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IN THE FOOTSTEPS OF A BIOCHEMICAL LUMINARY: THE SCIENTIFIC LEGACY OF YAKUB PARNAS

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The article is dedicated to commemorating Yakub Karol Parnas, an eminent figure in biochemistry and a professor in the Department of Physiological (Biological) Chemistry at Lviv Medical University. It underscores the profound impact of Yakub Parnas on Ukrainian biochemistry, shedding light on intriguing facets of his personality during his highly productive two decades at Lviv University. His research significantly contributed to unveiling anaerobic glucose metabolism, later acknowledged as the Embden-Meyerhoff-Parnas pathway. Professor Yakub Parnas and his Lviv school conducted pivotal studies on enzymatic transformations associated with anaerobic muscle function and alcoholic fermentation, glycogen phosphorolysis, revelation of ATP synthesis within glycolysis, pioneering use of radioactively labeled phosphorus in biological experiments.

K e y w o r d s: biochemistry, Yakub Parnas, Embden-Meyerhoff-Parnas pathway, Lviv.

Yakub Karol Parnas, born on 16 January 1884 in the village of Mokryani, was the progeny of Oskar, a landowner, and Gabriela, nee Bernstein. Mokryani, a small town situated in the Drohobytsky district of Galicia, now within the Lviv region, encapsulates the intricate historical tapestry of Central and Eastern Europe. Originally part of Poland until the late 18th century, the region subsequently fell under the Austro-Hungarian monarchy until the conclusion of the First World War. Between 1918 and 1939, it reverted to Polish control, and following the Soviet–German treaty in 1939, it became part of the Soviet Union. The period from 1941 to 1944 witnessed German occupation, and presently, it constitutes a segment of Ukraine [1].

Parnas' significant contributions, emerged as a noteworthy figure in biochemistry, unfolded during his two-decade tenure in Lviv, marking a period where he not only achieved paramount scientific milestones but also navigated through cultural transformations (Fig. 1) [2, 3]. His early works occupy a pivotal position in the annals of biochemistry, with each observation serving as a substantive contribution to the comprehension of tissue metabolism, its intricate pathways, and the pivotal role played by enzymes.

Fig. 1. Yakub Parnas (16.01.1884 – 29.01.1949)

In 1902, Yakub Karol Parnas graduated from the gymnasium in Lviv, and by 1904, he completed his studies at the Higher Technical School in Berlin-Charlottenburg (Germany), specializing in Strasbourg under the guidance of F. Hofmeister (1905) and in Zurich with R. Wilstetter (1906-1907). Sub-

sequently, in 1907, he defended his doctoral thesis on amphi-naphthoquinone in Munich, earning the degree of Doctor of Philosophy "About naphtoquinones. Dissertation" (In German). Following this, he worked in the laboratory of Prof. Franz Hofmeister from 1907 to 1913 and concurrently held a teaching position at the University of Strasbourg. By 1913, Parnas attained the title of associate professor at the University of Strasbourg. In 1914, he conducted research in the laboratory of Frederick Hopkins in Cambridge, and between 1916 and 1919, he served as the Head of the Department of Physiological Chemistry at the Institute of Physiological Chemistry at the University of Warsaw [4].

Upon returning to his homeland, Parnas ardently resumed his research activities, initially in Warsaw for a brief period, and subsequently at the Jan Kazimierz University in Lviv. In 1920, Parnas relocated to Lviv to join Jan Kazimierz University, drawn by its more democratic academic environment and international professorship [5]. Serving as the head of the Institute of Medical Chemistry at Lviv University from 1920 to 1941, he concurrently held the position of professor and head of the Department of Biological Chemistry in the Medical Faculty. During this period, Parnas established a renowned scientific school, particularly excelling in the field of carbohydrate metabolism in the body. Appointed as a full professor and the Head of the Department of Medical Chemistry at the Jan Kazimierz University's Medical Faculty, the ensuing two decades proved to be the most prosperous and prolific in Yakub Karol Parnas's life and work.

