Research Article

Thymus, and Understanding the Modified T cell (ADP-A2M4) Regards to 1st DNA Strand Rules of Function and How to Support Modified T cells with Proper Amino Acids Chain for Reactivating many Tissues and Cycles Functions in Strong Linkages to ATPase Activities.

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Abstract

Cytotoxic T Lymphocyte Antigens 4 (CTLA-4 or CD152) exerts inhibitory activity on T cells are due to mutation in alpha genes are deficiency in the way of translations to produce a beta chain that can be a deficiency in Leu availabilities or deficiency in Tyr and branched amino acids which are necessary for sestrin, AMPK, TOR, and MAPK activities and functions. The mRNA alpha represents the main coding gene from 1st DNA strand-specific for thymus activities which is the imp strand for controlling 2nd DNA strand and varies according to sex and according to human genetic rules, but beta mRNA represents a specific code from 2nd DNA strand which is controlled by 1st DNA strand and also varies due to genetic rules and sex types, that located in the membrane is formed by translations from alpha mRNA.

When 1st DNA strand differs due to sex generation, or due to genetic history and situations, the thymus alpha mRNA will differ in specific characters and specificities from individual to another, "and maybe look closer when are from the same 1st or 2nd degree of genetic Relatives rules ", the TMPO alpha coded gene will differ, and consequently, TMPO beta genes will differ between those individuals, even their characters in their functional processes, and will reflect differences between those individuals in their T-cells molecular structure and in the brain with neutral activities, and also in sestrin, Leu carrier molecular composition activities that carry specific codes have to Mach another in 1st DNA strand and in alpha TMPO will be different in their functions with thymus and with bone marrow functions too.

Acute thymic involution "ATI" is occurred due to increasing suddenly in ATPase activities and in cytochrome activities with unavailabilities of proper Leu activities in its sestrin tools, and deficiency in AMPK & TOR protein availabilities, that will lead to an increase in catabolic cycles within the thymus with no receiving of effective supply from other tissue as liver, brain and neuron cells.

Also, ATI can occur due to deficiency in sestrin Leu carrier activities may due to deficiency in some of its necessary amino acids for its full functions besides Leu activities and AMPK protein activities availabilities. May delaying in sestrin-Leu carrier tool activities to deliver the brain responds to cells due to many factors will give a chance to sestrin amino acids chain to be altered or to be changed that will lead to a wrong message reeds by alpha genes lead to a change in the beta genes productions consequently in antigen synthesis and production.

Materials

T-cells, thymus cells, Cytotoxic T Lymphocyte Antigens 4 (CTLA-4 or CD152, healthy thymus antigen, modified T cells, Thymopoietin (TMPO), CD90, Sestrin-Leu carrier tool(SLCt), ETRQβ-002 vaccine, Endothelin-1, Enkephalin Leu-pentapeptides.

Introduction

The thymus gland, despite containing glandular tissue and producing several hormones, is much more closely associated with the immune system than with the endocrine system. The thymus serves a vital role in the training and development of T-lymphocytes or T cells, an extremely important type of white blood cell. T cells defend the body from potentially deadly pathogens such as bacteria, viruses, and fungi **(**9**)**.

The thymus gland produces several hormones including Thymopoietin and thymulin: Hormones that assist in the process where T cells differentiate into different types. Thymosin: Accentuates the immune response as well as stimulating pituitary hormones such as growth hormone.

Thymopoietin is a protein involved in the induction of CD90 in the thymus. The thymopoetin (TMPO) gene encodes three alternatively spliced mRNAs encoding proteins (alpha), (beta) and (gamma) which are ubiquitously expressed in all cells... TMPO alpha is present diffusely expressed with the cell nucleus while TMPO beta and gamma are localized to the nuclear membrane **(**10, 11**)**.

The mRNA alpha represents the main coding gene from 1st DNA strand-specific for thymus activities which is the imp strand for controlling 2nd DNA strand and varies according to sex and according to human genetic rules, but beta mRNA represents a specific code from 2nd DNA strand which is controlled by 1st DNA strand and also varies due to genetic rules and sex types, that located in the membrane is formed by translations from alpha mRNA. When 1st DNA strand differs due to sex generation, or due to genetic history and situations, the thymus alpha mRNA will differ in specific characters and specificities from individual to another, "and may be looking closer when are from the same 1st or 2nd degree of genetic Relatives rules ", the TMPO alpha coded gene will differ, and consequently, TMPO beta genes will differ between those individuals, even their characters in their functional processes, and will reflect differences between those individuals in their T-cells molecular structure and in the brain with neutral activities, and also in sestrin, Leu carrier molecular composition activities that carry specific codes have to Mach another in 1st DNA strand and in alpha TMPO will be different in their functions with thymus and with bone marrow functions too.

