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RESEARCH ARTICLE

PROTON GRADIENTS AND THE MEMBRANE REDOXY POTENTIAL THREE STATE DEPENDENT 9 STEPPED FULL CYCLE OF PROTON CONDUCTANCE IN THE HUMAN BODY

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ABSTRACT

The Within reaction medium “Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂”, which is belong to the the membrane redoxy potential three state dependent 9 stepped full cycle of proton conductance have been conducted such processes as the oxygen will then consume four protons from the matrix to form water, while another four protons are pumped into the IMS), resulting to form of proton gradient. The normal functioning of reaction medium “Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂”, which is belong to the the membrane redoxy potential three state dependent 9 stepped full cycle of proton conductance is accompanied with these processes as protons and electrons are transferred from donors as fatty acids, glucose, and aminoacids, by using these complex reactions as Glycolysis, Oxidative deamination, Betta-oxidation followed by Krebs cycle, to electron acceptors such as oxygen in redox reactions, release the energy stored in the relatively weak double bond of O₂, lead to formation of proton gradient, followed by oxidative phosphorylation, resulting to ATP synthesis. Within reaction medium “Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂”, which is belong to the the membrane redoxy potential three state dependent 9 stepped full cycle of proton conductance the oxygen will then consume four protons from the matrix to form water while another four protons are pumped into the IMS), resulting to form of proton gradient. ATP synthase, also called complex V, is the final enzyme in the oxidative phosphorylation pathway, uses the energy stored in a proton gradient across a membrane to drive the synthesis of ATP from ADP and phosphate (P_i), this is expressed in following equation, supposed by us as “Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂”, which is belong to the the membrane redoxy potential three state dependent 9 stepped full cycle of proton conductance, described by us. The relationship between proton gradient generation and oxidative phosphorylation also have been appeared as the metabolic pathway in which cells use enzymes to oxidize nutrients as protons flow back across the membrane and down the potential energy gradient, through a large enzyme called ATP synthase with participation of process as chemiosmosis, the energy is tapped, the ATP synthase uses this energy to transform adenosine diphosphate (ADP) into adenosine triphosphate, named as phosphorylation reaction, which is driven by the proton flow, which forces the rotation of a part of the enzyme (ATP synthase is a rotary mechanical motor) within reaction medium as “Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂”, which is belong to the the membrane redoxy potential three state dependent 9 stepped full cycle of proton conductance, described by us. Firstly we are reporting that the generaion of proton gradients, preceded by oxidation of donators, which have been conducted in the left side of reaction medium expressed as “Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space”, meanwhile, the process of phosphorylation have been occurred in the right side of reaction medium expressed as “(ATP + heat energy) + H₂O + nH + matrix + CO₂” (M.Ambaga, A.Tumen-Ulzii, 2019) followed by the formation of proton gradients.

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INTRODUCTION

Proton gradients in particular are important in many types of cells as a form of energy storage., which is usually used to drive ATP synthase, flagellar rotation, or transport of metabolites and classified as bacteriorhodopsin and noncyclic photophosphorylation and oxidative phosphorylation). Generation of proton gradient preceded by the electron transport chain, Complex I (CI) catalyzes the reduction of ubiquinone (UQ) to ubiquinol (UQH₂) by the

transfer of two electrons from reduced nicotinamide adenine dinucleotide (NADH) which translocates four protons from the mitochondrial matrix to the IMS, Complex III (CIII) catalyzes the Q-cycle. The first step involving the transfer of two electrons from the UQH₂ reduced by CI to two molecules of oxidized cytochrome c at the Q_o site. In the second step, two more electrons reduce UQ to UQH₂ at the Q_i site, Complex IV (CIV) catalyzes the transfer of two electrons from the cytochrome c reduced by CIII to one half of a full oxygen. Utilizing one full oxygen in oxidative phosphorylation requires the transfer of four electrons. The oxygen will then

consume four protons from the matrix to form water while another four protons are pumped into the IMS). Proton gradients in particular are important in many types of cells as a form of energy storage., which is usually used to drive ATP synthase, flagellar rotation, or transport of metabolites and classified as bacteriorhodopsin and noncyclic photophosphorylation and oxidative phosphorylation. Generation of proton gradient preceded by the electron transport chain, Complex I (CI) catalyzes the reduction of ubiquinone (UQ) to ubiquinol (UQH₂) by the transfer of two electrons from reduced nicotinamide adenine dinucleotide (NADH) which translocates four protons from the mitochondrial matrix to the IMS, Complex III (CIII) catalyzes the Q-cycle. The first step involving the transfer of two electrons from the UQH₂ reduced by CI to two molecules of oxidized cytochrome c at the Q_o site. In the second step, two more electrons reduce UQ to UQH₂ at the Q_i site, Complex IV (CIV) catalyzes the transfer of two electrons from the cytochrome c reduced by CIII to one half of a full oxygen.

