ISSN:2249-5347
IJSID
International Journal of Science Innovations and Discoveries
An International peer Review Journal for Science

Nobel Prize in Medicines 1953

Hans Adolf Krebs

Fritz Albert Lipmann

The Nobel Prize in Physiology or Medicine 1953 was divided equally between Hans Adolf Krebs "for his discovery of the citric acid cycle" and Fritz Albert Lipmann "for his discovery of co-enzyme A and its importance for intermediary metabolism"

The Staff of the Karolinska Institutet has awarded this year's Nobel Prize in Physiology or Medicine to Professor Hans Adolf Krebs and Professor Fritz Lipmann. This is an acknowledgement of fast and significant contributions to the research into the functions of the living cell. Extremely complicated molecules take active part in the mechanisms of these cells. Their size can be several thousand times that of the largest metal atoms, those of the uranium group. Difficulties in understanding a machinery of that type are immense, especially so long as these giant molecules, the proteins, retain so many of the mysteries of an unexplored world. These active proteins are called enzymes. Certain specific smaller compounds which attach themselves to these enzymes, and which awaken their activity are called coenzymes.

This year's prizes which are presented here tonight were awarded for the discoveries of essential processes connected with the metabolism of the cell. It has long

been known that the main components of our foods (proteins, fats, and carbohydrates) are transformed by the living cell into compounds having much smaller molecules. It is a unique property of the cell that simultaneously its own components undergo processes of breaking down and building up which leads to the rejuvenation of the whole organism. The breakdown products from both the food and the cell components are used as building material for the working machinery of the cell. The energy necessary for this construction work is mainly derived from a transformation of a suitable amount of material to carbonic acid and water. That all these processes can take place simultaneously and in an extremely complex manner is due to the very far-reaching structural specialization of the microcosm of the cell.

Much had been known about all this before the advent of Hans Adolf Krebs, but this knowledge was concerned only with details and partial processes here and there. Nobody knew how these isolated reactions were related to each other, and no one could present a uniform picture of a logical overall reaction mechanism.

It was Krebs who discovered how these individual reactions are linked to each other in a cyclic process. He brought us a clear understanding of the essential principle of how the released energy is used for the building up processes which take place within the cell.

This energy is liberated by the oxidation of a 2-carbon compound to carbonic acid and water. This 2-carbon compound is derived from the foodstuffs and is introduced into the Krebs cycle. The nature of this compound and the mechanism of its incorporation were discovered by Fritz Lipmann. But for the moment let us not be concerned with this discovery since at that time it had not yet been made. In the beginning Krebs was quite alone with his idea, and when he first presented it, it was criticized by many. But soon he found an even greater number of supporters who were joined by his previous critics. Krebs' idea was that the mysterious 2-carbon compound is added on to a known substance with 4 carbon atoms yielding a 6-carbon compound. The 2-carbon compound, bound in this way, is then degraded stepwise to carbonic acid, water, and energy. When this degradation is completed, the 4-carbon compound is again free to react with another 2-carbon

molecule, which starts a new period in the oxidation cycle. Krebs could show that the 6-carbon compound formed at the onset of this cycle is citric acid which contains three carboxyl groups. The cycle is therefore also called the tricarboxylic acid cycle.

The Krebs cycle explains two simultaneous processes: the degradation reactions which yield energy, and the building-up processes which use up energy. This is in keeping with the above-named principle of a balance between these two kinds of cell reactions. Several other scientists, notably the Americans Werkman and Wood and the Spanish immigrant Ochoa, now working in New York, have furnished proof of the reversibility of the Krebs cycle.Out of the chaos of isolated reactions Krebs succeeded in extracting the basic system for the essential pathway of oxidation process within the cell. His penetrating intuition was so clear and true and his grasp of the problem so keen from the start that none of his original ideas had to be revised.

It is necessary to introduce compounds from the outside into the Krebs cycle in order to keep it in operation, because theoretically speaking the integral components are not used up in the process. The principal incorporation takes place through Lipmann's 2-carbon compound. It had been generally assumed that this compound was closely related to acetic acid. It was known that large amounts of acetic acid are formed in the metabolism of the cell. This acid possesses two carbon atoms and could fit well into the mechanism of the Krebs cycle. It seemed quite certain that the 2-carbon compound was acetic acid, but that it was active in some unknown form. Lipmann maintained for several years that acetyl phosphate, a compound formed from acetic acid and phosphoric acid was the active principle and he defended this idea against a growing scepticism of his colleagues. Just when most biochemists became convinced that this compound would not fit into the mechanism of the Krebs cycle, and were ready to abandon the whole idea, Lipmann announced his discovery of coenzyme A. Now suddenly everything fitted perfectly - the last notch of a combination lock fell into its place.

Coenzyme A is a compound with a rather small molecule, which, when united with the enzyme-protein, acquires the property of binding acetic acid. Acetic acid is normally

quite unreactive but when bound in this way it becomes labile and reactive and represents the previously mystical 2-carbon compound which combines with a 4-carbon compound to form citric acid. A new way for the transmission of energy in the cell was demonstrated by this discovery.

Recently the acetyl phosphate made a come-back, when Lipmann with his usual keen insight showed that it is used as the active 2-carbon compound in certain bacteria. Far from feeling triumphant Lipmann wrote in his otherwise very serious scientific paper that he was quite happy about this finding.

That Lipmann's discovery has an even wider scope became clear when he and others found that other acids than acetic acid are activated by coenzyme A bound to other enzyme proteins.

Some of the coenzymes belong to the class of vitamins, Lipmann's coenzyme for example is related to the B-vitamins, and vitamins B_1 and B_2 are also active as coenzymes. B_2, a yellow vitamin, has been used by the Swedish biochemist Hugo Theorell to demonstrate that an active enzyme can be formed when a vitamin becomes bound to a specific protein.

Doctor Krebs. The Staff of Karolinska Institutet is pleased to reward your achievement when with intuitive perception you were able to see in the chaotic and fragmentary mass of known enzymatic processes the way, the primary pathway, of combustion, and with consummate skill to prove the reality of your vision.

This prize is in corroboration of the general agreement that you have laid a foundation, which will last for all time and that we have already witnessed the great development of constructive work founded on your pioneer achievement.

On behalf of the Staff of Karolinska Institutet I ask you now to receive the award from the hands of His Majesty the King.

Doctor Lipmann. You are a fighter. Your opponent, and everybody knows you have only one, is an impersonal opponent namely the complexity of biochemical processes.

Your keen wish to make things understandable and distinct has been rewarded in the form of a clear-cut and far-reaching discovery.The importance of your discovery of coenzyme A was immediately realized in biochemical circles but in spite of the tremendous pace which was set in the purification and identification of the new activator, you have remained the leader throughout.

You have removed an obstructive confusion by the clear demonstration of a widespread reaction and have discovered simultaneously a new way for the transmission of energy in the cell.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/medicine/laureates/1953/press.html