Also, the stimulating mechanism of Thymus coding genes from actin filaments will differ according to sex types and depending on the degree of differences in TMPO alpha coding genes,

also their regulated closed enzymes that regulate the functions and compositions of the dendritic cells have to follow the same origin of TMPO alpha genes.

The effect of the ETRQβ-002 vaccine on pulmonary hypertension and remodeling of pulmonary arterioles and right ventricle (RV) was carefully evaluated **(**14**)**. Many investigators have shown that insulin administration reduces endogenous leucine appearance rates **(**17**)**. Where the increase in the ratio of total leucine flux to body weight in subclinical thyrotoxic state can be a reflection of Deficiency in AMPK protein activities and reduction in ATPase and deficiency in the sestrin-Leu carrier tool which contain two sites more with Leu for AMPK & TOR protein for activating Leu for genes synthesis in the favor of proper cells Metabolism.

Methods and Results

That Epithelial tissues and lymphatic tissues containing dendritic cells and macrophages make up the majority of both regions of the thymus.

Epithelial cells are receiving stimulation from other tissue then start to stimulate the two thymus parts by G-actin activities and by endothelin_1 stimulating activities which are depending mainly on actin & ribosomal ATPase activities, AMPK, and TOR protein functions pathways, that are in turn depending on sestrin Leu carrier molecular composition activities, that can accelerate signal transductions between tissues directly and indirectly.

Antigens in T-cells looking as are depending mainly on TMPO beta genes in the membrane but originally depending on the TMPO alpha genes molecular structure and compositions in the nucleus which are stimulated and activates by endothelin_1 productions through stimulation by G_actin and their ATPase plus cells ribosomal ATPase activities.

Where the function of the thymus is to receive immature T cells and train them into functional, mature T cells that will attack only foreign, and will not attack their main cells where TMPO alpha goes still inactive forms and still carry the main codes from 1st DNA strand and still have imp - ve phosphate linkages with its imp polarities that did by ATPase activities.

T cells first reside within the cortex of the thymus where they come in contact with epithelial cells "under the effect of endothelin-1" presenting various antigens through alpha translation to generate beta genes then translation and transcription to generate antigen peptides chain which

is controlled by sestrin-Leu carrier tools (SLCt) that carry the imp message within its chain from brain responds.

The immature T cells that respond to the antigens corresponding to foreign cells are selected to survive, mature, and migrate to the medulla while the rest die via apoptosis "according to metabolic cycles that passed through catabolic or Mata-anabolic processes ", and are cleaned up by survived macrophages and by endothelin_1 activities which have mainly the function of cleaning veins and interstitium fluid from inflammation and from any infections.

To stimulate thymus activities can be through stimulation directly by active endothelin-1 that will have a composition have to be matched with alpha subunits in that individual, with sestrin Leu carrier activities, and I prefer ET-1 stimulation will be through veins where it is the original sites for its normal functions.

Cytotoxic T Lymphocyte Antigens 4 (CTLA-4 or CD152) which exerts inhibitory activity on T-cells is due to a mutation in alpha genes and deficiency in the way of translations to produce a beta chain that can be a deficiency in Leu availabilities or deficiency in Tyr and branched amino acids which are necessary for sestrin, AMPK, TOR, and MAPK activities and functions, where there is a strong effect of amino acids on immune function **(**2**)**.

Several hormones are produced by the thymus to promote the maturation of the T cells prior to their release into the bloodstream.

Acute thymic involution (ATI) is usually regarded as a virulence trait. It is caused by several infectious agents (bacteria, viruses, parasites, fungi) and other factors, including stress, pregnancy, malnutrition and chemotherapy **(**12**)**.

ATI is occurred due to increasing suddenly in ATPase activities and cytochrome activities with unavailabilities of proper Leu activities in sestrin and deficiency, unavailabilities in AMPK & TOR protein, that will lead to a sudden increase in catabolic cycles within the thymus without receiving of effective peptides and genes supplies from other tissue as liver, brain and neuron cells.

Also, ATI can occur due to deficiency in sestrin Leu carrier activities may due to deficiency in some of its necessary amino acids for its full functions besides Leu activities and AMPK protein activities availabilities. May delaying in sestrin-Leu carrier tool activities to deliver the brain responds to cells due to many factors will give a chance to sestrin amino acids chain to be altered

or to be changed that will lead to a wrong message reeds by alpha genes lead to a change in the beta genes productions consequently in antigen synthesis and production, also delaying in ATPase activities will give the same result of a deficiency in beta and antigen molecular structure and functions.

