



RESEARCH ARTICLE

THE HISTORY OF DISCOVERY OF FULL CLOSED CYCLE OF PROTON CONDUCTANCE INSIDE HUMAN BODY

*Ambaga, M. and Tumen-Ulzii, A.

New Medicine Medical University, Ulanbator, Mongolia

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ABSTRACT

Our first imagination was that the evolution history of development of life processes in our planet during last billion year should build the full closed cycle of protons, with direct participation of this cycle have been formed more than 100 kg ATP during 24 hours and heat energy, enough to warm the human body until 36-37 Celsius degree, where protons have been recirculated, reutilized, making repeated circulation movement within concrete interval time. At first we had been succeeded to find the end 9-th stage of the full closed cycle of electron, proton conductance, which basic features may be described as entry of oxygen from lung, formation of HbO₂, 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, which we named as 9-th stage of the full closed cycle. In this connection it was raised the question as which basic features should be bear the 8-th stage of the full closed cycle. After this, it was became clear that the 8-th stage of the full closed cycle had been distinguished by the diffusion of proton from mitochondrial matrix of all cells in the form of HCO₃ as the protonated carbon dioxide, and metabolic water through plasma membrane of red blood cells with participation of aquaporin protein channels and by Na⁺/H⁺ antiport mechanism, also entry of CO₂ from all cells.

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INTRODUCTION

It is raised the principally important questions relating to as how protons made closed repeated movement by circulating through closed circle, where is started first point stage of proton conductance, where is ended the terminal stage and how the previous stage of circulation have been conditioned the following stage and in which relationship and interconnection existed both parallel existed stages of proton conductance.

Our first attempts was aimed to find the full closed cycle for protons, with direct participation of this cycle have been formed ATP and heat energy, as same as the Krebs cycle of electron, proton conductance. In early 1937, Krebs' team discovered that citrate acted as a catalyst, while researchers C. Martius and F. Knoop discovered another product of citrate oxidation as ketoglutarate. At Krebs' Sheffield laboratory revealed that another product of cellular respiration—oxaloacetate could combine with pyruvate or other compounds to form citrate, closing the circle. Bohr effect describing as an increase in blood carbon dioxide level or a decrease in pH causes hemoglobin to bind to oxygen with less affinity, a

decrease in carbon dioxide or increase in pH will result in hemoglobin picking up more oxygen and a decrease in blood pH or an increase in blood CO₂ concentration will result in hemoglobin proteins releasing their loads of oxygen have been given to us first imagination how to close the circle of proton conductance, proposed by us. Also, literature data, demonstrating that hemoglobins of vertebrate erythrocytes perform two major biological functions transport of O₂ from respiratory organ to peripheral tissues, and transport of CO₂ and protons from peripheral tissues to respiratory organ for subsequent excretion (Murray R.K, et al), respiration requires electron transport – redox reaction, also a membrane, proton pump, and an ATP-synthase, the main problem with respiration evolving early in the history of life is the need for a membrane (Nick Lane) affinity of hemoglobin to O₂ decreases when pH of blood falls-facilitates release of O₂ in tissues-increased CO₂ in blood- increased H⁺ production- H⁺ binds to deoxyhemoglobin- accessibility of O₂ to hemoglobin decreases - O₂ released was more useful scientific guide to us to find the such lawful processes as how protons made closed movement by circulating through closed circle, where is started first point stage of proton conductance. But, at first it was very difficult for us to describe that how occurred the conductance

*Corresponding author: Ambaga, M.

New Medicine Medical University, Ulanbator, Mongolia

of proton by closed cycle, starting from first stage of conductance and ending by repackaging of protons inside membrane surroundings of erythrocyte. During our investigation we had been succeeded to find first thestage of the full closed cycle of electron, proton conductance, which features may be described as release of proton, electron from food substrates under the undirect action of oxygen released from membrane surroundings of erythrocyte in the 9-th stage, which named by us as the first stage of the full closed cycle

RESULTS AND DISCUSSION

Our first imagination was that the evolution history of development of life processes in our planet during last billion year should build the full closed cycle of protons, with direct participation of this cycle have been formed more than 100 kg ATP during 24 hours and heat energy, enough to warm the human body until 36-37 Celsius degree where protons have been recirculated, reutilized, making repeated circulation movement within concrete interval time.