The Jan Kazimierz University, during those years, stood as a distinguished scientific and intellectual hub, hosting luminaries across various disciplines. Parnas, already a well-respected figure, received esteemed recognition and the requisite resources to maximize his scientific, intellectual, and creative potential. Over the course of a few years, he successfully established a thriving center for teaching and research, forming a dedicated group of collaborators commonly referred to as the 'Parnas School' (Fig. 2). Notable among them were J. Heller (currently a professor of biochemistry in Warsaw) and W. Mozolowski (presently holding the chair of biochemistry in Gdansk). Together, they contributed significantly to the discovery of the process of ammonia formation in the blood and muscle. This groundbreaking work elucidated that ammonia gen-

Fig. 2. Staff of Physiological Chemistry Department, Jan Kazimierz University, Lviv, Poland, 1929. Standing from left: J. Nuckowski, J. Jaworska, T. de Tesseyre, W. Chrząszczewski, W. Lewin'ski, P. Ostern, C. Lutwak-Mann, technician. Sitting from left: W. Mozołowski, A. Klisiecki, Y. K. Parnas, J. Heller, U. Mroczkiewicz, and down J. Sieniawski, T. Mann, K. Wajda

esis resulted from the deamination of adenylic acid to inosinic acid. The subsequent exploration of the physiological significance of this process in muscular contraction was markedly facilitated by the large-scale preparation method for adenylic acid, developed in Parnas's laboratory in 1932 by his pupil and collaborator, Paul Ostern.

The 1930s marked a zenith in Parnas's professional life, representing a period of remarkable productivity. Those fortunate enough to collaborate with him during this phase were left in awe of his leadership qualities, profound knowledge in chemistry and physiology, exceptional experimental design skills, and notably, his nearly encyclopedic memory. This remarkable gift enabled Parnas to master multiple languages, flawlessly recall the names and faces of numerous students, recite extensive passages of Greek and Latin poetry from his youth, and impart scientific facts and chemical formulas to his pupils.

As early as 1922, Prof. Parnas authored his textbook, "Physiological Chemistry with Special Reference to Animal Physiology", a seminal work and the first of its kind written in Polish. This text played a crucial role in educating physicians and biologists. Between 1922 and 1926, he contributed several chapters to textbooks such as the Textbook of Physiology edited by A. Beck, the Textbook of Biological Methods edited by E. Abderhalden, and the Textbook of Normal and Pathological Physiology edited by A. Bethe, G. Bergmann, G. Embden, and A. Ellinger. Demonstrating a keen interest in nutritional problems, Parnas co-authored a monograph with W. Mozołowski on the physiological and chemical aspects of dietetics. Many of Parnas's students willingly volunteered to work in his laboratory, where he, as a mentor, significantly influenced their subsequent scientific trajectories. Even clinical practitioners, including pediatricians, surgeons, and internists, underscored the invaluable impact of the biochemical training they received in Parnas's laboratory, expressing words of deep respect and admiration in their reminiscences.

Ammonia released during muscle activity was quantified using the Kjeldahl instrument, refined by Parnas and Heller. Contrary to expectations, ammonia was identified as a product of nucleotides rather than glucose metabolism. A significant finding emerged, indicating that ammonia is released from adenylic acid (AMP), not from adenosinetriphosphoric acid (ATP). All three nucleotides (ATP, ADP, and AMP) were found to be in equilibrium in skeletal muscle, with adenylate kinase catalyzing their interconversion.

In the academic years of 1929/1930, Parnas assumed the position of Dean of the Faculty of Medicine at Lviv University. Early in 1930, he conducted microchemical analyses at the Universities of Leipzig and Strasbourg, a venture unfeasible in his laboratory. Elected as a member of the Polish Academy of Arts and Sciences in Cracow in 1931, the same year saw Parnas appointed Head of the Division of Pharmacy at the Faculty of Medicine, along with the Directorship of the committee overseeing Premedical Departments.

During 1931-1932, he held a visiting professorship at the University of Zurich and received honorary doctorates from the University of Athens in Greece (1936) and the Sorbonne University in Paris (1936). As a testament to his scholarly eminence, Parnas became a member of the German Academy of Naturalists "Leopoldina" [6].

