

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

| | | | |
|---|----------------------------------|---------------------------------------|-------------------|
| NAME Phuoc T. Tran | | POSITION TITLE Assistant Professor | |
| eRA COMMONS USER NAME TRAN.PHUOC | | | |
| EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i> | | | |
| INSTITUTION AND LOCATION | DEGREE <i>(if applicable)</i> | YEAR(s) | FIELD OF STUDY |
| UC, San Diego (UCSD) | BS | 1993-1996 | Molecular Biology |
| Oregon Health & Science University | MD | 1996-2003 | Medicine |
| Oregon Health & Science University (OHSU) | PhD | 1996-2003 | Genetics |

A. Personal Statement

The goal of the proposed developmental project is to characterize a novel pre-clinical inducible lung specific Twist1 transgenic mouse model of metastasis. I have the expertise and motivation necessary to successfully direct the proposed work. I have a broad background in molecular biology and medicine, with specific training and expertise in key research areas for this application. As an M.D./Ph.D. student at OHSU, I carried out basic research on the mechanisms of DNA repair, a pathway critical for genome stability. As a resident and instructor of radiation oncology at Stanford, I treated cancer patients many of whom had lung metastases with therapeutic radiation often times in combination with systemic therapies. My research interests in the basic biology of metastasis and the clinical implications of tumor progression originated from this clinical experience and provided the impetus to seek out my post-doctoral mentor and develop the novel inducible mouse model that is detailed in my proposal. It was during my postdoctoral research fellowship at Stanford, where I expanded my research expertise by using small animal imaging and small animal therapeutic radiation to study the biology of oncogenes with inducible and conditional lung specific mouse models. As a new PI at Johns Hopkins I have developed a research group interested in the mechanistic role of epithelial-mesenchymal transitions (EMTs) in metastatic progression and have the expertise in utilizing and developing small animal imaging platforms, to conduct the studies relevant to this proposal. In summary, I have a demonstrated record of successful and productive research projects germane to the proposal and these experiences have prepared me well to conduct the proposed project.

B. Positions and Honors.**Positions and Employment**

1998-2001 Graduate Student, Molecular & Medical Genetics, OHSU, R. Michael Liskay (Advisor).
 2002-2003 Postdoctoral Research Fellow, OHSU, R. Michael Liskay (Advisor).
 2003-2004 Preliminary Internal Medicine Intern, St. Mary's Medical Center, San Francisco, CA.
 2004-2008 Radiation Oncology Resident, Stanford University Medical Center.
 2007-2008 Chief Resident, Radiation Oncology, Stanford University Medical Center.
 2005-2009 Postdoctoral Research Fellow, Stanford University Medical Center, Dean Felsher (Advisor).
 2008-2009 Instructor, Radiation Oncology, Stanford University Medical Center.
 2008-2009 Member, Stanford Cancer Center.
 2009- Assistant Professor, Radiation Oncology, The Johns Hopkins University School of Medicine.
 2010- Assistant Professor, Oncology (secondary appt), JHU SOM.
 2010- Member, Sidney Kimmel Comprehensive Cancer Center.

Honors

1995 John Muir College Caledonian Honor Society, UCSD.
 1995-1996 UC Regents Scholar; the most prestigious UC scholarship.
 1996 Graduated *magna cum laude* from UCSD.
 1996-2003 OHSU Laurel Merit MD/PhD Scholar.

Principal Investigator/Program Director (Last, First, Middle): PI Name Tran, Phuoc T.

