James V. Staros

Education. Staros received his undergraduate education at Dartmouth College, where he became hooked on laboratory research and co-authored his first published scientific paper with his undergraduate research advisor, David M. Lemal. He was a National Science Foundation Graduate Fellow at Yale, where he earned a Ph.D. in Molecular Biophysics & Biochemistry under the mentorship of Frederic M. Richards and was a Helen Hay Whitney Postdoctoral Fellow in Chemistry at Harvard, where he worked with Jeremy R. Knowles.

Early faculty career. Staros began his faculty career at Vanderbilt in 1978, earning tenure in 1983, promotion to Professor in 1986, and serving as a department chair 1988-2002. At Vanderbilt, he was active in faculty governance, serving as Chair of the Faculty Senate, and he was recognized with the Thomas Jefferson Award "...for distinguished service to Vanderbilt through extraordinary contributions as a member of the faculty in the councils and government of the University."

Administrative roles. In 2002, Staros was named Dean of the College of Arts & Sciences at Stony Brook University (SUNY) with a faculty appointment as Professor in the Department of Biochemistry & Cell Biology. In 2009, he became Senior Vice Chancellor for Academic Affairs & Provost of the University of Massachusetts Amherst, with a faculty appointment as Professor in the Department of Biochemistry & Molecular Biology, a position that he assumed full time in September 2014 when he stepped out of his administrative post and back into life as a faculty member until his retirement in September 2019.

Contributions to education. In addition to leading a vigorous research program (see below) that included mentoring many undergraduates, graduate students, and postdocs, Staros has been an innovator in undergraduate and graduate education. At the undergraduate level, he has been very active in bringing innovations into the science classroom and teaching laboratory. In 1991, in a successful proposal to the HHMI Undergraduate Biological Sciences Education Program, he designed a networked wet teaching laboratory as part of a total overhaul of introductory biology. In 1995, he posted his first hypertext syllabus for a course he taught in a computer classroom designed and built with support from another HHMI grant that he led. More recently as UMass Amherst Provost, he was a strong proponent of Team-Based Learning (TBL), with the result that UMass Amherst constructed seven IT-enhanced TBL classrooms on campus and provided support for faculty converting courses to TBL format through its Center for Teaching & Learning. After returning to the faculty, he taught regularly in this format until his retirement. He currently serves as Chair of the Governance Committee of the Bay View Alliance, a consortium of a dozen public research universities in the U.S. and

Canada committed to "exploring strategies for cultural change to support and sustain the widespread adoption of instructional methods leading to better student learning."

At the graduate level, Staros served on numerous federal graduate fellowship and training grant review committees and site visit teams, including a four-year appointment on the primary training grant review committee for the National Institute of General Medical Sciences, two of those years as its chair. He served on the advisory committee that recommended the creation of the Chemistry-Biology Interface program and chaired the panel that reviewed the first proposals to that program. He was one of the founding chairs of the Interdisciplinary Graduate Program at Vanderbilt, and he organized the first workshops on Responsible Conduct of Research for that program in 1990 and 1991 and continued to participate in RCR training for graduate students at Vanderbilt, Stony Brook, and currently, at UMass. As Provost at UMass, he commissioned the first in depth review of Ph.D. programs across the campus, and he elevated the Dean of the Graduate School position to a Vice Provost position, moving graduate education into the Provost's cabinet.

Diversity and inclusion. Staros has had a career-long commitment to diversifying the professoriate by enabling opportunities for underrepresented students to excel. In 1988 he created a program to bring underrepresented students to Vanderbilt for a summer research experience. He secured local seed funding to accept students for the summer of 1989 and 1990, securing funding from HHMI and NIH that supported the program from 1991 until (and after) he left Vanderbilt in 2002. It was largely for this program that he was recognized with the Vanderbilt University Affirmative Action Award in 1990, one of the first Vanderbilt faculty members to be so recognized. At UMass, he served as Principal Investigator for the NSF-funded Northeastern Alliance for Graduate Education and the Professoriate (NEAGEP), a consortium of ten public and private research-intensive universities in the Northeast and five affiliated minority serving institutions. The NEAGEP program greatly increased the number of underrepresented minority students in STEM discipline Ph.D. programs at UMass Amherst and greatly increased the retention and completion rates of those students.