Parnas has conclusively demonstrated for the first time that ATP can be regenerated at the expense of the energy derived from glycolysis in a process known as the "Parnas reaction". These groundbreaking results were initially presented at the 4th Congress of Biochemistry in Paris in 1933 and subsequently published in two papers in Nature in 1934. The Parnas reaction, unveiled in 1934, elucidated the direct involvement of adenosine triphosphate, the precursor to adenylic acid, in the enzymatic transfer of phosphate groups [7]. Following these pivotal discoveries, research in Professor Parnas' laboratory predominantly focused on investigations into glycogen and glucose metabolism. In summary, their most noteworthy achievements included: the identification of the reaction of glycogen phosphorolysis occurring in the presence of inorganic phosphate; the revelation that ATP synthesis, a process within glycolysis, involves the transfer of phosphate residues from molecule to molecule; pioneering the application of radioactively labeled phosphorus in biological experiments. Among the first to use radioactive phosphorus compounds, Yakub Parnas and his colleagues conducted groundbreaking research on the processes of phosphorylation in the body. The division of glycogen into glucose-6-phosphate in the presence of inorganic phosphate is the initial reaction of biological phosphorylation, which was identified at the Ya. Parnas department [7].

In assembling a sizeable group of bright young students in Lviv, Professor Parnas elevated the Lviv

Institute of Medical Chemistry to global prominence [8]. The Institute of Medicinal Chemistry at Lviv University swiftly gained worldwide recognition. Under Ya. Parnas' leadership, the Lviv School of Biochemists initiated research with a focus on ammonia production processes in blood and tissues, particularly muscles. The group contributed around 300 scientific articles. Yakub Parnas nurtured a significant cohort of bright individuals in Lviv, many of whom became distinguished scientists, heading labs and departments in Poland, England, and various other nations [8]. Unfortunately, this scientific institution faced near-destruction during World War II, leading to the dispersion of its staff across several countries.

In 1939, Jan Kazimierz University was renamed to Ivan Franko and the Soviet model for its functioning was adopted. In January 1940, the university underwent further changes aligned with the Soviet pattern, resulting in the separation of the Faculty of Medicine and the establishment of a new National Medical Institute. Parnas assumed leadership as the Head of the Chemical Department at this Institute. Parnas, in addition to ongoing studies on glycolysis, reignited his interest in naphthoquinones, the subject of his doctoral thesis. Collaborating with Baranowski, he synthesized methylnaphthoquinone, a vitamin K substitute, and applied it in medical practices, particularly in surgery and hemorrhages. These findings were communicated in an article on vitamins published in 1943. Toward the end of 1940, Parnas assumed the role of a member of the Regional Council of People, garnering respect from Russian and Ukrainian scientists. In 1943, he and Baranowski were invited to Moscow to present their work, receiving appreciation from prominent biochemists such as A. A. Bohomolec, A. E. Braunstein, A. W. Palladin, S. S. Medviediev, B. J. Zbarski, W. A. Engelhardt, and others [9,10].

In May 1943, with the relocation of refugees from Ufa to Moscow, Parnas took on the role of Director of the Chemical Department of the National Institute of Experimental Medicine. Swiftly reorganizing it into the National Institute of Biological and Medical Sciences of the Academy of Medical Sciences, he established a new Laboratory of Carbohydrate Metabolism. From 1943 to 1948, he served as the Director of the Institute of Biochemistry of the Academy of Sciences of the USSR, concurrently leading the Laboratory of Physiological Chemistry of the Academy of Sciences of the USSR from 1943 to 1949. Honored as an Academician of the Academy of Sciences of the USSR (1942) and the Academy of Medical Sciences of the USSR (1943), Parnas received accolades such as the Stalin Prize of the 1st degree (1942) and the Order of Lenin, the highest recognition in the USSR (1944).