The thymus is the first organ of the body that exhibits age-associated degeneration/regression, termed "thymic involution." A hallmark of this early phenomenon is a progressive decline of thymic mass as well as a decreased output of naïve T cells, thus resulting in impaired immune response **(**13**)**. Importantly, thymic activities are linked to AMPK proteins and Tyr and Leu amino acids activities and their availabilities in their necessary tool for their proper metabolic cycles, and are linked to cellular senescence which is a stress response induced through G-actin isoforms activities, that indicates the necessity of actin and endothelin-1 in thymus activities.

The gene expression level of mTOR in the duodenum decreased with increasing leucine level and the expression of mTOR, S6K1 in the jejunum and ileum increased with increasing leucine level **(**5**)**. Leucine can improve intestinal development by enhancing villus height and V:C ratio in the jejunum and ileum. Moreover, the expression of mTOR increased as the level of dietary leucine was elevated **(**5**)**.

As sestrin leu carriers activities increased in the duodenum, in the liver and in the spleen, as the % of mTOR and AMPK protein in that tissue area will be decreased due to functioning mTOR and AMPK proteins by sestrin Leu carrier activities for cells metabolism and for reactivating brain functions, neurons cells activities, and for main inner cells proliferation.

Leucine acts as a cellular signal, thereby stimulating muscle protein synthesis, leading to the inhibition of muscle catabolism, especially in an experimental model of cancer cachexia **(**6**)**, that sestrin Leu carrier tools act also as signal transmission carried from and to the brain within its molecular chain for completing enkephalin Leu pentapeptides functions, thus that is so important for protecting and maintained thymus activities in proper activities.

Where sestrin-2 (sesn2), has potential function on various inflammatory diseases, "that Sesn3 regulate podocyte mitochondrial dysfunctions and apoptosis under high-glucose conditions via AMPK" **(**7**)**.

Sestrin activities are strongly related & linked to ATPase activities and to enkephalin Leu pentapeptides activities in the brain which reflect transmitting messages between the brain, neuron, and gland cells, thus sestrin-leu is regulating biological tools for thymus activities

through AMPK protein availabilities, and through inhibiting Thymine hydroxylase "if appeared in vivo ", and for increasing the tyrosine-Leu activities in the coding genes hormones, thus increasing in thymus activities and in their proper Tcells production need sestrin Leu carrier tool proper activities, and need proper activation to enkephalin leu pentapeptides for pr hormone synthesis and functioning Tcells production too.

ADP-A2M4 which is made by removing white blood cells "T cells" from the patient, genetically then modifying them, and then giving again the modified T cells back to the patient that can be able to attack and kill cancer cells. Now the question is modified T cells will not attack alpha genes in the thymus or not, and its molecular arrangement will be able to accept translations from the antigen and from alpha genes for the favor of the patient's main living cells?

T-cells have to obey and follow the 1st DNA strand rules in sex types and in genetic rules, so if modified T cells will be different than the original composition of alpha genes in its specific sires 1st DNA strand in the individual patient rules, so will not follow their new 1st DNA strand regulatory rules steps, and maybe more active and having more binding energy contents in their molecular compositions than antigen and than alpha genes composition in thymus nucleus, that lead to attack the antigens and original alpha genes compositions, and will attack endothelin-1 in interstitium fluid too.

But if interstitium endothelin-1 from patient or individual will be examined and will start to be matched with modified T cells (MTc) in the vaccine, will indicate successful matching between MTc and neuron cells including thymus cells in vivo.

Endothelin-1 can not be modified, but Leu peptide in sestrin Leu carrier tools can be modified in specific sites with consideration of remaining the main imp sequence in sestrin that matched with enkephalin leu-pentapeptides in the brain to don't isolate sestrin from brain functions and activities to neuron and to glands cells.

Those modifications can be done through following several rules and modulations to other biological tools in plasma and in interstitium fluid eg increasing tRNAs with considerations of maintaining proliferations for antigen resynthesis and accelerating sestrin-leu functions with regards to of increasing brain activities with the increasing G_protein and proper availabilities of acetylcholine which are strongly linked with and protected by acetyl-CoA and availabilities of retinol in specific molecular genes for previous cycles and for other conjugated processes and for indirectly linked processes for gland secretions delivery and for AMPK proteins synthesis which can be varies to be liked with specific cycles for feeding other tissue.

May this fragment of gene molecular the structure can carry many advantages for some tissues functions with imp reactivating sestrin-Leu carrier tool for many other organs functions as brain, liver, and respiratory cells :(CGG) Arg, (ACC) Thr, Ile, Gly, (CGG) Arg (ATG) Met Ser, Tyr, Gly Gly, Phe, Leu,That fragment can accelerating tool to sestrin-leu carrier activities, with proper activation to brain functions in the availabilities of acetyl-CoA and AMPK protein that will have the main character of having Thr and Ser amino acids for MAPK pathways activities and proper phosphorylation by G_actin and ribosomal ATPase.

