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Nobel Prize in Medicines 1937

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The Nobel Prize in Physiology or Medicine 1937 was awarded to Albert Szent-Györgyi "for his discoveries in connection with the biological combustion processes, with special reference to vitamin C and the catalysis of fumaric acid"

The Staff of Professors of the Caroline Institute, pursuant to the task devolving upon them by the terms of the will of Alfred Nobel, have awarded the Prize for Physiology or Medicine for the year 1937 to Professor Albert von Szent-Györgyi, in recognition of his discoveries concerning the biological combustion processes with especial reference to vitamin C and to the fumaric acid catalyst. The wording of the above sentence indicates that the mechanism of biological oxidation has been investigated beyond the great discoveries in this field made by Otto Warburg, Heinrich Wieland, and their successors. Their systems of catalysts for oxidation have been shown to be dependent on Szent-Györgyi's new catalysts.

It was generally known before that combustion liberates energy in living cells which can be employed there without loss - directly for the building up of new substances - for storage or for the building of functioning cell structures. The building up of living

organisms then is dependent in essential respects on combustion, which is guided by catalyst systems. Thus catalyst systems are conditional for the building up of living organisms. Consequently in the unknown period during which organic life originated, the formation of these and other catalyst systems must have preceded the completion of the living animal organisms.

Preferably I should wish to confine my remarks to the new conquistador from Szeged. The survey is however of higher importance on this occasion, and moreover the course of the events is dramatically concentrated. Each one of the three has conquered new ground by intuitive daring and skill. Szent-Györgyi's greatest achievement has intimately linked up the accomplishments of the two others and of their successors, giving us for the first time a picture of a coherent oxidation process - of the interplay of three catalyst systems and the oxidation thereby in metabolism

Warburg, who always stood alone with some few faithful co-workers, is the foremost pioneer, and he had to overcome the greatest difficulties. At this day there is none who can any longer throw doubt on his discoveries, but that was not so, when in 1931 underestimated by the majority, he was awarded the Nobel Prize by the Caroline Institute. He has shown that the inert oxygen, with which the red blood corpuscles are fully loaded, is taken up from them by a catalyst system to which many red pigments belong (for brevity's sake called «the red system»). These are related to the red blood pigment. They contain as active groups (for the most part) iron and specific proteins. In this system the oxygen combines with the iron during varying periods of time. In the case of the most rapid catalysts, it combines with the iron, is converted into a lively, reactively disposed form and is delivered - all at a speed that gives a flowing stream of active oxygen from the catalyst system. One thought that this active oxygen oxidized directly. That is not the way however.

On the contrary, the active oxygen meetshydrogen - but that is another story, belonging to Szent-Györgyi's great discovery. The manner in which the life-giving active oxygen's dramatic encounter in the darkness of the cells ensues, had been unknown ever

since the morning of time until, in 1933, Szent-Györgyi carried out some experiments which proved to be the prelude to the revelation of the secret.

For the moment I will leave oxygen, and direct the attention to the first, apparently unimportant, experiments carried out by Wieland. These led him to the conception of an idea, which was destined to carry him on to the disclosure of an extensive part of the mechanism of oxidation. A large number of investigators were soon attracted by Wieland's opinion. This seemed to be at variance with the oxygen activation - at any rate that was the view of a majority. This apparent inconsistency was never considered by Szent-Györgyi, nor by Warburg.

Wieland had observed that palladium is capable of absorbing hydrogen from certain organic compounds, which means their partial combustion or oxidation. Through the cooperation of many investigators the presence was revealed of extensive metal-free catalyst systems, the effect of which was shown to consist in the removal of hydrogen from metabolic substances, in agreement with Wieland's concept. These catalysts were given a name in common:dehydrogenases (hydrogen-removers, hydrogen-absorbers, or hydrogen-transporters) and the idea was held pretty generally that the hydrogen activated by this system would be capable of reacting directly with the inert oxygen molecules. Hydrogen superoxide was supposed to form an intermediate product. That is not the highway of oxidation however. On the contrary, the hydrogen first meets Szent-Györgyi's catalyst system from a different side to the one where the activated oxygen flows into it from the «red system». That again is another story, which also belongs to Szent-Györgyi's great discovery. From 1925 onwards he had been investigating a number of hydrogen-absorbers. Previously to anyone else he formed the view of these as members of a catalyst system in the service of oxidation (in other quarters loosely conceived of as being auxiliary catalysts of some kind for fermentation). He was also occupied with experiments on a yellow substance, termed flave by him, while his investigation regarding vitamin C was being completed, and conducted on to the isolation of that substance, enabling him later to insert it in the catalyst system of certain hydrogen-removers. Vitamin C and another substance,