would meet protons separated from food substrates with oxygen as electron acceptors, which factors will cause the release of electrons and protons from food substrates, which factors will cause the release of oxygen from the erythrocyte membrane surroundings. Before discovery of the membrane - redox potential, a three state line system dependent - full 9 stepped closed cycle of proton conductance, we did not know which factors will cause the release of carbon dioxide from the erythrocyte membrane surroundings in the direction to respiratory organs, from which stage started the cycle of proton conductance inside human body, and by which stage ended the cycle of electron and proton conductance inside human body and from how many stages are consisted the closed cycle. At first time, we revealed the two stages and parameters of closed cycle of proton conductance inside human body, it was first and 9-th stages. In this connection, we proposed that the full 9 stepped cycle of proton conductance inside human body starts from the release of protons and electrons from food substrates (first stage) and ends by the final accumulation of free protons in the form of HbH inside the erythrocyte

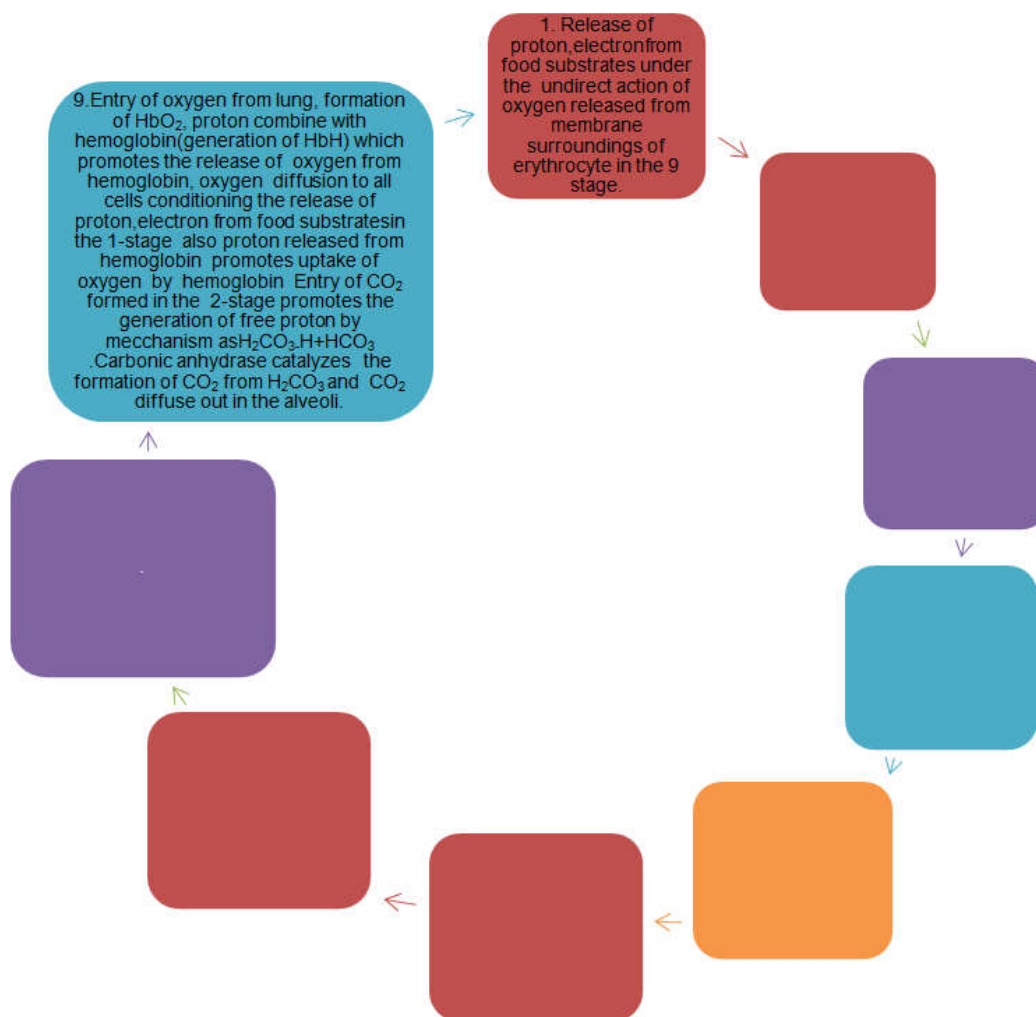


Figure 1. First revealed the basic two stage and parameters of closed cycle of proton conductance inside human body