Notice: as the end of the gene fragment contains Cytosine mean is for or will act as tRNAs to deliver the rest of the chain to other tissues for translations or for proper transcriptions which I consider it is filtrations and a way of acting on inflammation and on viral infections but has to be followed and conjugated with MAPK imp activities which are so linked to and with ATPase activities for many isoforms activities as G-actin filaments activities.

May, alpha genes in females will differ from males but will give the same results of the function, but their steps of producing beta genes will positively differ and their way of production will fully differ, that in females may depend on transcriptions to some endothelin-1 isoforms to be joined sestrin-Lue carrier genes (SLCg) under control of 2nd DNA strand for adjusting all released gene from SLCg at the front of alpha genes in the thymus through translations after filtering it by endothelin-1 by translations processes too. But in males may depend mainly on the received messages from the brain by sestrin-Leu carriers tool that the free peptide from SLCg will be translated directly interstitium and in thymus to give directly beta genes that can be modified later by antigen and by MAPK pathways to gain more other amino acids in specific sites for other pathway functions and activities.

The most imp in previous notes in the brain, in SLCg, in G-actin, and in endothelin-1 activities is the un-increasing in +ve cations which are the main of converting active anion mol to idle inactive molecules the can inhibited tRNAase and inhibit ribosomal and G_actin activities and can be the main for failure in brain arteries, in heart, in the liver and in respiratory cells proper activities.

Endothelin-1 has strong roles in pathogenicity, where ET-1 can clean veins and interstitium fluid from inflammations and from cytotoxic T Lymphocyte Antigens 4 (CTLA-4 or CD152), and consequently can adjust hypertension in the availabilities of acetyl CoA and proper active sestrin-Leu carrier activities availabilities, with the proper activations of ATPase in G-actin and in ribosomes.

ET-1 contain 21 amino acids :

H-Cys(1)-Ser-Cys(2)-Ser-Ser-Leu-Asp-Met--Lys-Glu-Cys(2)-Val-"Tyr-Phe-Cys(1)-Leu"-Asp-His-Ile-Ile-Trp-OH

Note that, the most imp amino acids in endothelin_1 are Tyr, Phe, Cys, and Leu, that during its effect on inflammation and foreign bodies will need the imp tool that can functioning the oxidized Leu with Phe and Tyr to be completed during matablic pathways with Gly & Gly for completing its active amino acids chains for brain enkephalin leu-pentapeptides reactivities endothelin and then for reactivating alpha genes in thymus nucleus for beta genes production for Tcells antigen resynthesis and for acting more efficiently on inflammation products.

Endothelin-1 have a role in the pathogenesis of M. tuberculosis infections, and ETA or ETB receptor signaling can modulate the host response to the infection **(**14**)**.

As,ETRQβ-002 vaccine on pulmonary hypertension and remodeling of pulmonary arterioles was carefully evaluated **(**15**)**.ETRQβ-002 vaccine and the mAb significantly decreased the RV systolic pressure **(**16**)**.

The Endothelin-1 can be used instead of T-cells from a healthy person to the patient but we have to follow sex rules which is so imp to me for insure increasing the patient life, that males for males and females for females, then ET-1 can be the pro stimulating peptide gene can be used as a primary vaccine for cleaning interstitium fluid & veins from inflammations and that can adjust hypertension and purify blood cells from +ve inflamed biological molecule which can increase Ca+ precipitations in veins, and then endothelin-1 can be used for resynthesis Tcells and reactivate thymus tissue in the availabilities of proper ses-leu carrier tool (SLCt) and proper ATPase activities, and acetyl-CoA which is necessary for reactivating acetylcholine in the brain and necessary for blood fluidity indirectly and in the availabilities of G_protein its identity will depend on the case health recovery. ET-1 can start the cycle of production T-cells from its pro-status, that will give the chances to many imp tools and cycles in the patient's body to react with the new arrived ET-1 and the stimulation to many cycles steps will begin, that finally the productions of new T cells in patients body will be from the 1st steps that'll stimulate the bone marrow, and will have deep origin in the patient body with neuron cells, with the brain, and with bone marrow too with thymus activities, that has to be supported by cofactor and coenzyme as I mentioned.

To prove the differences between female and males in the Tcells biological mechanism of synthesis will be indicated in the examinations of molecular composition of endothelin-1 in females and males in thymus and plasma in respiratory tissue and some other tissues.

Also, some G_actin isoforms in females differ from males as in liver, in heart, in breast and respiratory tissue. Also G-protein which is so imp for brain functions and neuron activities are characterized in females with some advantages than males as increasing in Gly and gln amino acids in some necessary genes for proliferation activities than males. And may Ser and Thr amino acids in males are much more than females.

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