BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Chu, Edward	Professor of Medicine and Pharmacology & Chemical Biology
eRA COMMONS USER NAME EDCHUED	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Brown University, Providence, RI	BS	06/80	Biology
Brown University, Providence, RI	MMS	06/83	Pharmacology
Brown University, Providence, RI	MD	06/83	Medicine
National Cancer Institute, Bethesda, MD	Fellow	06/89	Medical Oncology

A. Personal Statement

I have a broad background in cancer pharmacology, cancer drug development, and clinical investigations, with specific training and expertise in key research areas for this application. My main research efforts have focused on the design and development of novel agents and treatment approaches for the treatment of colorectal cancer and other GI cancers as well as in the early-phase I and II clinical development of novel small molecules for non-GI cancers as well as other solid tumors. As a result of my research experience, I presently serve as Co-Leader of the Cancer Therapeutics Program of the University of Pittsburgh Cancer Institute, Leader of the Phase I Drug Development Program, and PI of our NCI-UM1 Phase I grant. I am also the Co-PI of an NCI-P01 grant that is focused on the development of Chinese herbal medicine as a modulator of cancer chemotherapy in the treatment of colorectal cancer. I have a demonstrated track record of successful and productive research projects in the area of cancer drug development and clinical investigation. As such, I have the background, expertise, and commitment to serve as a member of the UPDDI internal advisory board.

The following list represents some of the recent manuscripts and/or reviews focused on cancer therapeutics and early-stage cancer drug development.

(1) Kummar S, et al. A phase I study of the Chinese herbal medicine PHY906 as a modulator of irinotecan-based chemotherapy in patients with advanced colorectal cancer. Clin Colorectal Cancer. 2011;10:85-96. PMID: 21859559.
(2) Kiesel BF, et al. LC-MS/MS assay for the quantitation of the HDAC inhibitor belinostat and five major metabolites in human plasma. J Pharm Biomed Anal. 2013;81:89-98. PMID: 23644904. PMCID: PMC3663884.
(3) Tawbi H et al. Calcium carbonate does not affect imatinib pharmacokinetics in healthy volunteers. Cancer Chemother Pharmacol 2014;73:207-11. PMID: 24170263. PMCID: PMC3880632.
(4) Parikh RA et al. The potential role of hepatocyte growth factor (HGF)-MET pathway inhibitors in cancer treatment. OncoTargets and Therapy 2014;7:969-983s. PMID: 24959084. PMCID: PMC4061161.
(5) Appleman LJ, et al. A phase I study of DMS612, a novel bifunctional alkylating agent. Clin Cancer Res. 2015;21:721-729. PMID: 25467180.

B. Positions and Honors

Positions and Employment

1990-1992 Senior Staff Fellow, Medicine Branch, National Cancer Institute, NIH, Bethesda, MD.
1992-1996 Senior Clinical Investigator, NCI-Navy Medical Oncology Branch, NCI, NIH, Bethesda, MD.
1996-2001 Assoc. Prof. of Medicine and Pharmacology, Yale Cancer Center, Yale School of Medicine, New Haven, CT.
1996-2005 Director, VACT Cancer Center, VACT Healthcare System, West Haven, CT.

1996-2010	Co-Director, Developmental Therapeutics Program, Yale Cancer Center, Yale School of Medicine, New Haven, CT.
2001-2010	Professor of Medicine and Pharmacology, Yale Cancer Center, Yale School of Medicine, New Haven, CT.
2004-2010	Chief, Section of Medical Oncology, Yale Cancer Center, Yale School of Medicine New Haven, CT.
2004-2010	Associate Director of Clinical Research, Yale Cancer Center, Yale School of Medicine, New Haven, CT.
2007-2010	Deputy Director, Yale Cancer Center, Yale School of Medicine, New Haven, CT.
2010-	Professor of Medicine, Chief, Division of Hematology-Oncology Deputy Director, University of Pittsburgh Cancer Institute, Pittsburgh, PA

