Synopsis on the Immunology article

The article, "Extensive RNA Editing and Splicing increase Self-Representation Diversity in Medullary Thymic Epithelial Cells," by Danan-Gotthold (2016) describes the process of establishing a central tolerance in the thymus. The immature T cells are trained by the thymic stroma to be immunocompetent. The prepared cells become capable of identifying recognizing invaders. The process which involved instruction of the T cells to discriminate between self and non–self while being potentially harmless. The experiment aims to determine the levels of medullary thymic epithelial cells. The article uses various research methods to analyze and describe the findings from the experiments conducted. The present review will examine the experimental approach, justification, and significance of the research.

Experimental approach

The experiment utilized various research methods in the preparation and analysis of the results. The research methods used help in the analysis and discussion of the findings from the research experiment. The approaches included;

RNA Sequencing

RNA sequencing refers to a tool for measuring a transcriptome. The experiment population, AireKO was separated from distinct strains. This separation was necessary for the extraction of RNA and its sequencing. The method was also important for the researchers to detect known and unknown features of genes, hence detecting the transcript isoforms (Danan-Gotthold, 2016, pg. 10). First, the researchers isolated the individual strains in library preparation. It was achieved by using an illumination. In the processing stage, the researchers used 13 different tissue types of genes. The approach was necessary to the research as since it required high accuracy levels to detect new changes that had not been identified by earlier researchers.

Alternative splicing

The alternative splicing was used to determine the differences in frequency between the cell type as and cell types and the tissues under examination. The method was significant in the comparison of the detected junctions within each cell and expressing them in mTECs. AS was useful in the editing of the variants using r-MATS, this method altered exons expressing them in forms where one was in the tissue under examination and the other forms in m-TEC.

Findings

mTECs Express High Coding Genome

Although expression of the gene in mTECs is a common phenomenon, the procedure has not been extensively experimented using the RNA sequencing methods. The RNA sequence analysis used on datasets achieved various mTECs populations within the body parts of the mouse i.e. the lungs, brain, testes, and the skin. Further analysis expressed that most body tissues had a 60-65% of the coding genome. Some parts also expressed a higher percentage of coding genome, i.e., the testes and the brain at approximately 85% coding gene. However, the testes and brain tissues with Aire-deficient mTECs expressed a relatively lower genome of 75%. This was, however, larger than the overall percentage of the other peripheral tissues. From this analysis, it was clear that mTECs expressed much of the coding genome. The mTECs population which is not Aire-deficient expressed a higher coding gene as compared to the Aire-deficient mTECs population.

Tissue Self-shadow in mTECs

The experiment analyzed the level of overlap of tissue that restricted gene in any particular peripheral tissue. Using the leave-one-out analysis, and TRA detection, all RNA -seq were analyzed. The results indicated that the peripheral tissues had a high tissue overlap with a 60-100% tissue signature. The tissues in parts such as the brain and testis expressed a low

percentage of tissue overlap of approximately 31%. However, the overlap of the mTECs and other tissues was low in the Aire-deficient mTECs.

The central tolerance of the testis in the brain and tests indicate a low tolerance as compared to periphery tissues. Self-shadow cells from these areas escape to the periphery where they are controlled by antigen sequestering. For instance, when cells from areas such as the brain or testis are exposed to antigens, i.e. after an injury, the T cells that escaped the central tolerance may be activated to attack these areas.

Alternative Splicing Events per Gene

An alternative splicing of a single gene gives rise to various protein variants. These variants differ in amino acid sequences. The use of alternative splicing of a gene leads to an increase in the diversity of antigens in these tissues. The difference in tissue antigens helps in a reduction in immune system self-reactivity. Using the RNA-seq., the experiment obtained that mTECs displayed a high splicing propensity to events per gene. For example, mTECs various variants which are tissue restricted, these variants are often expressed in different alternative forms in the hematopoietic system as well as the brain.

High RNA editing rate in mTECs

RNA editing expands the diversity of protein hence making changes to nucleotide sequences In an RNA molecule. From the experiment, the researchers obtained a high RNA editing in mTECs. Mature mTECs exhibited a high RNA editing which was similar to that of the brain. The brain and the colon have large RNA editing levels (Danan-Gotthold, 2016, pg.6). The high levels of RNA editing were also observed in Aire-deficient mTECs, but not in immature mTECs. It was achieved by editing the rate of each sample of RNA sequence, and compared them with other sites altered between mTECs.

Methods of Analysis

RNA Sequencing Analysis

The researchers opted to use the RNA sequencing method due to its high sensitivity and accuracy in measuring expressions across the transcription as well as its high visibility of previously undetected changes. In this research, various studies had been conducted on gene expression in different tissues including the brain and the testis. Thus, to ensure accurate independent results were achieved, the researchers opted for the RNA sequence analysis. This method took into consideration the prior findings from various investigators, an analysis of Aire-deficient mTECs and specific extracted tissue genes.

Alternative Splicing

Alternative splicing of genes was used in the research to obtain comparable samples. The splice gene junctions were compared with the mTECs. This was conducted using r-MATS. This analysis was important as it was used together with the RNA seq to determine the TRA ration in mTECs and the AireKO samples.

Leave-One-out Analyses

This expression analysis was utilized in this research to help compare the mTECs genes with other tissues. The research created samples which were randomly aligned. For instance, the research assessed the TRA gene expressions by mTECs by comparing a whole sample of FPKM values. The leave-one-out analysis was used to obtain the size of RNA sequence samples. This technique was important to the experiment as it helped assess the TRA genes using the mTECs.

Quality of Research

The article can be considered a quality research. The researchers vividly explain the methods used to analyze the research finding while explaining the research findings. The data used in the experiment was also well analyzed using graphs and tables. However, the research

did not provide the past reference of research conducted on the similar topic use them to be used as a comparison in the research. A paper that extensively examines and analyzes the previous scholarship is most likely to be reliable and credible compared to that which only presents its own research and presents it. The reason for this is that previous knowledge lays the foundation for any research work and acts as a go-to reference whenever issues of technicality need to be verified.

Significance of the Research to Immunology

This research was aimed at determining the extent of RNA editing and splicing t increase immune self-representation. Although much past research has been done to determine the immune manner in which transcriptome complexity differs from others, using RNA editing and alternative splicing, differ from other tissues. The research thus seeks to address this issues using different the alternative splicing and RNA editing of various tissue cells. From the experiments, it was observed that using the RNA seq analysis mTECs expressed a higher rate of protein coding genome. This indicates that mTECs have a strong ability to change to different forms capable of detecting invaders and avoiding self-reaction as compared to other tissues cells within the body. This is significance to the study of immunology as it extends the knowledge on the different reactions of abilities of genes in a body.

Conclusion

The article by Danan-Gotthold is critical in the determination of the extent of RNA editing and splicing in increasing the in self-representation diversity mTECs. Although similar experiments have been done in the past, the findings from the present article indicate that mTECs display high levels of cell alternative splicing. This comes as an advantage to this cells as they are capable of diversifying to various forms through splicing while being harmless to self-reaction. The propensity of mTECs is in tissue cells with a higher number of AS events per gene

and high RNA editing rate. These genes are often found in the brain and testis tissues as opposed to the peripheral tissues like the lungs and skin. The study is significant to the study of immunology as it gives more knowledge regarding RNA processing as a means of immune system self-representation. The self-representation is important in the establishment of different genes with no self-harm and autoimmunity prevention. This experiment serves as a stepping stone for any future research that will be conducted in an immunology topic. It also helps extend the studies regarding topics of immunology.