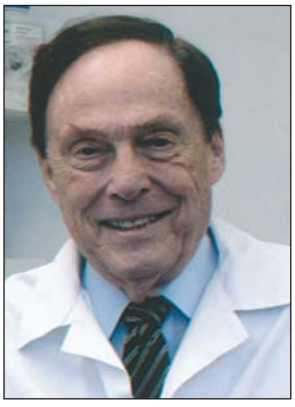
Cover legend: **Elwood V. Jensen;** a member of The Editorial Academy of The International Journal of Oncology



Elwood Jensen was born in 1920 in Fargo, North Dakota. In 1924, his family moved to Springfield, OH, where he attended high school, and graduated from Wittenberg College in 1940 with a major in chemistry. After a year of graduate study in chemistry at the University of Chicago, Pearl Harbor and the ensuing war interrupted his formal studies. He devoted the next three years to the search for more deadly chemical warfare agents and then a fourth year to research on synthetic rubber, where, mainly by accident, he made two unexpected discoveries in free radical chemistry that endeared him to his professor. By working extra hours, he managed to complete his PhD thesis in organic chemistry in 1944.

The studies of toxic substances awakened a dormant interest in things physiological, but, by the time the war was over, he was too old to consider four years of medical school. So, with the help of his professor, Morris Kharasch, he obtained a Guggenheim fellowship to go to Zürich to learn steroid chemistry with Leopold Ruzicka at the Swiss Federal Institute of Technology. While in Switzerland, he had an extracurricular experience that was to have a major influence on his later research. In the summer of 1947, he and his wife visited Zermatt to view the regal Matterhorn, with no intention of climbing since he had no previous experience. But the enchantment inspired by this peak led him to attempt the ascent anyway, in company with a Swiss guide and a student with climbing experience. When this was successful, he wondered why the Matterhorn was the last major peak in Europe to be climbed when even a novice could do it with the help of a guide. He later learned that the summit was reached only in 1865, when an English engraver and six companions decided to try the northeast face, which appeared from below to be a sheer wall of rock, rather than previous routes that had looked much easier. This was his introduction to the concept of 'alternative approach' that served him so well in his subsequent studies.

Returning to the University of Chicago, he joined the faculty of the medical school where Charles Huggins was in the process of establishing what, in 1951, became the Ben May Laboratory for Cancer Research. There he remained most of his career, serving as Director from 1969 to 1982 and taking mandatory retirement in 1990 as the Charles B. Huggins Distinguished Service Professor Emeritus. During this time he had joint appointments and graduate students in various basic science departments. On leave of absence, in 1983-87 he served as world-wide Director of the Ludwig Institute for Cancer Research, based in Zürich, and in 1988 as Fogarty Scholar at the National Institutes of Health in Bethesda.

In the early 1950s, Jensen was amazed when Dr. Huggins showed him how, after a few day's administration of sub-microgram doses of estradiol to the immature rat, its tiny uterus was induced to grow by a factor of nearly ten. At that time, when biochemistry was largely enzymology, it was assumed that estrogen must act on enzyme systems, but just how was not clear. Recalling the Matterhorn saga, Jensen took an alternative approach: not what does the hormone do to the tissue but what does the tissue do with the hormone?

Because estrogens are active in such tiny amounts, to find them in tissues after giving a physiological dose required labeled hormone of much higher radioactivity than had ever been known before. In 1957, the Jensen laboratory devised an apparatus for labeling estradiol with carrier-free tritium, permitting the detection of one-trillionth of a gram. During the early 1960s, he used this to show that estradiol stimulates rat uterine growth without itself undergoing chemical change and that hormone action results from its binding to an inactive form of a specific receptor protein, converting it to an active transcription factor. When analogous receptors were later discovered for other steroid hormones, Jensen's 'two-step' mechanism became the prototype for the action of all classes of these agents.

Having established that estrogens act in combination with a receptor protein (ER), Jensen reasoned that the one-third of human breast cancers that are hormone-dependent and respond to endocrine ablation (ovariectomy, adrenalectomy, hypophysectomy) must contain the receptor, but perhaps the two-thirds that proliferate even in the absence of hormone may no longer need or make this protein. In 1965, he undertook a collaborative study with surgeons at the University of Chicago, correlating the ER content of the tumor tissue with the patient's response to estrogen deprivation. As first reported in 1971, and with a larger study in 1978, the two-thirds of the patients whose cancers show low ER content rarely respond to endocrine manipulation, whereas, of the patients with high

receptor levels, most, but not all, show objective remission. These findings have been confirmed in many laboratories including studies with newer endocrine treatments, such as antiestrogens and aromatase inhibitors. Estrogen receptor analysis of excised breast tumor tissue as a guide to therapy selection is now standard clinical practice.

With the indentification of receptors for all classes of steroid hormones, several groups attempted, by conventional techniques of immunoprecipitation, to prepare antibodies to these proteins, but without success. Suspecting that the estrogen receptor might form soluble immune complexes, Jensen succeeded in obtaining the first antibodies to a steroid hormone receptor by the alternative approach of sedimentation in sucrose gradients, using the tritiated hormone as a marker for the receptor and the increase in sedimentation rate as an indicator of antibody bound to the estrogen-receptor complex. Monoclonal antibodies to human receptor have provided immunochemical procedures for determining ER in breast cancers with many advantages over steroid-binding assays. Jensen's antibodies, as well as the purified protein employed in their preparation, were used by others for cloning the estrogen receptor.

After retiring from the University of Chicago in 1990, Jensen spent one year as Scholar-in-Residence at Cornell University Medical College in New York City, nearly seven years as von Humboldt Visiting Professor at the University of Hamburg, three years as Nobel and then STINT Visiting Professor at the Karolinska Institutet in Huddinge and a half-year at the NICHD in Bethesda. In 2002, he came as Visiting Professor to the Department of Cell Biology of the University of Cincinnati College of Medicine, where he is currently Distinguished University Professor and holder of the Wile Chair for Cancer Research. In collaboration with Professor Sohaib Khan, he is studying the antagonist-specific binding site in ER, which he had discovered while in Hamburg and shown to be responsible for the anti-estrogenic action of tamoxifen.

For his discoveries, Elwood Jensen has received 27 national and international awards, including the Prix Roussel, Gairdner Foundation Award, Kettering Prize of the GM Cancer Foundation, Koch Award of the Endocrine Society, Axel Munthe Award in Reproduction, Landon Prize for Translational Cancer Research, Brinker Award for Breast Cancer Research, and, most recently, the Albert Lasker Award for Basic Medical Research. He was awarded honorary DSc degrees from Wittenberg University, Acadia University and the Medical College of Ohio and honorary MD degrees from the Universities of Hamburg and of Athens. He was elected to the U.S. National Academy of Sciences in 1974 and the American Academy of Arts and Sciences in 1975, and has served as President of the U.S. Endocrine Society (1980-81), on the Councils of the National Academy of Sciences, American Cancer Society, NICHD and NCI, advisory boards of several organzations, and editorial boards of eight different scientific journals. Some day he intends to retire to Zürich, where his German/Swiss wife can continue her musical performances, but, for the present, there is still much work to be done.