV irradiation. The transmissible spongiform encephalopathies (TSE), scrapie, kuru, mad cow disease and chronic wasting disease are some examples of prion related diseases.

## Questions:

1. What components does the virus bring in at the time of infection?

2. Why do HIV patients succumb to simplistic infections?

3. Why are HIV patients given combination therapy?

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