In such way, at first time we have had the imagination that inside human body should be the closed pathway, by which have been conducted the circulation of protons, but, in this time we did not know several facts about the full closed cycle of proton conductance inside human body. At example, we did not know which stage of the full cycle of proton conductance inside human body followed after Krebs cycle, in which part of full closed cycle of proton conductance inside human body

membrane surroundings, allowing the promotion of oxygen intake by all cells of human body and the removal of carbon dioxide from the human body. Meanwhile, we had been succeeded to find the end stage of the full closed cycle of proton conductance, which basic features may be described as entry of oxygen from lung, formation of HbO₂, 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, which named by us as 9-th stage of the full closed cycle.

The fifth stage of the full closed cycle have been connected with Mitchel discovery, relating to translocation of proton to intermembrane space of mitochondria without accompanying electron. After this, we revealed that translocation of proton to intermembrane space of mitochondria without accompanying



Figure 2. The final variant of closed cycle of proton conductance inside human body

In this connection it was raised the question as which features should be bear the 8-th stage of the full closed cycle. After this, it was became clear that the 8-th stage of the full closed cycle have been distinguished by the diffusion of proton from mitochondrial matrix of all cells in the form of HCO_3^- as the protonated carbon dioxide, and metabolic water through plasma membrane of red blood cells with participation of aquaporin protein channels and by Na^+/H^+ antiport mechanism, also entry of CO_2 from all cells. Also during our study we established that the second stage of the full closed cycle have been characterized by transfer of protons and electrons to NADH as hydrogen atom and formation of CO_2 in Krebs cycle in the result of release of protons and electrons from food substrates (carbohydrate, amino acids, fatty acids). After this, it was clear that third stage of the full closed cycle have been conducted as transfer of protons and electrons to KoQ as hydrogen atom from NADH and FADH₂. What about the fourth stage of the full closed cycle, this stage may be described as transfer of electrons to cytochrom C without accompanying proton.

electron should be lead to creation of proton gradient in the intermembrane space of mitochondria and following transfer of proton to matrix through ATP synthase, this stage named by us as the seventh stage of the full closed cycle of electron, proton conductance. The full 9 stepped cycle of proton conductance inside the human body was proposed by M.Ambaga is included the "Donators + membrane-redox potentials three-state line system + $\text{O}_2 + \text{ADP} + \text{Pi} + \text{H}^+ + \text{nH} + \text{membrane space} = (\text{ATP} + \text{heat energy}) + \text{H}_2\text{O} + \text{nH} + \text{matrix} + \text{CO}_2$ " reaction medium.

Basing in the our study, we concluded that the following close relationships existed between stages 1 and 9 of the full 9 stepped cycle of proton conductance inside the human body:

- Release of proton, electron from food substrates in the first stage have been occurred under the indirect action of oxygen released from membrane surroundings of erythrocyte in the end 9 stage.

- In the end 9-th stage proton combines with hemaglobin (generation of HbH), which promotes the release of oxygen from hemaglobin and the oxygen diffusion to all cells conditioned the release of proton and electron from food substrates in the 1st stage.
- The entry of CO₂ formed in the second stage of the full 9 stepped cycle of electron and proton conductance promotes the generation of free proton by mechanism as H₂CO₃ -H + HCO₃⁻, in such a way that promotes the release of oxygen from hemaglobin in the 9-th stage and the oxygen diffusion to all cells conditioned the release of proton and electron from food substrates in the 1st stage of the full 9 stepped cycle of electron and proton conductance.

Beside all this, protons released from erythrocyte membrane surroundings in the 9-th stage of closed cycle by incorporating into composition of HCO₃⁻ (bicarbonate ions) and bicarbonate ions have been participated in the biosynthesis of pyrimidine ribonucleotides, which have been conducted as ATP + HCO₃⁻ + glutamine + H₂O = carbamoyl phosphate, carbomoyl phosphate + aspartate = carbamoyl aspartate, carbamoyl aspartate = H₂O + dihydroorotate, dihydroorotate + quinine = orotate, orotate + PRPP = orotidine monophosphate (OMP), OMP = CO₂ + uridine monophosphate (UMP). Protons released from erythrocyte membrane surroundings in the 9-th stage of closed cycle is mostly transported within HCO₃⁻ (bicarbonate ions) and H₂CO₃ (carbonic acid).