1998-2001 OHSU Molecular Hematology Research Training Fellow (NIH grant 5-T32-HL07781).
2003 OHSU Dean's Medical Student Research Award recipient.
2006 Radiological Society of North America (RSNA) Roentgen Resident Research Award.
2006 RSNA Research Resident (RR0601).
2007 ASCO/AACR Methods in Clinical Cancer Research Workshop Scholarship.
2007 Malcolm A. Bagshaw Award.
2007 Henry S. Kaplan Research Fellow (SUMC grant 1046297-100-KAVWO).
2007 ASTRO Resident Poster Recognition Award (Top 3 posters of the national meeting).
2008 RSNA Research Fellow (RF0801).
2008-2011 Parker B. Francis Fellow.
2009 RSNA Research Scholar (RSCH0915): Declined.
2009-2011 ASTRO Junior Faculty Career Research Training Award.
2011 The Epithelial-Mesenchymal Transition (EMT) International Association Best Poster Award.
2011-2013 The Phyllis & Brian L. Harvey Scholar-Patrick C. Walsh Prostate Cancer Research Fund Award.
2011-2016 DoD Prostate Cancer Physician Research Training Award (PC101555).
2012-2014 Uniting Against Lung Cancer Junior Investigator Award.
2012-2016 American Cancer Society Research Scholar.

C. Selected peer-reviewed publications (selected from 33).

Most relevant to the current application

1. **Phuoc T. Tran***, Alice C. Fan*, Pavan K. Bendapudi*, Shan Koh, Kim Komatsubara, Joy Chen, George Horng, David I. Bellovin, Sylvie Giuriato, Criag S. Wang, Jeffrey A. Whitsett and Dean W. Felsher. Combined Inactivation of MYC and K-ras Oncogenes Reverses Tumorigenesis in Lung Adenocarcinomas and Lymphomas. *PLoS ONE* 3 (2008) e2125. PMID: 18461184. * - these authors contributed equally.
2. Hu Zhou, Manuel Rodriguez, Fred van den Haak, Geoffrey Nelson, Rahil Jogani, Jiali Xu, Xinzhi Zhu, Yongjiang Xian, **Phuoc T. Tran**, Dean W. Felsher, Paul J. Keall, Edward E. Graves. Development of a MicroCT-Based Image-Guided Conformal Radiotherapy System for Small Animals. *Int J Radiat Oncol Biol* 78 (2010) 297-305. PMID: 20395069; PMCID: PMC2906632.
3. Edward E. Graves, Marta Vilalta, Ivana K. Cecic, Janine T. Erler, **Phuoc T. Tran**, Dean Felsher, Leanne Sayles, Alejandro Sweet-Cordero Quynh-Thu Le and Amato J. Giaccia. Hypoxia in models of lung cancer: implications for targeted therapeutics. *Clin Cancer Res* 16 (2010) 4843-52. PMID: 20858837; PMCID: PMC2948600.
4. Carsten H. Nielsen, Richard H Kimura, Nadia Withofs, **Phuoc T. Tran**, Zheng Miao, Jennifer Cochran, Zhen Cheng, Dean Felsher, Andreas Kjær, Juergen K. Willmann, Sanjiv S. Gambhir. PET Imaging of Tumor Neovascularization in a Transgenic Mouse Model with a Novel ⁶⁴Cu-DOTA-Knottin Peptide. *Cancer Res* 70 (2010) 9022-30. PMID: 21062977.
5. Jing Zeng, Alfred P. See, Khaled Aziz, Saravanan Thiyagarajan, Tarek Salih, Rajendra P. Gujula, Michael Armour, Jillian Phallen, Stephanie Terezakis, Lawrence Kleinberg, Kristen Redmond, Russell K. Hales, Roberto Salvatori, Alfredo Quinones-Hinojosa, **Phuoc T. Tran+**, Michael Lim+. Nelfinavir induces radiation sensitization in pituitary adenoma cells. *Cancer Biol Ther* 12 (2011) 657-63. PMID: 21811091. + - corresponding authors.
6. **Phuoc T. Tran***, Pavan K. Bendapudi*, H. Jill Lin*, Peter Choi, Shan Koh, Joy Chen, George Horng, Nicholas P. Hughes, Lawrence H. Schwartz, Vincent A. Miller, Toshiyuki Kawashima, Toshio Kitamura, David Paik+ and Dean W. Felsher+. Survival and Death Signals Can Predict Tumor Response to Therapy After Oncogene Inactivation. *Sci Transl Med* 3 (2011) 103ra99**. PMID: 21974937. * - these authors contributed equally; + - corresponding authors; and ** - Highlighted by Comments in *Sci Transl Med*, *Cancer Res*, *Nat Rev Clin Oncol* and *Cancer Discovery*.
7. **Phuoc T. Tran*+**, Emelyn H. Shroff*, Timothy F. Burns*, Saravanan Thiyagarajan, Sandhya T. Das, Tahera Zabuawala, Joy Chen, Yoon-Jae Cho, Richard Luong, Pablo Tamayo, Tarek Salih, Khaled Aziz, Stacey J. Adam, Silvestre Vicent, Carsten H. Nielsen, Nadia Withofs, Alejandro Sweet-Cordero, Sanjiv S. Gambhir, Charles M. Rudin and Dean W. Felsher+. *Twist1* suppresses senescence programs and thereby accelerates and maintains mutant *Kras*-induced lung tumorigenesis. *PLoS Genet* 8 (2012) e1002650. PMID: 22654667. * - these authors contributed equally; and + - corresponding authors.

