# Professor W.K. Alfred Yung

## *A Biographical Sketch*

Professor W. K. Alfred Yung, M.D., received his undergraduate degree from the University of Minnesota, Minneapolis, in 1971, graduating summa cum laude. For his medical training, he attended the University of Chicago Pritzker School of Medicine and received his M.D. degree in 1975. Internship and residency training followed at the University of California, San Diego from 1975-1978, and chief residency and fellowship at Cornell University School of Medicine and Memorial Sloan-Kettering Cancer Center from 1978-1981. Dr. Yung currently holds the title of Professor of Neuro-Oncology and Cancer Biology, as well as the Margaret and Ben Love Chair of Clinical Cancer Care. He has served as Chair of the Department of Neuro-Oncology since 1999. He is also Professor of Neurology at the University of Texas Health Sciences Center at Houston Medical School and serves on the faculty of the University of Texas Graduate School of Biomedical Sciences in Houston.

His research program at M. D. Anderson Cancer Center spans more than two decades and includes basic, translational, and clinical research. Along with 23 years of continuous funding by NCI, his work has also been funded by foundations and industry grants. His primary research interest focuses on development of molecular therapeutic strategies targeting the EGFR and PTEN/PI3 kinase pathways and the angiogenic regulatory mechanisms that are crucial to human glioma genesis and progression. The translational research effort has developed several adenoviral vectors that are capable of down-regulating TGF-$\alpha$ and VEGF production and angiogenesis in glioma cells. More recently, his laboratory has focused on investigating the biological activity of a series of new PTEN/PI3K pathway inhibitors in glioblastoma in vitro and in vivo models. Another research project investigates the subcellular localization of the tumor suppressor MMAC/PTEN gene and its nuclear signaling pathway. Highlights of his major research projects and grants include:

- Subcellular localization and nuclear signaling of PTEN: As a continuation of work started by the late Dr. Peter Steck, we have cloned the PTEN promoter region and has demonstrated that PTEN is sequestered in the nucleus during Go resting phase and is summoned to the cytoplasmic membrane when cells are stimulated by growth factor. This nuclear export of PTEN is self-regulated by the PI3K (mTOR)/S6K1/2 pathway. More importantly, nuclear PTEN is capable of inducing growth arrest independent of p-Akt activation suggesting PTEN may have a separate signaling pathway in the nucleus.
- Development of new targeting agents against the PTEN/PI3K pathway: Parallel to our work on the biology of PTEN signaling, we are developing a comprehensive approach to identify and assess the efficacy of signal transduction agents targeting the PTEN/PI3K pathway. We have ongoing collaborations with several biotech and pharmaceutical companies to study several new molecules such as QLT, TAE-226, RAD001, PX866, and BEZ-235. Using the reverse phase protein lysate array technique, we can rapidly assess the downstream effect of these molecules. Tumor stem cell and human tumor explants are being used in our animal experiments since they are more reflective of human tumor genotype. More importantly, we have initiated a SiRNA library synthetic lethality screening project to rationally identify synergistic gene targets that will potentiate PI3K agents.
- In collaboration with Dr. Candelaria Gomez-Manzano, we are investigating the role angiopoietin-2 (Ang-2) and Tie-2 plays in the angiogenesis process of malignant glioma. We have shown high Ang-2 expression can significantly inhibit the ability of endothelial cells to form vascular-like structures, thus destabilizing the angiogenesis process. The ultimate goal of this project is to combine an oncolytic viral delivery system with anti-angiogenesis molecules to produce a synergistic effect.