Lecture 16: Expression of Ab, mRNA Editing, T-cell Independent Antigens, Regulation

Expression of Ig Genes:
1. Promoter selection is obtained by proximity to enhancer sequences, which enhance the level of transcription from the closest promoter.
2. Unused V/D/J segments removed from mRNA by splicing.
3. Leader (signal) peptide signals export to rough ER. Removed during transport across ER membrane.

Events that Rely on polyA addition:
   i. Production of Membrane Bound and Soluble Immunoglobulin with the same specificity.
      The 3' end of every constant region contains the following elements:
      1. S exon codes for the carboxy-terminal sequence found in soluble IgM, a hydrophilic sequence.
      2. polyA: poly A cleavage and addition sites
      3. M1, M2 exons that code for the membrane domain. Hydrophobic sequences.
      4. 2nd polyA site.
      Alternate use of the two polyA sites results in the expression of soluble IgM (\(\mu 4-S\)) or membrane bound (\(\mu 4-M1-M2\)) IgM.

   ii. Co-expression of IgM and IgD: These two isotypes are expressed at the same time in the mature B-cell. The two constant domain gene segments are adjacent to each other on the chromosome. The 3' end of the \(\mu\) gene and the 3' end of the \(\delta\) gene have two polyadenylation sites. Alternative use of two of these sites leads to expression of membrane bound IgM or IgD.
Other Aspects of B-Cell development:

"Original Antigenic Sin" –
Regulation of B-cells.
i) B-cells also have Fc receptors.
ii) Binding of antibody to Fc receptors attenuates ability of B-cell to become active due to dephosphorylation of activated BCR-antigen complex.
iii) Mechanism is in place to turn off B-cell activation when pathogen is cleared by the acquired system.
iv) "Sin" because it prevents an active immune response to related pathogens with similar epitopes if some of the original antibody is still present. This antibody will bind to the related antigen and prevent a B-cell response.

Secondary B-cell Response:
i) B & T_h-memory cells can live for decades
ii) Clonal expansion during activation of B-cells produces large number of memory cells.
iii) Formation of antigen-B-cell/T-cell complex in 2° organs enhanced by larger number of cells.
iv) Activation process faster.
v) Heavy chain type (isotype) and high affinity are preserved on memory B-cells.

T-cell Independent Antigens:
i) Repeating epitopes on pathogen can activate B-cells to differentiate into plasma cells. Clustering of BCR can provide a sufficiently strong signal for the cell to differentiate into IgM secreting plasma cells.
ii) No direct contact with T_h cells, (response can be aided by proliferation cytokines from T_h cells.)
iii) No class switching
iv) No affinity maturation
v) No memory cells.