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Braunstein as a Strategist

O. L. Polyanovskii

Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, ul. Vavilova 32, Moscow, 119991 Russia; fax: (095) 135-1405; E-mail: pol@eimb.ru

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From my student days in the late 1940s, the name of Alexander Evseevich Braunstein was tightly associated with concepts of complicated processes which regulate amino acid metabolism. His finding of transamination and of transaminase became the most important landmark in modern biochemistry. His studies on the action mechanism of pyridoxal enzymes published in coauthorship with M. M. Shemyakin were no less significant. However, aspartate transaminase remained his beloved creation.

I made my acquaintance with A. E. Braunstein at home drinking tea in 1959. This was the period when V. A. Engelhardt was organizing a new institute, and Braunstein was one of founders drawn in by Engelhardt to form the strategic lines of the institute. Certainly, Braunstein was himself a great strategist (that was confirmed by his whole life). And he solved problems of the general line development not by phrases but by quite concrete solutions (or proposals) that were the same thing. First of all, he sensed and precisely assessed the moment when and what work should be started not to be late.

Thus, after the tea drinking Braunstein took from a shelf a fresh journal (that was *JBC*) and showed me articles of American authors about purification and features of aspartate transaminase. From that time aspartate transaminase was entrusted to me. I had to learn to prepare the enzyme in a highly purified state and in sufficient amounts to provide studies not only of its catalytic properties but also physical parameters and the structure. This was the time when into the institute furniture was being brought, the researchers were hanging oak shelves over their three-post tables (these shelves are still retained in some rooms) and providing themselves with all necessities. During my work I had to synthesize carboxymethyl cellulose, granulated calcium phosphate, etc. In less than a year a transparent yellow (because of pyridoxal phosphate bound) solution of aspartate transaminase stood on the laboratory table. Braunstein was glad no less than we. He clearly understood that a new stage had come: from a virtual biocatalyst the enzyme became quite a material object and a search for keys to its active site should be started. The first step in this line was realized with the help of Czech colleagues. Braunstein who was known and respected by everybody arranged my scientific mission to Prague, and in several months I succeeded in the isolation of a pyridoxyl-containing peptide. This was the peptide from the active site of transaminase. Then, in the middle 1960s, only a few proteins and enzymes were available for studies. Braunstein clearly understood that the most elegant studies on principles of biological catalysis should be based on the knowledge of the enzyme structure in detail. And, consequently, one had to go further and not postpone the determination of the primary structure of aspartate transaminase.

Then there was then no equipment in the Institute of Molecular Biology. However, in the Institute of Natural Compound Chemistry headed by M. M. Shemyakin and located under the same roof similar studies were in progress, and Braunstein decided that it would be the least expensive to organize the work in cooperation with the neighbors. The year 1967 started. We already knew much about transaminase and might vouch for success in the isolation of trypsin and chymotrypsin peptides and also provide a high purification degree of large amounts of the protein that was of no less importance. I went to Yu. A. Ovchinnikov, the youngest Deputy Director. He was likely to know about our work, and my proposal did not seem unexpected to him. But Yurii Anatol'evich said that the Academicians should speak to one another (reasonably considering our agreement to be insufficient for such a large-scale work). The Academicians called up the same evening and gave their consent. Even in the next morning we discussed the details in the study of Braunstein. And during the following two years although the number of participants was not great, Braunstein conducted joint working conferences in his study. We also studied concurrently and very intensively functionally important groups of the enzyme and their locations on the polypeptide chain of aspartate transaminase were determined. Various

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approaches were used, but first of all we used covalently binding mono- and bifunctional reagents. The most successful work in this series resulted in the establishment of the distance between Lys, Tyr, and Cys residues in the active site region. This result was subsequently confirmed by X-ray crystallographic analysis. In 1974 the primary structure of aspartate transaminase was published. And some months later a similar structure was published by our colleagues from Italy and England. During all the time they were working in parallel but were some months behind. The work had been performed. We felt us winners, and the young participants were awarded with the Lenin Komsomol prize.

When the works were presented in total at the Biochemical Congress in Stockholm, F. Straub, who was then President of the Hungarian Academy of Sciences, said that such abundant data seemed to be obtained by workers of the whole institute. We had to say that the workers were not of one, but of two institutes.

While we were taking congratulations including those of colleagues from other countries, Braunstein soberly weighed the situation and came to a decision. He invited me and with his usual reserved smile said that it was time to be ready for X-ray crystallographic analysis and to crystallize our transaminase, but I already had other plans.