Study Questions:

• Review some basic concepts in protein structure. What do you mean by primary, secondary, tertiary, and quaternary structure?

Primary structure : the linear sequence of amino acids. It starts from the amino-terminal (N) end to the carboxyl-terminal (C) end.
Secondary structure: alpha helices and beta sheets. Secondary structure is formally defined by the pattern of hydrogen bonds between the amino hydrogen and carboxyl oxygen atoms in the peptide backbone.
Tertiary structure is the three-dimensional shape of a protein. The tertiary structure will have a single polypeptide chain "backbone" with one or more protein secondary structures, the protein domains.
A few tertiary structures may fold into a ***quaternary structure***.

• Outline the domain structure of an IgG antibody.

IgG antibodies are the large globular proteins. It contains 2 ***heavy chains*** and 2 ***light chains***. The 2 heavy chains are linked to each other and to a light chain.
Each chain has a ***constant*** *and* ***a variable*** *parts*.
The nature of the heavy chains determines classes of immunoglobulins.
There are five types of heavy chains:

- IgG or γ (gamma) (IgG1, IgG2, IgG3, IgG4),
- IgA or α (alpha (IgA1, IgA2),
- IgM or μ (mu),
- IgD or δ (delta),
- IgE or ε (epsilon),

There are two types of light chains:

- κ (kappa),
- λ (lambda).

• What is BCR?

BCR (B cells receptor) is a transmembrane protein on the surface of a B cell. Each B cell expresses a single B cell receptor (BCR). The BCR is linked with molecules responsible for signal transmission after contact with the antigen: the Igα or CD79a and Igβ or CD79b.

• Describe the pre-B receptor and outline its functional roles during B cell development.

Pre-B receptor is in charge of signaling that a H chain has successfully emerged. After that, the cell enters to pre-B2 stage of development, in which L chain rearrangement occurs.

• What is receptor editing? At what stage of development is clonal deletion of B cells presumed to occur?

It occurs at the pro-B cell stage? Where H chain rearrangements occurs. // Cycling pre-B: We generate different chains and in this stage we “select” the H chain. It is important to know that cells with favorable H chain will be divided more times that cells with a not favorable H chain. H with not favorable H chain will die.

• What is B cell repertoire?

The B-cells repertoire of a human is a diverse range of B-cells distinguished by their unique immunoglobulin (BCR).
There are several checkpoints at different stages of B-cell maturation at which expanded clones could be molecularly defined:

- pro-B to pre-B cell : H chain rearrangements
- pre-B2 to transitional B cell : might be H chain and L chain rearrangements
- mature B cell : combinatorial and junctional diversity of the H and L chain + SHM

• What is a clone in B cell repertoire context?

Clone is a collection of genetically similar cells defined by similarities in their antibody heavy chain, light chain or a combination of both.

• Why is studying the B cell repertoire important?

B cells are an important part in studying causes and dynamics of autoimmune diseases (there was something about leukemia in the article). B cells population provides a BCR repertoire. Understanding of the BCR repertoire in the context of autoimmune diseases (and some others) is incomplete, and defining this could provide new insights for their therapy.

• Why is studying the B cell repertoire diversity important?

The analysis of mutations of clones might be useful to create a lineage of mutations that describes the process of clonal development. Analyzing the patterns of these lineages can give insights into the diversification and selection processes that lead to clonal evolution.