Summary of Papers

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Summaries

1. Berland Et Al finds that sub-optimal V(D)J recombination activity can cause partial immune defects and/or DNA repair defects. He discovers this through an analysis of the TCRα repertoire, which also helped him to reveal a possibility of early diagnosis of patients presenting with hypomorphic DNA repair defects inclined to experience acute toxicity during prehematopoietic stem cell transplantation conditioning[1].

2. Bolland Et Al successfully developed a method to measure antigen receptor diversity. He achieves this through discovering the underlying logic of the recombination rates of V gene segments, chromatin states. In this paper, it was found that chromatin states were based on clan evolution and not geographical location, which was found out because of the ability of VDJ-seq to report on DNA rather than downstream RNA expression[2].

3. In this paper, Dash Et Al describes the analytical tools they developed to characterize epitope-specific repertiores. The analysis demonstrates that each epitope-specific repertiore contains a group of receptors that share core sequence similarities. They were able to highlight key conserved residues driving TCR recognition[3].

4. TCRβ subunits can be identified by their hypervariable $CDR3$ sequence, whihc encodes the principal site of antigen contact. Freeman Et Al was able to identify 33,664 TCRβ clonotypes and retrieve precise measurements of $CDR3_\beta$ length diversity, usage of nontemplated bases, sequence convergence, and gene usage and pairing[4].

5. In this paper, Gellert Et Al discusses the role of enhancers, histone acetylation, and chromatin remodeling factors in controlling accessibility. This paper explains how RAG proteins, repair factors, and regulation affect V(D)J Recombination[5].

6. Livak and Schatz analyze V(D)J Recombination by-products by using murine TCRα locus as a model system. This analysis revealed many retained DNA sequences which were previously thought to have been lost during intrathymic T-cell development.They also discovered that strict regulation of V(D)J recombination is required to prevent the loss of functionally selected, assembled antigen receptor genes[6].

7. This paper focuses on TCR activation and the application of TCR-engineered T cells and how to further enhace the function of TCR-engineered T cells and increase their lifespan in tumor

areas.T cells using combined recognition pathways showed greater efficacy by by-passing the mechanisms by which tumor cells escape immune recognition. Yu Ping Et Al finds that in combination with drugs targeting chemokines, cytokines, and immune checkpoint proteins, TCR-engineered T cells can obtain better clinical response in future treatments[7].

8. Ramesh Et Al discovers an inherent T cell defect in Common Variable Immune Deficiency(CVID), which displays unique V gene usage. They found that the CVID CDR3 repertoire is strikingly deficient in junctional modifications in V–D and D–J segments. Because TCR abnormalities like this in CVID don't seem to be associated with specific clinical issues, they concluded that there must be inherent defects in T cells[8].

9. It was found that bladder cancer exomes with productive TCRβ recombinations in tumor resident T cells showed a positive response to drug treatments. The detection of these recombinations were discovered to be useful for prognosis in bladder cancer because the approach for using exome files to assess the immune status of tumor samples was validated[9].

10. This paper utilizes sequence repertoire analysis to underline the impact of selection on the V(D)J recombination process. They quantify the changes with time in the way receptors are generated and selected for function as well as a strong increase in repertoire diversity. Sethna Et Al also finds that selection is weaker in lab mice than in humans and it doesn't affect the diversity of the repertoire[10].

11. A high frequency of CDR3s are found in type 1 diabetes patients, suggesting that early events in thymic cell development and repertoire generation are abnormal in type 1 diabetes. Short CDR3s are also found to increase risk for autoimmune disease. Random VDJ gene rearrangement typically yields a pre-selection repertoire of TCRB CDR3s across a range of lengths, but shorter lengths are favored in type 1 Diabetes.These findings are consistent with the idea that antigen-receptor repertoire should be included as a major contributor to disease risk[11].

12. Zhao Et Al used a linear-amplification VDJ-seq method to measure T cell receptor diversity. This paper used linear-amplification because it reduces the bias in the PCR process.This method contributes to further understanding of the antigen receptor rearrangement process because they are able to obtain millions of clean sequence reads efficiently[12].

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