Utilizing one full oxygen in oxidative phosphorylation requires the transfer of four electrons. The oxygen will then consume four protons from the matrix to form water while another four protons are pumped into the IMS). Owing to this process as life hydrogenates carbon dioxide, attaches hydrogen atoms to CO₂ converting carbon dioxide into organic molecules as glucose, fatty acids, aminoacids was the evolution basis of generation of proton gradient with participation of a reaction medium as “Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂”, which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance described by us. All cells "breathe" by pumping protons (hydrogen ions) across a membrane, would burn food - donators with oxygen, these all are conditioned the generation of ATP (the universal energy currency of life) by using Fatty acid oxidation included reaction medium as “Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂”, which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance described by us.

Generation of proton gradient preceded by the electron transport chain, Complex I (CI) catalyzes the reduction of ubiquinone (UQ) to ubiquinol (UQH₂) by the transfer of two electrons from reduced nicotinamide adenine dinucleotide (NADH) which translocates four protons from the mitochondrial matrix to the IMS, Complex III (CIII) catalyzes the Q-cycle. *J. E. Walker (1982)* clarified the three - dimensional structure of the enzyme, which consists of one protein group (the F₀ portion) embedded in the inner membrane and connected by a sort of protein stalk or shaft to another protein group (the F₁ portion). The passage of hydrogen ions through the membrane causes the F₀ portion and the stalk to rotate, and this rotation changes the configuration of the proteins in the F₁ portion. *J. E. Walker's* results supported Boyer's “binding change mechanism,” which proposed that the enzyme functions by changing the position of its protein groups in such a way as to change their chemical affinity for ATP and its precursor molecules.

RESULTS AND DISCUSSIONS

At first time, we revealed that the full 9 stepped cycle of proton conductance inside human body, which starts as release of proton, electron from food substrates under the undirect action of oxygen released from membrane surroundings of erythrocyte in the 9 stage by a closed loop figure.



Figure 1. The final variant of closed cycle of proton conductance inside human body

In the framework of biological events as “the membrane redox potential three state dependent 9 stepped full cycle of proton conductance” would be conducted a following processes as:

1. First stage - Release of proton, electron from food substrates under the undirect action of oxygen released from membrane surroundings of erythrocyte in the 9 stage
2. Second stage - Transfer of proton, electron to NADH, FADH₂ with release of CO₂ in Krebs cycle
3. Third stage - Transfer of electron to KoQ with the transfer of protons across a membrane to intermembrane space
4. Fourth stage - Transfer of electron from reduced KoQ to cytochrom C with the transfer of protons across a membrane to intermembrane space
5. Fifth stage - Formation of metabolic water in the mitochondrian matrix by oxidation of proton by molecular oxygens i.e, by protonation of molecular oxygen by matrix proton with participation cytochrome C oxidase within complex IV
6. Sixth stage - Final creation of proton gradient in the mitochondrial intermembrane space with participation of complex I, III, IV
7. Seventh stage - Transfer of proton to mtochondrial matrix through ATP synthase with synthesis of ATP and generation of heat energy
8. Eighth stage - Entry of three important factors to erythrocytes as protons are exited in the form of metabolic water from mitochondrial matrix of all cells and entered in the form of HCO₃ through plasma membrane of red

blood cells, also entry of CO₂ formed in the 2-stage of closed cycle and entry of oxygen from lung

9. Ninth stage - Proton combine with hemoglobin (generation of HbH) which promotes the release of oxygen from hemoglobin, oxygen diffusion to all cells conditioning the release of proton, electron from food substrates in the 1-stage also proton released from hemoglobin promotes uptake of oxygen by hemoglobin, CO₂ promotes the generation of free proton by mechanism as H₂CO₃ = H+HCO₃, carbonic anhydrase catalyzes the formation of CO₂ from H₂CO₃ and CO₂ diffuse out in the alveoli.

Firstly we are reporting that the generation of proton gradients, preceded by oxidation of donors, which have been conducted in the left side of reaction medium expressed as "Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space", meanwhile, the process of phosphorylation have been occurred in the right side of reaction medium expressed as " (ATP + heat energy) + H₂O + nH + matrix + CO₂" (M.Ambaga, A.Tumen-Ulzii, 2019) followed by the formation of proton gradients. The final step of cellular respiration is the electron transport chain, four complexes embedded in the inner membrane would pump protons from the matrix to the intermembrane space (IMS), ten protons translocated from the matrix to the IMS which generates an electrochemical potential of more than 200mV, this drives the flux of protons back into the matrix through ATP synthase which produces ATP by adding an inorganic phosphate to ADP as $\text{NADH} + 11 \text{H}^+_{(\text{matrix})} + 1/2 \text{O}_2 \rightarrow \text{NAD}^+ + 10 \text{H}^+_{(\text{IMS})} + \text{H}_2\text{O}$, in all these processes the proton gradient have been played a more important role owing to participation of a reaction medium as "Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance.

