Lieber Seminar 1: The Mechanism of Human Nonhomologous DNA End Joining and Its Role in Chromosomal Translocations. (50 min + 10 min discussion)

Most pathologic double-strand DNA breaks are repaired by either of two pathways: nonhomologous DNA end joining (NHEJ) or homologous recombination (HR). HR appears to function only in late S or G2 of the cell cycle. NHEJ functions throughout the entire cell cycle. Therefore, most double-strand breaks (DSBs) are repaired by NHEJ, and all breaks where there is no long homology (<25 bp) are repaired by NHEJ.

I will describe what is known about the mechanism of NHEJ and how one can identify sites where NHEJ has occurred in the genome, as opposed to HR or some other repair pathway. I will also describe how NHEJ joins the breaks most chromosomal translocations.

Lieber Seminar 2: The Mechanism of Lymphoid Gene Rearrangements and Their Role in Chromosomal Translocations. (50 min + 10 min discussion)

V(D)J recombination is the programmed gene rearrangement process that occurs in pre-B and pre-T cells in all vertebrates. I will describe the normal process, its mechanism and the proteins involved in this mechanism. I will also describe how V(D)J recombination sometimes goes awry and causes chromosomal translocations in human lymphomas such as follicular lymphoma, mantle cell lymphoma and some pre-B cell lymphomas.**s**

Class switch recombination (CSR) is the programmed gene rearrangement process that occurs in mature B cells so as to change the antibody from IgM to IgG, IgA or IgE. I will describe the mechanism of class switch recombination and the known proteins involved. I will explain how R-loops provide an efficient target for the enzymes that initiate CSR, and I will discuss the DNA and RNA nucleotide sequence features that are necessary for R-loop formation. I will also describe how class switch recombination sometimes goes awry and causes chromosomal translocation in sporadic Burkitt's lymphoma and multiple myeloma.