containing sulphur as a hydrogen-removing group and defined by Sir Frederick Gowland Hopkins and others, were however until 1934 the only substances belonging to the hydrogen-transporters in the oxidation-chain that had been isolated. The rank that they possess as catalysts is dependent on the velocity of the hydrogen-transportation and the degree of the activation of the hydrogen - problems that still await a satisfactory solution. On the other hand, Hugo Theorell succeeded in 1934 in isolating, in Warburg's laboratory, the first really rapid hydrogen-transporter, called «the yellow enzyme». He could also show that it was a phosphoric-acid ester of vitamin B_2, linked to a specific protein. Warburg and Christian, in 1935, defined the nature of the active group in two other dehydrogenases, colourless and metal-free (co-ferment and co-zymase), which had long frustrated the attempts of other investigators. One of them was the catalyst that Szent-Györgyi had placed in this section of the oxidation-chain.

The magnificent series of Szent-Györgyi's discoveries commenced in 1933. They were carried out and pursued at Szeged with extraordinary rapidity and precision. His clear vision for essentials induced him, in spite of his isolation of ascorbic acid and of his identification of it with the so-termed vitamin C - a feat that was justly hailed with enthusiasm - to hand over to others for the time being the tempting pursuit of the further development of that discovery, and to devote the whole of his energy to the problem of combustion, notwithstanding the difficulties it presented. Many investigators had been working at the so-called plant acids in the muscular system, and had observed their capacity for intensifying oxidation in that tissue. The readiest explanation however of how that came about, viz. that they are easily combusted themselves, simply did not fit in with Szent-Györgyi's intuitive perception. By elaborating reliable methods of analysis for the substances in question, and by means of consistent experiments, he and his co-workers proved that the plant acids were not consumed by combustion, were not ordinary nutrient substances, but were on the contrary themselves active groups of catalysts which served to maintain the combustion without themselves suffering any diminution thereby. The process involves a peregrination of hydrogen more intricate than the adventurous journeys

of Odysseus, though more rapid. Hydrogen is released out of the metabolic substances, probably through cooperation between Szent-Györgyi's and Warburg's co-ferment and Theorell's yellow enzyme, and encounters the plant acids, entering in that way Szent-Györgyi's's system. These acids transfer the system into the order: oxalacetic acid, malic acid, fumaric acid, and succinic acid, then, in the form of active hydrogen, to encounter the active oxygen from «the red system» and form water and free energy - a series of providentially subdued explosions which I alluded to before as a dramatic encounter. The plant acids act as catalysts by cooperation with specific proteins, and the effect of the yellow enzyme probably extends some way into this Szent-Györgyi's intermediate system.

Thus, the oxygen-activation in the red iron system and hydrogen-transfer from nutrients by the yellow metal-free system along with co-agents have been united by Szent-Györgyi through the discovery of this intermediate system. The interplay of «the red system»'s cytochrome-group and the yellow enzyme might probably also, according to Theorell, proceed directly. The flaws are numerous, but not of a character to constitute any essential breach in the highway of the oxidation-chain. Numerous ramifications of the latter however already begin to be discernible.

It is of especially great importance that at least two vitamins - C and B_2, and possibly B_1, and P - are in cooperation in the oxidation chain and are catalysts, illustrating the way in which these vitamins act in the organism. It may be that development in the near future will reveal the importance for our organism of copper concerning oxidation and of vitamin C with certain followers in plants, viz. oxidating enzyme, and oxidizable and reducible substances (Szent-Györgyi's flavonoles, termed vitamin P), which are capable of forming a sensitively attuned system with the vitamin, hydrogen-superoxide and proteins, or parts of them, with active and activating sulphur in the molecule. The sulphur of the alchemists of old, out of which everything was to radiate, is destined to experience a renaissance.

Professor Albert von Szent-Györgyi. As a representative for the Caroline Institute on this occasion, I am commissioned to give expression to our high estimation of your researches.

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You never swerved from your unyielding purpose to study the primary and fundamental processes of biological oxidation. Entering upon this difficult field of biochemical research you soon became a pioneer by interpreting the position and real function of co-ferment as an important link in the chain of dehydrogenating catalysts. Not even your important discoveries regarding vitamin C could deter you from following a certain strain of thought. I am deducing now from a close observation of your work that you were drawing distinctions in your mind at this occasion between your interesting discovery of ascorbic acid and the bare possibility of some other audacious plans of yours coming true. At this early stage they must have involved the investigation of the fundamental mechanism of connecting hydrogen activation with that of oxygen activation. Your intuitive mind decided in favour of the possibility of success, and you won through. In the year 1933 the first signs became visible for outsiders, and from then on the pace set by you and your co-workers at Szeged was astonishing, and your results were fundamentally new and highly important. In the midst of fervent research work with most promising aspects you are the discoverer and idealist to the mind of Alfred Nobel.

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http://www.nobelprize.org/nobel_prizes/medicine/laureates/1937/press.html