Stanford

Albert J. Wong, M.D.

Professor of Neurosurgery

Bio

ACADEMIC APPOINTMENTS

- Professor, Neurosurgery
- Member, Stanford Cancer Institute

PROFESSIONAL EDUCATION

- B.A., Johns Hopkins University , Bioengineering/Medicine
- M.D., Johns Hopkins School of Medicine

LINKS

- Lab website of Albert Wong: https://awonglab.web.app/#home

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The goal of this laboratory is to define targets for cancer therapeutics by identifying alterations in signal transduction proteins and then translate these findings into important clinical tools, including one of the first effective peptide vaccines against cancer. The major type of cancer that we study is glioblastoma multiforme, the most common and devastating of the human brain tumors, but this work has also had implications for lung, breast, ovarian and prostate cancers.

Our research direction originated when we first identified a spontaneously occurring mutant EGF receptor in glioblastoma. Known as EGFRvIII (pronounced “E-G-F-R-v-three”), this molecule represents a deletion of exons 2 through 7 in the extracellular domain of the EGF receptor. This removes 273 amino acids and creates a novel glycine at the fusion junction. We have engaged in both very basic studies on the signal transduction pathways initiated by EGFRvIII, as well as translational work to create diagnostic tools and therapies around EGFRvIII.

Our basic science studies on understanding EGFRvIII signaling have led us to discover the Gab1 docking protein. Orignially discovered as a substrate for the EGF receptor, we and others have found that Gab1 is a substrate for numerous tyrosine kinase receptors, and in turn Gab1 recruits several proteins with SH2 domains. It is now clear that it is a vital link for multiple growth factor and cytokine pathways and has a role in diverse phenotypes such as cell survival, the cellular response to stress, and the cellular entry of parasites.

As another result of our efforts on signaling pathways, we have discovered that glioblastoma tumors preferentially utilize the JNK pathway, unlike many other tumors that use the ERK pathway. More specifically, only one of the 12 known JNK isoforms is highly expressed, JNK2a2. Co-incidentally, we have uncovered

that this isoform is constitutively active and that it has a specific activation domain. JNK2a2 also upregulates TGF-a, a ligand for the EGF receptor that is frequently overexpressed in glioblastomas.

Our translational work has encompassed both diagnostics and therapeutics. We have developed antibodies that specifically recognize EGFRvIII and not EGF receptor and have also developed rapid RT-PCR based assays to detect EGFRvIII. Using these tools, we have discovered that expression of EGFRvIII is not limited just to glioblastoma tumors but it is also found in breast, lung, prostate and ovarian tumors.

We were the first to show that a peptide vaccine based on the cancer specific epitope found in EGFRvIII is an effective anti-tumor drug (originally called ALT-110). In animal models, this vaccine can both prevent tumors and induce the regression of existing tumors. We also played a major role in initiating the first clinical trial in humans using this peptide vaccine. Three trials have now been completed with highly interesting results. A Phase II clinical trial at Duke and MD Anderson for glioblastoma patients has shown median survival of 30 months vs. 14 months for conventional therapy in a matched cohort.

An expanded Phase II/III trial for brain tumors using the vaccine (now called CDX-110) is currently enrolling which is sponsored by Celldex Therapeutics. If you have questions about this trial, please visit the NCI trials website at http://clinicaltrials.gov/ct/show/NCT00458601 or www.avantimmune.com.

Disclosure: Dr. Wong is the inventor of EGFRvIII and CDX-110, holds other patents related to EGFRvIII, and owns equity in Celldex.

CLINICAL TRIALS

- Phase I Rindopepimut After Conventional Radiation in Children w/ Diffuse Intrinsic Pontine Gliomas, Not Recruiting

Teaching

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)

Publications

PUBLICATIONS

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- **Immunohistochemical discrimination of wild-type EGFR from EGFRvIII in fixed tumour specimens using anti-EGFR mAbs ICR9 and ICR10** *BRITISH JOURNAL OF CANCER*
  Modjtahedi, H., Khelwatty, S. A., Kirk, R. S., Seddon, A. M., Essapen, S., Del Vecchio, C. A., Wong, A. J., Eccles, S.
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- **Targeting EGF receptor variant III: tumor-specific peptide vaccination for malignant gliomas** *EXPERT REVIEW OF VACCINES*
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- **Hedgehog-responsive candidate cell of origin for diffuse intrinsic pontine glioma** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
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