Honors

2005	Fellow, American Association for the Advancement of Science (AAAS)
2005-2012	New York Magazine Top Doctor for Cancer (Medical Oncology)
2005-present	Castle Connolly American's Top Doctor for Cancer
2013	Chao Foundation Asian Leadership Award
2014	UPCI Merrill J. Egorin Excellence in Scientific Leadership Award
2014	Scott Wadler Memorial Lectureship, Visiting Professor, Weill Cornell Cancer Center
2014	Visiting Professor, Peking University Cancer Hospital
2014	Visiting Professor, Shanghai University Traditional Chinese Medicine Hospital

Committee Memberships

1998	Chairman: AACR Special Memberships Committee
2000-present	Editor-in-Chief, Clinical Colorectal Cancer
2000-present	Member, Scientific Advisory Board, Taiwan National Institute of Cancer Research
2004-2007	Member, ASCO Program Committee
2005-2007	Member, ASCO Grants Committee
2009-2014	Presidential Science Prize of Taiwan, Life Sciences Selection Committee
2011-present	AACR Scientific Program Committee
2012-2015	ASCO Scientific Program Committee
2012-present	AACR Exhibits Committee
2013-present	AACR Basic Cancer Research Fellowships Scientific Review Committee
2014-2015	ASCO Scientific Program Committee (Track Leader, Colorectal Cancer)
2014-2016	AACR Clinical Research and Experimental Therapeutics Awards Committee
2014-present	AACR Colon Cancer Research Fellowships Scientific Review Committee (Chair)

Federal Government Committees

1996-2000	Full Member: NIH Experimental Therapeutics I Study Section
1998-2001	Chairman: NIH Experimental Therapeutics I Study Section
1999-2001	Chairman, NIH/NCI Special Emphasis Panel Experimental Therapeutics I/II Study Section
2008-2013	Full Member: NIH/NCI IRG Subcommittee A Study Section
2011-2013	Chair: NIH/NCI IRG Subcommittee A Study Section
2011-present	Full Member: NCI Investigational Drug Steering Committee (IDSC)
2012-present	Full Member: NCI Experimental Therapeutics Committee (NeXT)

Member/Reviewer, International Grant Review Committees

2005-present	National Health Research Council of Italy
2005-present	University of Hong Kong, University Grants Committee
2008-present	Singapore National Medical Research Council Grants Committee
2013-present	Taiwan NHRI Cancer Center Review Committee

Member, NCI Cancer Centers Scientific Advisory Boards

2006-present Albert Einstein Cancer Center
2007-present Dartmouth-Hitchcock Norris-Cotton Cancer Center
2012-present Herbert Irving-Columbia Cancer Center
2012-present USC Norris Cancer Center
2012-present Univ. of Vermont Cancer Center (Chair)
2013-present Case Western Seidman Cancer Center
2013-present Medical University of South Carolina Hollings Cancer Center
2014-present Indiana University Simon Cancer Center
2014-present Univ of Wisconsin Cancer Center

C. Contributions to Science

(1) Translational Regulation of Gene Expression

My lab was the first to demonstrate that the expression of the folate-dependent enzyme thymidylate synthase was controlled by a translational autoregulatory mechanism whereby the thymidylate synthase protein binds to cis-acting regulatory elements on the cognate TS mRNA and regulates translation. This was a seminal finding as this was the first description of this type of translational autoregulatory mechanism in a eukaryotic organism. My lab then followed up on this observation to demonstrate that the expression of another folate-dependent enzyme dihydrofolate reductase is controlled in an identical translational autoregulatory manner. It has now been well-established that translation autoregulation is a common mechanism by which cellular gene expression can be controlled in a very efficient and rapid manner.

(1) Chu E, et al. Autoregulation of human thymidylate synthase messenger RNA translation by thymidylate synthase. Proc Natl Acad Sci USA. 1991;88:8977-81. PMID: 1924359. PMCID: PMC52634.
(2) Chu E, et al. Specific binding of human dihydrofolate reductase protein to dihydrofolate reductase messenger RNA in vitro. Biochemistry. 1993;32:4756-60. PMID: 8490020.
(3) Chu E, et al. Identification of an RNA-binding site for human thymidylate synthase. Proc Natl Acad Sci USA. 1993;90:517-21. PMID: 8421684. PMCID: PMC45694.
(4) Chu E, et al. Identification of a thymidylate synthase ribonucleoprotein complex in human colon cancer cells. Mol Cell Biol. 1994;14:207-13. PMID: 8264588. PMCID: PMC358371.

