The Lighter Side

Ketone Body Metabolism: Love and Survival

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Abstract

The following story tells the details of the ketone body metabolism, focusing on the needs of the brain in prolonged fasting conditions. This literary composition highlights the use of ketone bodies as an important metabolic adaptation that avoids excessive protein degradation and allows for greater survival. The liver produces ketone bodies that are released into the bloodstream and exported to the brain, which then absorbs and transforms them into acetyl-CoA. These molecules with central role in metabolism generate energy through the Krebs cycle, electron transport chain, and oxidative phosphorylation. This tale is a valuable tool for biochemistry teachers and students because it can help with a deeper understanding of the physiological roles of ketone bodies and their metabolism. © 2019 International Union of Biochemistry and Molecular Biology, 00(00):1–2, 2019.

This is a story of love and patriotism that occurred in times of scarcity.

These were crucial times, poor times where there was no food. The red flag was up which meant that the glucagon was active. Everything was chaotic because different survival methods were required, in which energy should be generated without turning to an excessive degradation of the precious proteins. The brain, the boss! Asked and asked, in fact, he demanded ATP. But how to achieve it? Everything possible was already being done. But no, the old man commanded it anyway.

The poor liver left its own consumption of the delicious and exquisite glucose to satisfy the requirements, not only of the tyrant brain who threatened to stop fulfilling its role as leader, but also of its accomplices, the extrahepatic tissues that followed in the footsteps of the dictator and said they would resort to drastic measures if they were not given glucose. Oh no! Hepatic glycogen is running out. That meant needing to use more and more of the most beautiful and important jewels, the proteins.

This would cause a tragedy and a half. NO! There had to be another way!

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Suddenly a light of hope illuminated the gloomy horizon. It was two molecules of acetyl-CoA that professed an immense love, which could not be fulfilled for lack of an accomplice that allowed them to condense. Oh surprise! Looking at the beautiful act was a friend, thiolase, who listened to everything and decided to help them. She approached the couple and told them that she had the power to realize their dream on one condition, one of the molecules had to leave part of its belongings as payment. Then, one of them said that she preferred sacrificing her possessions instead of living away from her soul mate and immediately discarded her CoA-SH. But this generated a problem, her name, her distinction, basically her last name was lost. This is why the happy couple decided to change their name to acetoacetyl-CoA, after all, they were already united.

Upon learning of the good news another friend, acetyl-CoA, wanted to visit them. But of course! A visitor like her cannot come alone. So she took with her a molecule of water and the HMG synthase that decided to tag along. Once they were all together, the gossip began with laughter and jokes, until they touched on the topic of the situation in which they lived. Suddenly, their hearts filled with patriotism and decided to fight against the oppressors. Due to her occupations, the synthase could not accompany them, but she put the perfect name to the group, a name that in fact gave fear, "β-hydroxy β-methylglutaryl-CoA" (HMG-CoA for the friends).

Right on! With this name they could join other similar molecules and generate a super monster called cholesterol. But nah, the option was good, nobody denies it, but they

preferred to fight. Then, an unexpected visitor showed up. It was a HMG-CoA lyase with a message that said "Dear acetyl-CoA, stop messing around and go help elsewhere". It was quite funny to see the temper tantrums that she put up but in the end she left after asking for one huge favor, to change the name of the amazing group to acetoacetate because nothing would ever be the same. Without realizing it, they had formed something very important in the fight against the tyrants, the first ketone body! How exciting!

Seeing this emotion, patriotism, goodwill, and craziness, two soldier enzymes approached the group to give them two options. The first one was to become acetone by a non-enzymatic decarboxylation or with the help of acetoacetate decarboxylase in exchange for a suitcase of CO_2. The second one, go with 3-hydroxybutyrate dehydrogenase, consume a delicious NADH and become 3-hydroxybutyrate.

The group wanted to be part of the elite fighters, so they opted to go with the dehydrogenase. Alright! Now they could go to the horrific brain and silence him once and for all. The road seemed easy. However, nothing is free in life. Upon arriving at the battle site, they were received by an enzyme identical to the previous one, 3-hydroxybutyrate dehydrogenase. She told them that they should prepare an NADH just as delicious as the one they consumed initially. Also, she told them that they must change their name back to acetoacetate so that they would not be discovered. How awful, it would seem that all the trouble they went through was for nothing!

Then an immense sadness reigned within the happy couple. They knew that the worst was about to happen but their loyalty to the cause was greater. Suddenly, a succinyl-CoA arrived accompanied by the general β-ketoacyl CoA transferase, who made him deliver the CoA package and return as succinate to his own route. As a *déjà vu*, the group returned to be acetoacetyl-CoA. They were almost there! Just a little more was needed, an act of heroism and incredible love. The molecules of acetyl-CoA had to be separated, in order to silently enter a pathway that would generate enough energy to satisfy the brain and stop the tyranny. With unbelievable grief, the couple asked for help from the one friend that once fulfilled their dream, the thiolase. She gave them the CoA-SH and separated the two molecules, who followed the same route with the hope that one day, not too distant, the same friend will reunite them once more.

Although this may never happen, their heroism will be remembered because their decisions were made during a life or death moment, literally. Due to this, the oxidation of acetyl-CoA molecules generated ATPs and the brain will be able to maintain its vital functions. In this land, hope for the future will be accompanied by a wave of glucose that will raise the beloved queen, insulin, to the throne. The hope for better days, moments of joy, and abundance are still on the line.

THE END.