During the wartime period, experimental endeavors were unattainable for Parnas [1]. Utilizing this interval, he produced exceptional reviews on enzymes, coenzymes, and hormones, which found publication in biochemical journals. Parnas orchestrated conferences, colloquially termed 'Parnas' Thursdays, celebrated for captivating lectures and lively discussions. Advocating active engagement of young researchers, he assigned them the task of preparing lectures on diverse topics. Notably, these seminars drew attendance not only from the departmental staff but also from distinguished scientists such as A. E. Braunstein, W. Bielew, M. Lyubimova, M. Shelagin, A. Szent-Gyorgy from Hungary, and B. Hastings from the USA [1, 9].

Post the war's conclusion, experimental work recommenced, albeit with limited reagent availability. Glycogen, myosin, nucleotides, and other organic compounds were isolated from rabbit muscle. Borys Stepanienko, under Parnas' supervision, explored the reaction of polysaccharides with iodide. Anna Petrova and later Eugenia Rosenfeld isolated phosphorylase, glycogen 1,6-glucosidase, and myokinase from muscles and tissues, delving into glycogen interactions with proteins. The study of AMP, ADP, and ATP was pursued, culminating in the establishment of the difference between "muscle AM" (adenosine 50-phosphate) and "yeast" adenosine-30-phosphate [10].

In 1947, Parnas faced declining health, marked by diabetes and heart disorders. Consequently, he resigned from the position of Director of the Institute in May 1948. On January 29, 1949, Parnas failed to attend a seminar at the Institute. Post-midnight that day, MGB (later known as KGB) officers apprehended Yakub Karol Parnas from his apartment. Following his arrest and extensive interrogation, Parnas fell ill and, despite medical assistance, succumbed to a heart attack.

Yakub Parnas left behind a significant scholarly legacy, including five textbooks and monographs, numerous scientific publications, and a global reputation as an outstanding researcher in the field of biological chemistry. His accolades encompassed membership in the Leopoldine Academy in Gale,

membership-correspondent of the Polish Academy of Sciences, valid membership in the Academy of Sciences of the USSR, membership in the Paris and Vienna Biological Societies, an honorary doctorate in Athens and the Sorbonne, and foreign membership in the French Academy of Medicine.

In 1996, Prof. Y. Parnas received official recognition for the first time in Ukraine. A memorial plaque honoring Yakub Parnassus was placed at the Lviv National Medical University building's entrance, which houses the Biochemistry Department where Yakub Parnas worked from 1920 to 1941 (Fig. 3) [11]. Concurrently, the First Parnassus Conference on Biochemistry and Cell Biology took place, marking the beginning of these conferences being organized on a regular basis. Conferences named after Yakub Karol Parnas were organized every two years. Subsequent conferences were hosted in Gdansk (1998), Lviv (2000), Wroclaw (2002), Kyiv (2005), Krakow (2007), Yalta (2009), Warsaw (2011), Jerusalem (2013), Wroclaw (2016), and Kyiv (2018). These conferences were jointly organized by the biochemical societies of Poland, Ukraine, and Israel.

Fig. 3. Commemorative plaque dedicated to Prof. Yakub Parnas was opened at 1st Parnas conference in Lviv (Ukraine) in September 1996

СЛІДАМИ БІОХІМІЧНОГО СВІТИЛА: НАУКОВА СПАДЩИНА ЯКОВА ПАРНАСА

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Стаття присвячена вшануванню Якова Оскаровича Парнаса, видатної постаті у біохімії, професора кафедри фізіологічної (біологічної) хімії Львівського медичного університету. Стаття висвітлює вплив Якова Парнаса на українську біохімію, досліджуючи цікаві аспекти його особистості впродовж найпліднішних двадцяти років роботи у Львівському університеті. Його дослідження значно сприяли розкриттю анаеробного обміну глюкози, визнаного пізніше як шлях Ембдена-Мейергофа-Парнаса. Центральними у численних наукових працях Якова Парнаса та його львівської школи були дослідження ензимних перетворень, пов'язаних із анаеробним функціонуванням м'язів та спиртового бродіння, ідентифікація реакції фосфоролізу глікогену, відкриття синтезу АТР в рамках гліколізу, першість застосування радіоактивно міченого фосфору в біологічних експериментах.

Ключові слова: біохімія, Яків Парнас, шлях Ембдена-Мейергофа-Парнаса, Львів.

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