A. The cellular mechanism responsible for synthesis of gastric HCL with participation of released protons from erythrocyte membrane surroundings and repackaged in the erythrocyte membrane surroundings in the 9-th stage of closed cycle.

- In the chloride shift as HCO₃⁻ (bicarbonate ions) eventually bearing proton released from food substrates diffuse out erythrocyte membrane surroundings into the plasma
- After this in bloodstreams HCO₃⁻ (bicarbonate ions) reacted with H⁺ and formed H₂CO₃ (carbonic acid)
- After this H₂CO₃ (carbonic acid) dissociates to form of H₂O and CO₂
- After this carbon dioxide (CO₂) diffuses into the gastric parietal cells
- After this carbon dioxide (CO₂) combines with water formed H₂CO₃ (carbonic acid)
- After this H₂CO₃ (carbonic acid) dissociates in to a HCO₃⁻ (bicarbonate ions) and hydrogen ion (H⁺)
- HCO₃⁻ (bicarbonate ions) are transported back into bloodstream
- H⁺-K⁺ exchange proton pump moves H⁺ into duct of gastric gland and K⁺ into the parietal cell
- Chloride ions diffuse into gastric gland duct.

In such way hydrogen ions (proton) are derived from carbon dioxide and water, which enter the parietal cell and participated in the synthesis of HCL.

The cellular mechanism responsible for secretion of HCO₃⁻ (bicarbonate ions) in pancreas with participation of released protons from erythrocyte membrane surroundings. HCO₃⁻ (bicarbonate ions) in pancreatic juice are neutralized the acidic chyme that enters the small intestine from the stomach. HCO₃⁻ (bicarbonate ions) and hydrogen ions (proton) are derived from carbon dioxide and water enter the pancreatic duct cell.

Carbon dioxide and water, which enter the pancreatic duct cell have been beared protons released from food substrates and repackaged in the erythrocyte membrane surroundings in the 9-th stage of closed cycle and released from this.

- Water (H₂O) and carbon dioxide (CO₂) combine to form H₂CO₃ (carbonic acid)
- H₂CO₃ (carbonic acid) dissociates to form HCO₃⁻ (bicarbonate ions) and hydrogen ion (H⁺)
- Hydrogen ion (H⁺) are exchanged for Na ions
- HCO₃⁻ (bicarbonate ions) are transported into the intercalated ducts in exchange for CL ion.

The cellular mechanism responsible for proton dependent acid – base balance with participation of released protons from erythrocyte membrane surroundings:

- Water (H₂O) and carbon dioxide (CO₂) combine to form H₂CO₃ (carbonic acid) within lung capillary blood circulation
- H₂CO₃ (carbonic acid) dissociates to form HCO₃⁻ (bicarbonate ions) and hydrogen ion (H⁺)
- Carbon dioxide and water, which enter the lung capillary blood circulation have been beared protons released from food substrates in the 1-th stage of closed cycle and repackaged in the erythrocyte membrane surroundings in the 9-th stage of closed cycle and released from this.

D. The cellular mechanism responsible for kidney regulation of proton dependent acid – base balance with participation of released protons from erythrocyte membrane surroundings

- H⁺ combine to form HCO₃⁻ (bicarbonate ion) to form HCO₃⁻ (bicarbonate ions) within kidney peritubular capillary blood circulation
- H₂CO₃ (carbonic acid) is converted to water (H₂O) and carbon dioxide (CO₂)
- In the tubular cells carbon dioxide (CO₂) combine with water (H₂O) to form H₂CO₃ (carbonic acid)
- H₂CO₃ (carbonic acid) dissociates to form HCO₃⁻ (bicarbonate ions) and hydrogen ion (H⁺)
- By antiport mechanism H⁺ is secreted into filtrate in exchange for Na from the filtrate

In such way carbon dioxide and water, which enter the kidney peritubular capillary blood circulation have been beared protons released from food substrates in the 1-th stage of closed cycle and repackaged in the erythrocyte membrane surroundings in the 9-th stage of closed cycle and released from this.

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