Other publications relevant to application

1. Tsutomu Nobori, Kenji Takabayashi, **Phuoc Tran**, Lisa Orvis, Ayse Batova, Alice L. Yu, and Dennis A. Carson. Genomic cloning of methylthioadenosine phosphorylase: A purine metabolic-enzyme deficient in multiple different cancers. *Proc Natl Acad Sci USA* 93 (1996) 6203-6208. PMID: 8650244; PMCID: PMC39214.
2. Hiroki Hori, **Phuoc Tran**, Carlos J. Carrera, Yasuko Hori, Michael D. Rosenbach, Dennis A. Carson and Tsutomu Nobori. Methylthioadenosine Phosphorylase cDNA Transfection Alters Sensitivity to Depletion of Purine in A549 Lung Cancer Cells. *Cancer Research* 56 (1996) 5653-5658. PMID: 8971171.
3. **Phuoc T. Tran** and R. Michael Liskay. Functional Studies on the Candidate ATPase Domains of *Saccharomyces cerevisiae* MutL-alpha. *Mol Cell Biol* 20 (2000) 6390-6398. PMID: 10938116; PMCID: PMC86114.
4. **Phuoc T. Tran**, Jeffery A. Simon and R. Michael Liskay. Interactions of Exo1p with components of MutL-alpha in *Saccharomyces cerevisiae*. *Proc Natl Acad Sci USA* 98 (2001) 9760-9765. PMID: 11481425; PMCID: PMC55526.
5. **Phuoc T. Tran**, Naz Erdeniz, Sandra Dudley and R. Michael Liskay. Characterization of nuclease-dependent functions of Exo1p in *Saccharomyces cerevisiae*. *DNA Repair* 1 (2002) 895-912. PMID: 12531018.
6. **Phuoc T. Tran**, Naz Erdeniz, Lorraine S. Symington and R. Michael Liskay. EXO1 – a multi-tasking eukaryotic nuclease. *DNA Repair* 3 (2004) 1549-1559. PMID: 15474417.
7. Diane Tseng*, Leeland P. Rachakonda*, Zheng Su, Ranjana Advani, Sandra Horning, Richard T. Hoppe, Andrew Quon, Edward E. Graves, Billy W. Loo, Jr, **Phuoc T. Tran**. Interim-treatment quantitative PET parameters predict progression and death among patients with Hodgkin's Disease. *Radiat Oncol* 7 (2012) 5. PMID: 22260710. * - these authors contributed equally.
8. **Phuoc T. Tran**+, Russell K. Hales, Jing Zeng, Khaled Aziz, Tarek Salih, Rajendra P. Gajula, Sivarajan Chettiar, Nishant Gandhi, Aaron T. Wild, Rachit Kumar, Joseph M. Herman, Danny Song and Theodore L. DeWeese. Tissue Biomarkers for Prostate Cancer Radiation Therapy. *Curr Mol Med* 12 (2012) 772-787. PMID: 22292443. + - corresponding author.

C. Research Support

Ongoing Research Support

O'Brien Center Pilot Tran (PI) 11/1/10-10/31/12

George M. O'Brien Center for Benign Prostate Hyperplasia/LUTS Research

“TWIST1 and Embryonic Reawakening in benign prostatic hyperplasia revisited”

The goal of this proposal is to establish a link between prostate luminal cell specific *Twist1* overexpression and increased prostate stem cells.

