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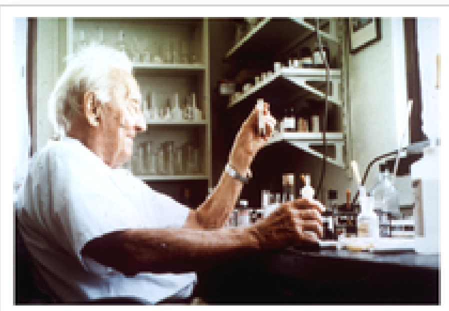
The Albert Szent-Gyorgyi Papers

The National Foundation for Cancer Research, 1973-1986



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By 1970, Szent-Györgyi's circumstances were looking desperate again. Stephen Rath, his friend and administrator of the Institute for Muscle Research, had died in 1962, leaving behind a huge financial mess. Szent-Györgyi found himself responsible for unpaid payroll taxes, NIH research funds that were unaccounted for, and income taxes on royalties from a centrifuge he and a colleague invented. Worse yet, most of his research funding had dried up. Though he would seem an obvious candidate for some of the federal government's "war on cancer" money, Szent-Györgyi flatly refused to write the kind of grant applications that such funding now required. Investigators were expected to explain in detail the work they planned to do, the results they expected to achieve, and how long it would take. Szent-Györgyi, still doing basic research, maintained that if he already knew what he would do and what he would find, he would not need the funding for research! Even had he been willing to submit further applications, Szent-Györgyi was nearly eighty years old, long past retirement age, and this may have counted against him. Besides this, Szent-Györgyi's ideas about cancer--which incorporated quantum physics--seemed bizarre to many grant reviewers. Cancer was considered a problem of molecular biology, not quantum mechanics. Consequently, Szent-Györgyi spent several years depending on the generosity of friends (and the MBL) to continue his research.

In April 1971, he gave a talk at the National Academy of Sciences and was interviewed afterward by the Washington *Evening Star*. He discussed his current funding dilemma in the interview, and was surprised, several weeks later, to get a letter from Washington, D.C. attorney Franklin Salisbury, asking where he could send a donation for the research. Szent-Györgyi told him to send it to MBL. Salisbury sent $25 and was startled to received a heartfelt letter of thanks from Szent-Györgyi. Salisbury had worked as a corporate counsel and businessman, and thought it very odd that a Nobel laureate should be so touched by so small a contribution. A year later, he offered to put together a non-profit cancer research organization, built around the cause of this older scientist who still had so much to offer. Salisbury's wife, Tamara, who had worked at NIH and at the Office of Naval Research, also joined the effort. Within several years, mainly through direct-mail solicitation, the National Foundation for Cancer Research (NFCR) had raised enough money to support not just Szent-Györgyi's research, but that of others working on the cancer question from a biophysics perspective. The NFCR became a "laboratory without walls," in which scientists could work in loose collaboration, with Szent-Györgyi as intellectual leader.

Szent-Györgyi's approach to cancer grew out of his longstanding belief that the many subtle processes in living systems must depend not just on "clumsy macromolecules" that make up body structures, but on small, highly mobile and responsive entities: delocalized electrons. (He had first proposed such an approach as early as 1941.) Molecular biology looked only at the *soluble* proteins in living systems, he noted. His theory (variously called "bioelectronic," "bioenergetic," biophysics, electronic biology, or quantum biology) attempted to explore cell activity on a submolecular level by looking at electron transfers between molecules connected together in *structures*. How else, he asked, could energy be turned into muscle motion, secretions, or nerve impulses? Regarding cancer, which is characterized by abnormal cell proliferation, Szent-Györgyi sought to understand not why cancer cells grow, but what stops normal cells from proliferating except when it is required. He suggested that the regulatory mechanism had originated very early in the earth's evolution; early living systems, before light and oxygen were available, existed in an "alpha state" in which their main functions were fermentation and proliferation. Oxygen changed everything, making proteins reactive and enabling them to link together in increasingly complex systems, differentiating structures and functions, and reaching a "beta state." Cells in the beta state, he said, resist proliferation partly because they are complex, and partly because they utilize compounds such as methylglyoxal to facilitate energy transfers between molecules, and thus carry out normal functions. When such cells need to proliferate, the methylglyoxal is temporarily inactivated by glyoxylase, an enzyme present in all living cells; the cell regresses to the alpha state and divides. Normally, this enzyme system is self-reversing, but a shortage of methylglyoxal or an excess of glyoxylase might keep the cell permanently in a proliferative state, i.e., cancer. Therefore, anything that disrupted the charge-transfer processes in structural proteins, might, according to Szent-Györgyi, push cells into the alpha state. He also believed that a vitamin C salt, ascorbate, played a crucial role in maintaining the "beta" state.

The last decade or so of Szent-Györgyi's career was spent working with biophysicists and others who could quantify these underlying theories about electrons and cancer. Much of the work involved using electron spin resonance (ESR) technology to detect free radicals in structural proteins, and thus demonstrate that the proteins could indeed act as semi-conductors with the help of methylglyoxal or similar compounds (many scientific colleagues were skeptical that proteins could serve as conductors at all). But he and his colleagues also looked at the affinity of tumor cells for certain kinds of free radicals.

As he had in his work with biological respiration cycles, Szent-Györgyi came very close to fitting together pieces of important biochemical puzzles. Free radicals (atoms or molecules with unpaired electrons) are generated by oxidation-reduction reactions within cells, and are often quickly inactivated by enzymes within the cells. But they also enter the body as environmental pollutants (e.g., smog and tobacco smoke), drugs, chemicals, or radiation. Because of the unpaired electron, free radicals are extremely reactive, i.e., they will steal electrons from other molecules, often breaking bonds in the process, including the covalent bonds in enzymes and other proteins, DNA, and the lipids in cell membranes, thus damaging those structures. Protection is provided by cell enzymes, and by antioxidant vitamins such as vitamin C (ascorbic acid) and vitamin E (tocopherol), which disarm free radicals by bonding with them. Szent-Györgyi's investigations, while often inconclusive, opened up new research perspectives on the processes involved in cancer.

In 1983, Szent-Györgyi began to have serious disagreements with the NFCR, mainly about funding contracts for his own operation at MBL. By the spring of 1986, he and the Salisburys had parted ways, and no alternative funding had been found. Szent-Györgyi's legendary good health declined; he had developed leukemia, followed by kidney and heart problems. He died on October 22, 1986, at the age of 93.