(2) Development of Antisense and siRNAs as Novel Therapeutic Molecules

The Chu lab has been investigating the potential role of antisense and siRNA's as novel therapeutic molecules for the treatment of colorectal cancer. The goal of these studies is to identify novel molecules to prevent and/or overcome the development of cellular drug resistance to inhibitor compounds that target thymidylate synthase, a well-established target for cancer chemotherapy. The Chu lab observed that siRNA's were significantly more potent and specific in their ability to repress TS mRNA translation, resulting in potent inhibition of TS synthesis. Moreover, they were able to completely restore chemosensitivity to anticancer agents that target TS, including the fluoropyrimidines and TS antifolate inhibitors.

(1) Schmitz JC, Agrawal S, Chu E. Effect of 2'-O-methyl antisense ORNs on expression of thymidylate synthase in human colon cancer RKO cells. Nucleic Acids Res. 2001;29:415-22. PMID: 11139611. PMCID: PMC29681.
(2) Mulkeen A et al. Short interfering RNA-mediated gene silencing of vascular endothelial growth factor: effects on cellular proliferation in colon cancer cells. Arch Surg. 2006;14:367-74. PMID: 16618894.
(3) Schmitz JC and Chu E. Effect of small interfering RNA 3'-end overhangs on chemosensitivity to thymidylate synthase inhibitors. Silence. 2011;2:1-6. PMID: 21247442. PMCID: PMC3035029.
(4) Wu SY, et al. Development of modified siRNA molecules incorporating 5-fluoro-2'-deoxyuridine residues to enhance cytotoxicity. Nucleic Acids Res. 2013;41:4650-4659. PMID: 23449220. PMCID: PMC363218.

(3) Investigate the Potential Role of Chinese Herbal Medicine as a Modulator for Cancer Chemotherapy

The Chu lab has been actively involved in studies to investigate the potential role of Chinese herbal medicine in cancer treatment either as monotherapy or to be used in combination with other anticancer agents. Significant efforts have focused on pre-clinical animal model studies to investigate the potential biological mechanisms of action. In addition, the Chu lab has been conducting early-phase clinical studies on a 4-herb Chinese herbal medicine PHY906, which has found to be an effective modulator of irinotecan-based chemotherapy. Based on pilot clinical trials, Dr. Chu and colleagues are now conducting a randomized placebo-controlled, double-blinded study looking at the effect of PHY906 on the toxicity and clinical efficacy or irinotecan chemotherapy in the treatment of metastatic colorectal cancer. This clinical study is the foundation of a P01 grant that is presently supported by the NCI.

(1) Yen Y et al. Phase I/II study of PHY906 /capecitabine in advanced hepatocellular carcinoma. Anticancer Res. 2009;29:4083-4092. PMID: 19846955.
(2) Zhang W et al. Identification of chemicals and their metabolites from PHY906, a Chinese medicine formulation, in the plasma of a patient treated with irinotecan and PHY906 using liquid chromatography/tandem mass spectrometry (LO/MS/MS). J Chromatogr A 2010;1217:5785-5793. PMID: 20696432. PMCID: PMC3668335.
(3) Kummar S et al. A phase I study of the Chinese herbal medicine PHY906 as a modulator of irinotecan-based chemotherapy in patients with advanced colorectal cancer. Clin Colorectal Cancer 2011. 10:85-96. PMID: 21859559.
(4) Liu H et al. Clove extract inhibits tumor growth and promotes cell cycle arrest and apoptosis. Oncology Res 2014;21:247-259. PMID: 24854101 [PubMed - indexed for MEDLINE] PMCID: PMC4132639.

(4) Role of Palliative/Supportive Care in the Treatment of Human Cancers

Over the past 3 years, I have been actively involved in developing and integrating pallative care services within the context of a medical oncology outpatient clinic as well as conducting clinical research in the area of palllative and supportive care of cancer patients.

