Sung-Hou Kim

From Daegu to Berkeley: Six Decades of Structural and Genomic Biology

A Toast to Sung-Hou Kim

Assembled by Debanu Das and Steve Muskal

To Sung-Hou Kim — born in Daegu in 1937, the eldest surviving son of eight children, who grew up under Japanese occupation and survived the devastation of the Korean War. A young man who moved from poetry to philosophy to religion before finding his calling in Science and who learned crystallography by performing Fourier transforms by hand at Seoul National University (SNU), Korea, using the diffraction data collected at the Korean Military Research Institute because there were no computers or X-ray diffraction equipment at SNU.

To the Fulbright scholar who left Korea in 1962 and arrived at the University of Pittsburgh, where George Jeffrey's crystallography program became his gateway to American science. To the postdoc who joined Alex Rich's laboratory at MIT and, unaware that the world's best labs had already failed, used polyamines from a virology textbook to obtain high quality single crystals of transfer RNA — a trick that became standard for every nucleic acid crystallographer who followed.

To the young assistant professor at Duke who, with Joel Sussman as his first postdoc and George Church as his first Research undergrad, solved the L-shaped structure of tRNA in 1973 — a discovery that made the front page of the New York Times and immediately illuminated how the genetic code is physically translated. To the mentor who saw a spark in George Church, rescued him from academic failure, and told him: "You are not destined to be a research assistant. You really have to apply to a top graduate school who can recognize your unusual talent." Church went to Harvard and helped invent genomics.

To the Berkeley professor who, with Bart de Vos, Liang Tong, Michael Milburn, and Pedro Matias, determined the structures of Ras oncoproteins that revealed why a single mutation causes uncontrolled cell growth — the molecular foundation for what has become one of the most active areas of cancer drug development. To the inventor, with Jarmila Jancarik, of the sparse-matrix crystallization screen, announced at a Gordon Conference where the audience ran out during the break to call their laboratories.

To the scientist who has many other curiosities, like a kid in a toy store, using one class of sweet proteins. His group determined the structures of sweet proteins such as Monellin and Thaumatin; engineered a more stable Single-Chain Monellin and introduced the gene to produce a "sweeter" tomato; determined the 3-D structure of a combined complex of D-Monellin and L-Monellin, looking for the possible difference between the right-handed protein universe and the left-handed universe.

To the structural biologist who spent a decade dissecting the bacterial chemotaxis receptor — from the first crystal structure of the ligand-binding domain in 1991, through the frozen dynamic dimer model, to the 200-angstrom cytoplasmic coiled-coil in 1999 and the receptor-clustering model in 2002 — delivering one of the most thorough structural dissections of a signaling system ever accomplished by a single group.

To the visionary who, with the 1998 MJ0577 paper, proved that three-dimensional structures could assign biochemical functions to hypothetical proteins when sequence analysis alone could not — the founding proof-of-concept for structural genomics as a discipline. Who then led the Berkeley Structural Genomics Center and helped build the biological beamlines at the Advanced Light Source, arguing that the synchrotron needed dedicated lines for biology — a contribution he credits with saving the facility when DOE reviewed whether to shut it down.

To the entrepreneur who co-founded Plexxikon, built on scaffold-based drug design from the very first day of discovery, and watched vemurafenib — Zelboraf — receive FDA approval in 2011 for BRAF-mutant melanoma under accelerated review, now approved in over sixty countries. The most prominent validation of structure-based drug discovery since the method's emergence.

To the computational genomics scientist who, in his final active years, applied feature frequency profiles to build whole-genome phylogenies that challenged conventional ribosomal RNA trees, and who brought machine learning to predict individual genomic susceptibility for complex diseases, such as 20 common cancers, from germline sequence variation.

To the man honored with the Lawrence Award, the Princess Takamatsu Award, the Ho-Am Prize, a Guggenheim Fellowship, and election to both the National Academy of Sciences and the American Academy of Arts and Sciences. Who in 2023 stood as one of four honorees at the Republic of Korea Science and Technology Merit Commemoration, reflecting: "Looking back now, it amazes me that my parents so readily allowed me — the eldest son — to study abroad."

To Sung-Hou Kim — teacher, crystallographer, entrepreneur, and architect of molecular understanding. Here's to the life of the mind and the structures it reveals.