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Résumé

Ioav Cabantchik is Professor Emeritus of Biochemistry and Biophysics at the Institute of Life Sciences of the Hebrew University of Jerusalem, Israel, where he held the Adelina and Massimo della Pergola Chair in Life Sciences. IC is a graduate of the Hebrew University of Jerusalem in Chemistry and Biology (BSc, 1964) and Biochemistry (MSc, 1966) and bio-medical programme in Radiation Biology and Biophysics of the University of Rochester School of Medicine, NY, USA, from where he got his doctoral degrees (*cum laude*). He later trained as Medical Research Fellow at the Research Institute of the Hospital for Sick Children (Toronto) (1975–1976) and was a Visiting Scientist in Membrane Physiology and Biophysics at the NIH (Kidney and Electrolyte Metabolism) (1976–78). In 1978, IC joined the Hebrew University of Jerusalem as Senior lecturer in Biochemistry and Biophysics in the Institute of Life Sciences. He was promoted to Associate Professor with tenure in 1984 and appointed Full Professor in 1987. He served as Head of Biochemistry (1987-90), Head of Life Sciences Teaching Program (2002-06) and Head of the Institute of Life Sciences (2007-09).

Teaching. He lectured in Cell Physiology and Advanced Biochemistry, Membrane Biology and Metal Biochemistry and was elected as most prominent teacher at HUJI. In 1994 he was nominated as Cystic Fibrosis NIH Scholar and in 1998 visiting INSERM professor at the Faculty of Medicine Claude Bernard - Hôpital Bichat (Molecular Biology of Erythropoiesis). He was on the Faculty of FEBS, NATO, ICRO and EMBO courses/workshops in Membrane Physiology and Biochemistry and organized international workshops/symposia in Iron in Health and Disease. He was Thesis advisor and/or co-advisor of both PhD and MSc students.

Research. The studies he conducted in Membrane Biochemistry in the initial stages of the scientific career led to the identification of the first mammalian membrane transporter—the anion exchange protein (**band 3**) of red blood cells—and to the delineation of its physiological role in the removal of CO₂ from tissue to lungs (for which he was awarded the Medical School *Metzger Medal for Distinguished Thesis*). Following an invitation by the WHO and subsequently by NIH, he gradually switched his research endeavours towards malaria pathophysiology, focusing on recently discovered permeation pathways induced in parasitized cells as potential avenues for targeted drug delivery. A unique target chosen was the parasite haemoglobin/iron handling machinery, whose molecular features differ markedly from those of host cells, thus offering a

promising window for rational therapy. However, meeting the new challenge demanded the introduction of novel experimental tools (metalo-probes and tailored protocols) for the dynamic iron tracing of iron in living cells and also in biological fluids, particularly the labile forms of iron that are redox-active (i.e. potentially toxic when prompted with pro-oxidants) and also chelatable (i.e. therapeutically targetable). The methodologies developed proved important not only for studying malaria pathophysiology and pharmacology, but also for exploring the wide area of mammalian iron metabolism in health and disease-an area that was about to explode in terms of new discoveries of both basic and clinical value. Thus the tools "ironically" developed for malaria proved instrumental for optimizing treatment of systemic iron overload (transfusional) with newly developed iron chelators suitable for oral administration (such as Exjade by Novartis or Deferiprone by Apopharma).

A new phase of translational and clinically oriented research begun with work done initially on malaria followed by application of the diagnosis and therapeutic tools to systemic siderosis. Those were further extended in the last 10 years to the treatment of siderotic disorders of more regional nature, such as cardiosiderosis and neurosiderosis in Friedreich ataxia-FRDA and neurosiderosis in various neurodegenerative disorders. These diseases which we collectively refer as NBIA (neurodegeneration with brain iron accumulation) comprise generic NBIA associated PKAN-deficiency or Parkinson's disease, MS, HD and AD and recently also Wolfram syndrom2- work in progress at HUJI). A characteristic feature identified in all those disorders is not merely regional siderosis in specific neurons or specific organelles like mitochondria, but a demonstrable **maldistribution of the metal**. That in turn posed a challenging question regarding the etiopathological factor (siderosis or iron deficiency or perhaps both!) and the prospects for its pharmacological correction. The contribution made by the group in Jerusalem is that iron maldistribution is a pharmacologically correctable condition whereby selective scavenging of toxic iron by specific chelators can be complemented by internal redeployment, thus sparing iatrogenic iron losses. That concept was translationally taken from bench to bed, establishing a moderate or conservative modality of chelation as a promising therapeutic option in various disorders of NBIA.

Methods developed in IC's laboratory for the identification of labile iron forms in biological fluids materialized also into clinical diagnostic kits that were patented and licensed to Aferrix Ltd (Tel Aviv Israel) for production and worldwide distribution for assessing systemic iron overload disorders.

Most of the achievements in Bioiron, basic and clinical, were the result of collaborations with Israeli leaders in iron pathophysiology and with various European groups with whom binational or multinational collaborations were established, many under the EU umbrella for the study of iron disorders (transfusional/

iatrogenic siderosis, anemia of chronic disease) and recently in NBIA (neurodegeneration with brain iron accumulation). Is the author of about 200 publications, mostly peer reviewed and based on original research. The research projects were funded over the years by NIH (1980-1994), WHO and US-AID (1984-1990), the Israel Science Foundation (1979-2006), BSF, GIF and EU (fr- 4 and 5 and Horizon) and also by contracts with Pharma. He is the founder and scientific director of Aferrix, Israel, a Yissum licensed company devoted to clinical and basic applications of analytical and diagnostic tools for early detection of toxic transition metals in biofluids. IC serves/d as consultant or scientific advisor for Novartis (Basel), Apopharma (Toronto), Aferrix (Tel Aviv), Hinoman (Or Yehudah) and Dexcel Pharma (Jerusalem).

IC organized several international workshops/conferences in Membrane Biochemistry and on Iron in Health and Disease, he was in the Board of Directors of the International Bioiron Society **IBIS** 2009-2013 and 2015-2021 and was elected President of IBIS for the 2017-2019 period. In 2015, he was awarded the Marcel Simon Prize for excellence in Research at the 5th Bioiron Congress held in Hangzhou China.

Additional information can be found at:

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