(1) Schenker Y et al. Oncologist factors that influence referrals to subspecialty palliative care clinics. J Oncol Pract. 2014;10:e37-44. PMID: 24301842. PMCID: PMC3948709.
(2) Maciasz R et al. Does it matter what you call it? A randomized trial of language used to describe palliative care services. Supportive Care in Cancer 2013;21:3411-3419. PMID: 23942596. PMCID: PMC3823760.
(3) Schenker Y et al. Care management by oncology nurses to address palliative care needs: a pilot trial to assess feasibility, acceptability, and perceived effectiveness of the CONNECT intervention. J Palliative Medicine 2015;18:232-240. PMID: 25517219. PMCID: PMC4347888.

Complete List of Published Work:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1XYt9nJKAb2Ql/bibliography/47241962/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIH/NCI: UM1 CA186690 (P.I.) 3/1/14 – 2/28/19 2.25 calendar months
Title: NCI ET-CTN with Phase I Emphasis at UPCI.
The major goal of this project is to be part of the new NCI ET-CTN as a lead academic organization and to develop early-phase clinical trials at the University of Pittsburgh Cancer Institute.
Role: P.I.

NIH/NCI: UM1 CA099168-03S1 (Chu) 03/01/16 - 02/28/19 0.24 calendar months *
** concurrent with parent UM1CA186690-03*

Title: Early clinical trials of new anticancer agents with phase 2 emphasis.
The major goal of this project is to design and develop phase 2 clinical trials of novel anticancer agents and/or combination regimens with incorporation of translational correlative science.
Role: PI

NIH/NCI: P01 CA154295 (Chu, Co-P.I.) 9/1/11 – 8/15/17 3.3 calendar months
Title: Chinese Herbal Medicine as a Novel Paradigm for Cancer Chemotherapy.
The goal of this interdisciplinary, clinical- and translational-based program project grant is to investigate the role of a novel Chinese herbal medicine PHY-906 as a modulator of cancer chemotherapy in the treatment of metastatic colorectal cancer.
Role: Co-P.I.

NIH/NCI: P30 CA147904 (Davidson, P.I.) 8/1/010 – 7/30/20 0.9 calendar months
Title: Comprehensive Cancer Center Core Support Grant.
The major goal of this project is to provide support and oversight over the research efforts of the Molecular Therapeutics Drug Discovery Research Program of the University of Pittsburgh Cancer Institute.
Role: Co-Director, Molecular Therapeutics Drug Discovery Research Program.

NIH/NCI: P30 CA147904 (Davidson, P.I.) 8/1/010 – 7/30/20 1.2 calendar months
Title: Comprehensive Cancer Center Core Support Grant.
The major goal of this project is to provide administrative support and oversight over the clinical and translational research efforts of the University of Pittsburgh Cancer Institute.
Role: Deputy Director.

NIH/NCI: T32 CA193205 (P.I.) 7/1/15 – 6/30/20 (no support requested)
Title: Training in Cancer Therapeutics Research
The main goal of this Training Program is to train the next generation of physician-scientists in the area of cancer therapeutics and provide them with a strong scientific foundation to discover, design, and develop novel anticancer agent and/or therapeutic regimens for the treatment of human cancers. The strategy for successfully carrying out this mission requires a training faculty and research environment that encompasses the entire continuum of basic, preclinical, and clinical/translational cancer therapeutics research at UPCI.
Role: P.I.

PENDING FUNDING:

NIH/NCI: R01 CA203347-01A1 (Chu) 12/01/16 - 11/30/21 0.90 calendar months
NIH/NCI
Title: The Chinese Herbal Medicine Huang Qin (HQ) as a Novel Modulator of Fluoropyrimidine Chemotherapy.
The goal of this grant is to investigate the biological mechanisms of the Chinese herbal medicine HQ using both in vitro and in vivo model systems and to determine the in vitro cytotoxicity and in vivo antitumor activity of HQ in CRC models.
Role: PI

OVERLAP:

NONE