Fatty acid oxidation and Glycolysis, Krebs cycle, also the reaction medium as "Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance, described by us these all are very important components of the generation of proton gradient, followed by oxidative phosphorylation. In such way, the electron transport chain carries both protons and electrons, passing electrons from donors as fatty acids, glucose, and aminoacids, by using these complex reactions as Glycolysis, Oxidative deamination, Betta-oxidation followed by Krebs cycle to acceptors, transporting protons across a membrane ,within the inner mitochondrial membrane, coenzyme Q10 (Q) carries both electrons and protons by a redox cycle Q accepts two electrons and two protons, it becomes reduced to the ubiquinol form (QH₂); when QH₂ releases two electrons and two protons, it becomes oxidized back to the *ubiquinone* (Q) form lead to the formation of proton gradient with using the membrane redox potential three state dependent 9 stepped full cycle of proton conductance in the human body. The normal functioning of reaction medium "Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix

+ CO₂", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance is accompanied with these processes as protons and electrons are transferred from donors as fatty acids, glucose, and aminoacids, by using these complex reactions as Glycolysis, Oxidative deamination, Betta-oxidation followed by Krebs cycle, to electron acceptors such as oxygen in redox reactions, release the energy stored in the relatively weak double bond of O₂, lead to formation of proton gradient, followed by oxidative phosphorylation, resulting to ATP synthesis. The relationship between Proton gradient generation and oxidative phosphorylation have been appeared in the framework of two sets of coupled reactions - the chain of redox reactions driving the flow of electrons through the electron transport chain, from electron donors such as NADH to electron acceptors such as oxygen and hydrogen (protons) thereby releasing the chemical energy stored into produce adenosine triphosphate (ATP). within reaction medium as "Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance, described by us.

The relationship between proton gradient generation and oxidative phosphorylation also have been appeared as the metabolic pathway in which cells use enzymes to oxidize nutrients as protons flow back across the membrane and down the potential energy gradient, through a large enzyme called ATP synthase with participation of process as chemiosmosis, the energy is tapped, the ATP synthase uses this energy to transform adenosine diphosphate (ADP) into adenosine triphosphate, named as phosphorylation reaction, which is driven by the proton flow, which forces the rotation of a part of the enzyme (ATP synthase is a rotary mechanical motor) with participation of reaction medium as "Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance, described by us. It should be say that both the electron transport chain and the ATP synthase are embedded in a membrane, and energy is transferred from the electron transport chain to the ATP synthase by movements of protons across this membrane from the negative N-side of the membrane to the positive P-side through the proton-pumping enzymes within reaction medium as "Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance, described by us. ATP synthase, also called complex V, is the final enzyme in the oxidative phosphorylation pathway, uses the energy stored in a proton gradient across a membrane to drive the synthesis of ATP from ADP and phosphate (P_i), all these are expressed in following equation, supposed by us as "Donators + membrane - redox potentials three - state line system + O₂ + ADP + Pi + H⁺ + nH + membrane space = (ATP + heat energy) + H₂O + nH + matrix + CO₂", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance.

It may be say that chemical reactions utilizing donors as fatty acids, glucose, and aminoacids, by using Glycolysis, Oxidative deamination, Betta-oxidation followed by Krebs cycle and in same time followed by proton gradient formation and oxidative phosphorylation, all these reactions have been conducted with "binding change" mechanism, by changing the position of protein groups, connected with change their chemical affinity for ATP confirmed by J.Walker and P. D. Boyer with participation of reaction medium as "Donators + membrane - redox potentials three - state line system + O_2 + $ADP + Pi + H^+ + nH$ + membrane space = (ATP + heat energy) + $H_2O + nH$ + matrix + CO_2 ", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance, described by us. It is more interesting that energy-releasing chemical reactions to drive energy-requiring reactions, utilizing donors as fatty acids, glucose, and aminoacids, by using these complex reactions as Glycolysis, Oxidative deamination, Betta-oxidation followed by Krebs cycle and also followed by oxidation phosphorylation, all these reactions are functioned normally with the passage of protons - hydrogen ions through the membrane, resulting to the F_0 portion and the stalk to rotate, by changing the configuration of the proteins in the F_1 portion confirmed by J.Walker and P. D. Boyer with participation of reaction medium as "Donators + membrane - redox potentials three - state line system + $O_2 + ADP + Pi + H^+ + nH$ + membrane space = (ATP + heat energy) + $H_2O + nH$ + matrix + CO_2 ", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance, described by us. Within reaction medium "Donators + membrane - redox potentials three - state line system + $O_2 + ADP + Pi + H^+ + nH$ + membrane space = (ATP + heat energy) + $H_2O + nH$ + matrix + CO_2 ", which is belong to the the membrane redox potential three state dependent 9 stepped full cycle of proton conductance have been conducted such processes as the oxygen will then consume four protons from the matrix to form water, while another four protons are pumped into the IMS), resulting to form of proton gradient.

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