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The Role of Transcription and Gene Expression in the Evolution of T-Cell Lymphocytes

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Abstract
This research will concern on discussing transcription and gene expression impact in the T-Cell lymphocytes evolution, by discussing the composition of the lymphatic system, specifically the receptors of the T-cell lymphocytes. As well as, both transcription and gene expression will be discussed.To achieve that aims, Inductive Approach will be used by collecting information from different studies until reaching the final results.The study found that decreasing of LEF-1 does not affects the evolution of the Thymus, but affects non-lymphatic parts, deteriorates severely and leads to death. But, decreasing of TCF-1 transcription factors affects the differentiation of thymus cell, resulting in a pool of cells with its immature single positive $CD8^+$ SP/ $CD4^+$ SP, which migrate to different parts of the body.

1. Introduction

Immunity is defined as the ability of the body to recognize and discriminate, then to eliminate the foreign elements of the body's cells, whether external elements which are outside the body, such as bacteria, toxins, chemicals, or internal elements, such as senescent cells or abnormal cells, like cancer cells. And finally form a memory to be able to fight theses foreign elements again easily (Parham, 2009).

The body's means to resist pathogens are not confined to one type of immune response, but it includes Innate Non-Specific Immunity, which is the immunity that the human inherits from his parents, and develops its effectiveness naturally with the development of human life. It works since birth began in resisting pathogens. It does not depend on cellular or specific Humoral mixtures, and there is no need to be specifically identified for microorganisms or exotic organisms to perform its immune role (Alberts et al., 2002). Acquired (Specific) Immunity is the second type of immunity, which is the immunity that an individual acquires while in the womb through the placenta, or through breastfeeding, or by diseases infection and treat it through the injection of bacterial vaccines, Vaccines Viral, or serums (Szakal et al., 1989).

This research will focus on the role of transcription and gene expression in the evolution of T-Cell lymphocytes, by discussing the composition of the lymphatic system, in particular the receptors of the lymphatic T-cell, in addition to discuss both transcription and gene expression. To achieve this, Inductive Approach will be used by collecting information from different studies to reach a final result.

2. Lymphatic System

The lymphatic system consists of organs spread throughout the body that cooperate with each other in a consistent manner and thus functionally as one unit, and there is no correlation between them in the anatomical side as in the digestive system, respiratory system, or circulatory system (Katakai et al., 2004).

The first component of lymphatic system is the lymph, which is a colorless liquid containing all the components of blood plasma except proteins and leaching from the blood as it passes through the blood vessels (Shayan et al., 2006). The second component is the lymphatic capillaries, which is closed-end lymphocytes, and are composed of a single layer of squamous epithelium cells and are spread in the tissue near blood vessels (Shayan et al., 2006). The third component is the lymphatic vessels; the lymphocytes are associated with each other to form the lymphatic vessels before they enter the venous cycle, then two ducts will be here, Thoracic duct, and Right duct. The forth component is Lymph nodes, which is oval structures in the shape of clusters, as the size of the head of the pin. It is located along the lymphatic vessels in different parts of the body, including the armpit, elbow, and neck (Katakai et al., 2004). The fifth component is the lymphoid organs, which are the primary sites for the production of lymphocytes. It born from Lymphoid Progenitor, then it proliferates and matures to functional effector (Nairn and Helbert, 2002). The fifth component is the lymphocytes immune, which are the center of specialized immune response, giving the immune system the ability to distinguish between self and non-self as well as remembering characteristics (Winslow, 2006).

3. Transcription's and Gene's Expression Role in T-Cell lymphocytes Evolution

The lymphocytes stem from the red bone marrow and differentiate in the thymus gland under the influence of thymus hormones, which include Thymosin, Thymopioetin, and Thymic humoral factor. These hormones are small metabolites that regulate the differentiation and maturation of lymphocytes that migrate to the lymph nodes, spleen and liver, as the large part of them circulates in the blood because they play an important role in the cell-mediated immune response (Hanabuchi et al., 2010).

The selection process of T-cell occurs when is matured into thymus gland, that has the same quality as MHC to avoid damaging the body's components. When genetic mutations occur in T-cell receptors after leaving the thymus gland, it may lose its ability to bind MHC, or become a reactive-self.

The receptor of the cell T-Cell, is a heterotimer molecule, consists of two series of sugary proteins: alpha and beta (αβ) T-cell receptor, or gamma and delta (γδ) T-cell receptor, which bind together at the connecting piece through bonds Disulphide (Schatz and Spanopoulou, 2005).

Each gene at the beginning contains regulatory zones that determine when and where proteins are produced, called enhancers, transcription factor, and promoters. These regions are responsible for controlling the expression gene, which gives different cells different properties, such as liver and nerve cells. Although all cells of the body contain the same version of the gene, each cell produces special proteins to complete its functions (Richardson, 2002).

