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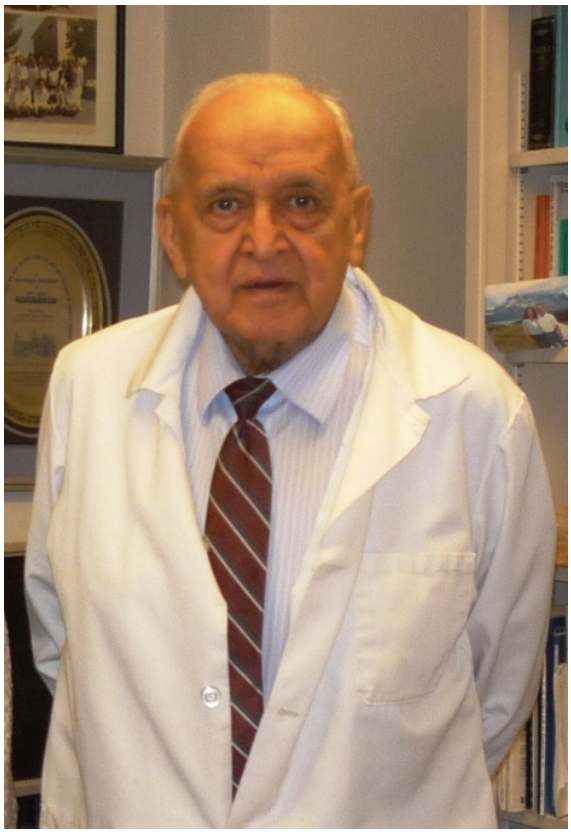
NEWS

Celebrating Franz Halberg's 90th birthday



The birth of *chronobiology* and *chronomics* as transdisciplinary scientific disciplines in their own right stems from Franz Halberg's unveiling of lawful variations within the physiological range and his vision that they were not trivial but had far-reaching implications. These sciences would not have come about without a key principle Franz followed throughout his life's work, namely to "measure in time what is measurable and render measurable what as yet is not". Toward this goal, he not only gathered a critical mass of data, himself and with a steadily extending network of disciples worldwide, he also developed inferential statistical methods for their analysis and interpretation.

By adding TIME to the existing body of knowledge in all of biology and medicine, and by recognizing the crucial role this new element was to play in all matters of life, Franz Halberg developed the new science of *chronobiology*. By insisting on an inferential statistical foundation, a microscopy in time was born. He later added a telescopy in time by his methodical scrutiny of non-photic as well as photic environmental influences on biota, from which *chronomics* flourished.

Born on July 5, 1919 in Romania, Franz Halberg became interested in the adrenal as a university assistant in post-World War II Innsbruck, Austria. He studied it at Harvard Medical School, where he held a World Health Organization fellowship in clinical endocrinology in 1948. In 1949, he moved to the University of Minnesota, which saw his breakthrough experiments that led to the important discovery that circadian rhythms are partly endogenous and can be manipulated by environmental synchronizers. His results were published in 1969 in a citation classic (Halberg F: Chronobiology. Ann Rev Physiol 31:675–725, 1969). By 1958, Franz had recognized the important role played by the cell's RNA and DNA cycles, which he was first to demonstrate as complementing the hypothalamic-pituitary-adrenal system as mediator of photic inputs. In an era when RNA and DNA were considered to be the most stable and constant entities in biology, Franz showed that both underwent a circadian variation and that it was RNA that led DNA in the sequence of events within the cell cycle. Realizing the implications of this finding for cancer treatment, Franz proceeded to demonstrate that both tumor regression rate and disease-free survival could be improved two-fold by timing the administration of radiotherapy in accordance to the circadian rhythm in tumor temperature used as marker rhythm. It is the privilege of only very few to have an impact in science, not only by original findings but primarily by a vision of their implications, that lead beyond a scientific breakthrough to a new way of thinking. By his deep sense of humility and his ability to sit in front of the facts without preconceived ideas, Franz has made a lasting dent in the history of medicine.

His work earned him numerous awards. Apart from holding professorships in Laboratory Medicine and Pathology, Physiology, Biology, Bioengineering and Oral Medicine at the University of Minnesota, he received honorary doctorates from the University of

Montpellier (France), Ferrara (Italy), Tyumen (Siberia), Brno (Czech Republic), L'Aquila (Italy), and most recently People's Friendship University of Russia (Moscow, Russia). At 90 years of age and still active 7 days a week in the Center named after him at the University of Minnesota, he is one of the last two recipients of a lifetime career award from the National Institutes of Health.

Singled out from accomplishments summarized in over 3,000 published titles in cooperation with colleagues from all five continents are the following highlights. First, rhythms are not trivial as they can tip the scale between health and disease and even between life and death. Franz Halberg's rigorous assessment of rhythm characteristics and their alterations in the presence of an elevated disease risk or overt disease attempts to achieve a better health care at a reduced cost by a timely chronodiagnosis followed by prophylactic interventions aimed at primary prevention and, when needed, by timed treatment (chronotherapy) optimized for the individual patient. Second, after suggesting the hypothalamus mediated light information, Franz fought from the start the idea that the suprachiasmatic nuclei were "the" master clock. After a debate that lasted more than a decade, Franz's view has been vindicated now that modern molecular biological techniques have shown the presence of oscillators in practically every cell, in the brain as well as in the periphery. Third, as the crowning of a distinguished career, Franz's early vision that rhythms were not trivial but rather constituted the founding block of life itself is being unveiled by findings that alterations in clock genes are not only responsible for alterations in circadian rhythms but are fundamentally involved in a host of diseases from addiction and cancer to cardiovascular disease. Last but not least, his mapping of a much broader time structure includes cycles with frequencies covering 10 orders of magnitude, aligned between biology and physics by means of an armamentarium of analytical procedures, including a remove-and-replace approach extended from endocrinology to a true transdisciplinary endeavor. Aligning spectral components shared between physiology (living matter) and the natural physical environment (physics) led to the concept of congruence. Franz demonstrated the presence of both photic and non-photic influences of the sun and broader cosmos on life on earth, suggesting that cyclic aspects of the environment underlie the cycles that constitute life. His view that each biological cycle stems from an environmental one underlies the evolutionary process in theory. In practice, it is both the indispensable control information for whatever is done in time and a new transdisciplinary broad and useful spectrum in its own right. A sample of recent findings illustrating both the applied and basic aspects of his research is included in this journal.

After entering his tenth decade, Franz remains a human dynamo, with ambitious projects to tackle the next scientific frontier of *chronobioethics*, shifting emphasis from the well-being of individuals to that of societies. Franz's most recent work addresses wide-ranging applications from the optimization of individualized health care to concerns for the health of societies. Toward this goal, the monitoring of vital signs such as blood pressure and heart rate serves the double purpose of advancing both the biomedical field and physics, enlarging the scope of Humboldt's purely physical monitoring into a transdisciplinary endeavor. Franz's vision to use the same data collected within the scope of health surveillance for a biologic monitoring of photic and non-photic solar effects worldwide provides another facet of a space weather report. His incredible persistence and intellectual clarity in the face of entrenched thinking, which established procedures and fields that transcend disciplinary boundaries, sets him apart as an extraordinary human being and a truly great scientist. It is a very great honor and privilege to have him as my teacher and as my most trusted friend.

Germaine Cornélissen