Research synopsis. The Staros laboratory focused on mechanisms by which the binding of polypeptide hormones to their cell surface receptors are transduced into signals in the cell and mechanisms by which those signals are regulated. The primary biological systems studied were the ErbB receptor family and their ligands, the archetypes of which are epidermal growth factor (EGF) and its receptor. The Staros group applied methods from protein chemistry, spectroscopy, and molecular biology in these investigations, often employing new chemical and spectroscopic reagents developed in Staros' laboratory.

Protein chemical studies in the Staros laboratory in the early 1980's showed that the EGF receptor and the EGF-stimulable Tyr-specific protein kinase are two functions of a single molecule, making the EGF receptor the first recognized receptor tyrosine kinase. Using

affinity labeling methods, they identified Lys721 as an important residue in the kinase active site. Subsequently, using site-directed mutagenesis, they showed that Asp813 functions as the catalytic base of the kinase in phosphoryl transfer. A surprising outcome of these studies was that the kinase-negative mutant receptors with Asp813 replaced with Ala or Lys 721 replaced with Arg, when expressed in cells without endogenous EGF receptors, are still capable of signaling for DNA replication, but only if ErbB2 is present. When the EGF receptor was expressed in 32D cells, a cell line that normally requires interleukin-3 (IL-3) for survival and proliferation and is devoid of endogenous ErbB receptors, EGF binding to the wild-type receptor could replace the functions of IL-3 binding to the IL-3 receptor. In the absence of EGF, the EGF receptor prevented apoptosis in these cells. Unexpectedly, the kinase-negative mutant in which Lys721 is replaced with Arg also prevented apoptosis; however, the kinase-negative mutant with Asp813 replaced with Ala did not retain this function.

A variety of spectroscopic studies were employed to investigate the dynamic interaction of EGF with its receptor and the state of the occupied EGF-receptor complex in the membrane. For example, the Staros group employed fluorescence homo-transfer, a specialized form of fluorescence resonance energy transfer (FRET) in which the same fluorophore is used as both donor and acceptor, to show that FRET between EGF molecules bound to receptors in cells arises not from transfer within occupied receptor dimers, but between occupied receptors within higher order oligomers. They built a specialized stopped-flow fluorimeter for investigating the kinetics of EGF-receptor binding and dissociation in <u>living cells</u> by fluorescence anisotropy. They expressed the EGF receptor in 32D cells, which do not express any endogenous ErbB receptors and showed that binding and dissociation isotherms can best be fit to two classes of receptors, indicating that the two affinity states of the receptor that are commonly observed are an intrinsic property of the receptor and disproving the then current hypothesis that the two states were due to heterodimerization with other members of the ErbB family. Studies in 32D cells expressing both the EGF receptor and ErbB2 suggested that the main effect of heterodimerization is to increase the population of high affinity receptors; however, the high affinity state of the EGF receptor in the presence of ErbB2 is different from the high affinity state in its absence. When the EGF receptor was expressed in the absence of ErbB2, the high affinity state is defined by a fast on-rate; however, in the presence of ErbB2, the high affinity state is defined by a very slow off-rate.

Using mass spectrometry to study the glycosylation state of the receptor, they found that Asn579, one of the eleven canonical asparagine-linked glycosylation sites, is not glycosylated in a fraction of the receptors expressed in A431 cells. This site is especially interesting because Asn579 lies in a part of the receptor that controls the transition between the inactive (tethered) state of the receptor and the active (untethered) state. By making a site-directed mutant receptor in which Asn579 is substituted with Gln, resulting in a receptor that cannot be glycosylated at that site, they studied the properties of this

subclass of receptors. Kinetic studies showed that the Asn579→Gln mutant EGF receptor when expressed alone in 32D cells has kinetic characteristics more closely resembling those of the wild-type receptor in the presence of ErbB2 than in its absence, *i.e.,* a higher proportion of high affinity receptors than for the wild-type receptor expressed alone, and a high affinity state that is defined by a slow off-rate rather than a fast on-rate. These results suggest that glycosylation at Asn579 contributes to stabilizing the inactive (tethered) state of the receptor.

In an independent series of studies, they employed computational methods to study the molecular evolution of the ErbB family of receptors and of the EGF family of ligands. One end result of these studies is the prediction of previously unrecognized ligands for the ErbB family of receptors.

Representative publications.

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