Transcription Factor is a protein that binds to a specific sequence of DNA and thus controls the copying of genetic information from DNA to mRNA (Latchman, 1997). Transcription Factors perform this task alone or with other proteins in groups by activating or blocking the direction of polymerase RNA, which is an enzyme that copies genetic information from the DNA of the RNA to specific genes. Transcription Factors perform several functions, most notably directing RNA Polymerase II to the promoter, and separating two DNA sequences to facilitate the transcription process (Roeder, 1996).

The Eukaryotes contains an important class of transcription factors known as General Transcription Factors (GTF), which are necessary for transcription and gene regulation. Many of GTFS are not actually linked to DNA, but are in fact a large part of the initialization phase of complex replication which interacts with RNA polymerases directly (Dillon, 2006). GTFS contains several of the most common TFIIA, TFIIB, TFII, TFIIIF, and TFIIH types, which are necessary to initiate the transcription process (Reese, 2003).

There are many factors governing the control of gene transcriptions, including the protein family called the High-Mobility group (HMG), are one of those factors expressed in T-lymphocytes (Laudet et al., 1993; Grosschedl et al., 1994). It contains two components, namely the Lymphoid Enhancer Binding Factor LEF-1, and T Cell Factor 1 TCF-1 which have been identified at all different levels of evolution of the lymphocytes (Oosterwegel et al., 1991).

LEF-1/ TCF-1 is transcript as a pre-B cell and T cell that is encoded into a LEF-1/ TCF-7 protein, which enhances its identification of the 59 CTTTGAA sequence in the TCRα Eα , and LEF-1/ TCF-1, and have identical properties in DNA binding, both of them activate the TCRα Eα. Additional binding sites for LEF-1 and TCF-1 have been identified in the transcription control areas of several T-lymphocytes, including CD4, TCRβ, and TCRδ (Travis et al., 1991).

In order to maintain the balance between life and death of cells, two factors known as TCF1 and RORγt, which regulate the levels of expression of Bcl-xl factor, to keep the critical cell of the binary positive cell (Xie et al ,2006).

4. Methods and Results

In this study, all chemicals, equipment and all laboratory facilities obtained from King Faisal Specialist Hospital and Research Center in Riyadh will be used for characterization aim of promoters in the T-Cell receptors of Alpha and Delta gene locus.

Following materials will be used: animal tissue sample of mouse Rag β (Rxβ), bacteria cells, human cell lines, Antibody, Enzymes, Kits, Plasmids, specific tools and chemicals, in addition the preparation of: (1X) TBE buffer, (1X) TDT Reaction buffer, 70% Ethanol, 10x annealing buffer, Medias for Bacteria Culture, SDS PAGE, DNA Polyacrylamide Gel Electrophoresis, and Dual-Luciferase Reporter Assay System.

Depending on Cloning PCR product into vector, DNA was extracted from Thymus Gland, and its concentration was measured. After that, primers were designed. DNA was doubled using a special kit (Qiagen, USA), by mixing the substances in specific quantities. After DNA doubling process, Electrophoresis process and Phenol / Chloroform extraction and Ethanol precipitation were done.

In cloning process, DNA PCR product and plasmid was digested using restriction enzyme, DNA PCR product and plasmid ligated using ligation enzyme, and Bacteria was transformed using DNA plasmid.

Finally, Biotin 3´ End DNA was labeled and Electrophoretic Mobility Shift Assay (EMSA) was done by DNA Polyacrylamide gel Electrophoresis.

A genetic relationship between the length of the catalyst and the gene expression was found. The lower the genetic length of the TEA and Jα49 promoters, the greater the gene expression in adult T lymphocytes and it is ineffective in embryos. In other words, the higher the length of the gene, the fewer the transcription factors associated with the catalyst. This reduces the activity of the catalyst that helps RNA polymerase inhibition for starting the transcription process.

After electrophoretic mobility shift assay process, radiated DNA was able to interact with different transcription factors to produce different proteins to meet cellular needs, while non-irradiated DNA produced no

protein.

Thus, the study showed that the TEA and Jα49 promoter were more active only in the binary positive cells during the rearrangement of the alpha TCRα lymphocyte in the adult stages of T lymphocytic maturation within the thymus gland, consistent with the results of Eα and TEA.

5. Conclusion

The research stated that decreasing percentage of LEF-1 has no impact on the evolution of the Thymus; it affects non-lymphatic parts, deteriorates hardly and leads to death. But, decreasing percentage of TCF-1 transcription factors have an impact on the thymus cell differentiation, which resulting in cells with its immature single positive $CD8^+$ SP/ $CD4^+$ SP, which migrate to different parts of the body.

The immobilization of immature single positive is an effective, systematic, and stimulating process of differentiation, as it leads to the generation of a large group of binary positive cells and is regulated by LEF-1 and TCF-1 transcription factors.

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