Role: PI

W81XWH-11-1-0272 Tran (PI) 3/21/11-3/20/16

Dept of Defense CDMRP Prostate Cancer Research Program

“Evaluating the Efficacy of ERG-Targeted Therapy in Vivo for Prostate Tumors”

The goal of this proposal is to validate an inducible *ERG* prostate specific mouse model and examine for cooperation with *AKT* for prostate tumorigenesis.

Role: PI

PCW Award Tran (PI) 4/1/11-3/31/13

Patrick C. Walsh Prostate Cancer Research Fund

“MYC as a biomarker to direct statin targeted therapy for definitive treatment of prostate cancer”

This is a phase 0 trial of pre-prostatectomy lovastatin to downregulate MYC in localized prostate cancer.

Role: PI

W81XWH-11-1-0336 Schaeffer (PI) 11/1/11-10/31/14

Dept of Defense CDMRP Prostate Cancer Research Program

“*RNASEH2A* - a Putative “Non-Oncogene Addiction” Gene Target and Marker for Radio-sensitivity in High Risk Prostate Cancer”

Principal Investigator/Program Director (Last, First, Middle): PI Name Tran, Phuoc T.

This proposal aims to demonstrate the association of *RNASEH2A* with lethal prostate cancer and determine if *RNASEH2A* modulates radio-sensitivity in prostate cancer cell lines and xenograft models.

Role: Co-I

1R01CA158100 Wong (PI) 7/1/11-6/30/14

NIH/NCI

“An integrated x-ray/optical tomography system for preclinical radiation research”

The goal of this proposal is to construct an integrated x-ray/bioluminescent tomography (BLT) system that can function as a standalone research apparatus and also on-board the SARRP to guide focal irradiation.

Role: Co-I

2P50CA103175-06A2 Bhujwalla (PI) 10/1/2011-9/30/2016

NIH

“Lung specific Twist-mediated EMT in lung premetastatic niche”

The goal of this pilot project is determine whether *Twist1* expression in the normal lung can increase colonization of fluorescently-tagged breast cancer cell line, NT2.5.

Role: Pilot project investigator for year one

Personalized Med Pilot Award Rudin (PI) 1/1/2012-12/31/2013

Commonwealth Foundation

“Individualized therapy for KRAS mutant lung cancer through triggering oncogene-induced senescence”

The goal of this proposal is to determine KRAS dependency in KRAS mutant NSCLCs and whether oncogene-induced senescence by TWIST1 inhibition is a therapeutic strategy in KRAS mutant NSCLC.

Role: Collaborator

Junior Investigator Award Tran (PI) 3/1/2012-2/28/2014

Uniting Against Lung Cancer

“Screening for TWIST1 inhibitors as treatment for lung cancer”

The goal of this proposal to identify compounds that inhibit Twist.

Role: PI

Research Scholar Tran (PI) 7/1/2012-6/30/2016

American Cancer Society

“Twist1 structure-function studies of Kras-induced senescence inhibition”

The goal of this proposal to characterize the domains of Twist1 required for suppression of *Kras* oncogene-induced senescence (OIS) and activation of OIS *in vitro* and *in vivo* using inducible *Twist1* transgenic lung tumor mice.

Role: PI

Research Scholar Ewald (PI) 7/1/2012-6/30/2016

American Cancer Society

“Regulation of mammary dissemination by cell adhesion and the myoepithelium”

The primary goal of this proposal is to dissect the molecular requirements for the barrier function of myoepithelial cells for breast epithelial dissemination using an inducible *Twist1* and conditional E-cadherin deletion mouse models.

Role: Co-I

PrTK03 DeWeese (PI) 7/01/2011-6/30/2016

Advantagene, Inc

A Randomized Controlled Trial of Prostatok as Adjuvant to up-front Radiation Therapy for Localized Prostate Cancer

Major Goal: A Randomized Controlled Trial of Prostatok as Adjuvant to up-front Radiation Therapy for Localized Prostate Cancer

Role: Co-I