Beth Israel Deaconess Medical Center
Center for Life Sciences
3 Blackfan Circle
Boston, MA. 02215

Harvard Medical School
Department of Medicine
Tel: 281-804-2378
E-mail: btrinh@bidmc.harvard.edu

October 31th, 2021

The RNA Society
7918 Jones Branch Drive, Suite 300
McLean, VA 22102, USA

Letter of Application for the RNA Society Outstanding Career Researcher Award

Dear Awards Committee:
My name is Bon Trinh (RNA Society member # 6027). I am writing to apply for the RNA Society Outstanding Career Researcher Award. Currently, I am an instructor at Harvard Medical School and a staff scientist at Beth Israel Deaconess Medical Center. In these roles, I have been conducting mentored research, applying for funding from government and non-government organizations to support my research, and participate in training the next-generation of life science researchers. With regard to research, I have been investigating the molecular mechanism underlying RNA regulation of gene expression via chromatin remodeling and determine the role chromatin-structure-regulated RNAs in normal and malignant hematopoiesis and as biomarkers and drivers of cancer drug sensitivity. This resulted in a first-author and co-corresponding paper, and a co-author paper that were published recently (Trinh et al, *Blood J*, 2021; van der Kouwe et al, *Blood J*, 2021) and a patent application (Trinh and Tenen, US/63/054,531, 2020). I have been a principal investigator of a Mentored Research Scientist Career Development Award (K01) from the National Cancer Institute. I participate in mentoring and training junior graduate students with experimental methodology and research design. I mentor intern students for the Undergraduate Internship Program of Harvard Stem Cell Institute (HIP) and Harvard Undergraduate Research Opportunities in Science (HUROS).

At Harvard Medical School Initiative for RNA medicine, I have been building my long-term research direction that focus noncoding RNA regulation of chromatin structure in myeloid development and AML. In my first- author and co-corresponding author paper published recently, I discovered a novel long noncoding RNA originating from the myeloid master gene *PU.1* locus. I demonstrated that this polyadenylated and enhancer-derived long noncoding RNA (eRNA) interacts with the broadly-expressed transcription factor RUNX1 and promotes docking of a RUNX1-bound enhancer to the *PU.1* promoter resulting in induction of *PU.1* long-range transcription and myeloid cell differentiation. In core binding factor acute myeloid leukemia (CBF-AML), I found that the oncogenic transcription factor fusion RUNX1-ETO reduces chromatin accessibly at the enhancer causing inhibition of the *PU.1* eRNA (Trinh et al, *Blood J*, 2021). In a collaborative study, we found that RUNX1-ETO induces expression of a *PU.1* antisense noncoding RNA that functions as an RNA inhibitor of *PU.1* mRNA translation (van der Kouwe et al., *Blood J*, 2021). Thus, noncoding RNAs play critical roles in RUNX1-ETO-mediated chromatin remodeling that inhibits *PU.1* transcription and translation in CBF-AML. Because targeting transcription factors and their oncogenic transcription factor derivatives remains a technical challenge, my finding of RNA-modulators of these molecular player reveals potential intervention points for chromatin-structure based therapeutic development. In recognition of my scientific findings, I was awarded an Abstract Achievement Award from the American Society of Hematology. My work was also selected for featuring at an early career highlight seminar for instructors and assistant professors of Beth Israel Medical Center.

My goal is to become an independent expert in RNA regulation of gene expression in normal development and cancer and a successful science teacher/mentor. Receiving an RNA Society Outstanding Career Researcher Award is a great honor that recognizes my RNA research contribution at international level. I appreciate your time and consideration.

Yours sincerely,

Bon Quy Trinh, Ph.D.

BON Q. TRINH, Ph.D.

Department of Medicine, Center for Life Sciences, Harvard Medical School, Beth Israel Deaconess Medical Center, 3 Blackfan Cir, Boston MA 02215, Phone: (281)-804-2378, Email: btrinh@bidmc.harvard.edu, Website: https://tinyurl.com/bontrinh

EDUCATION

Degree-Granting Education

University of Texas Graduate School of Biomedical Sciences, Houston, TX, USA
Doctor of Philosophy in Biomedical Sciences 05/2011

Vietnam National University, Hanoi, Vietnam
Bachelor of Science in Biotechnology 06/2002

Continuing Education and Certifications

Society for Hematopathology/European Association for Hematopathology, Houston, TX
Workshop on Progress in Acute Myeloid Leukemia, Myelodysplastic Syndromes and Acute Lymphoblastic Leukemia: Classification and Molecular Pathogenesis, 18.50 AMA PRA Category 1 Credits 10/2013

The Texas Advanced Computing Center, Houston, TX
Bring Your Own Code & Data Workshop 03/2013

Epigenome center, Baylor College of Medicine, Houston, TX
The 5th Epigenome Informatics Workshop 10/2012

RESEARCH EXPERIENCES

Harvard Medical School, Boston, MA

- **Instructor** in Medicine 03/2020 - present
- **Research Fellow** in Medicine 03/2016 - 02/2020

Projects: 1) RNA-mediated regulatory mechanisms underlying cancer-associated gene expression in blood development and leukemia, 2) Identifying molecular markers and drivers of cancer drug sensitivity (ASH Abstract Achievement Award, NCI K01 Career Development Award (2017-2022), co-corresponding and first-author paper (Trinh et al. 2021 ***Blood J***), **US Patent Application** (63/054,531).

UT MD Anderson Cancer Center, Houston, TX

- **Postdoctoral Fellow** 06/2011 - 02/2016

Projects: 1) Molecular control of signaling pathways in development of blood cells (Trinh et al. J Cell Sci. 2015), 2) Molecular abnormalities that disturb normal growth and differentiation of blood cells in leukemia (resulted in 2 R21 grants), 3) Molecular regulations of intracellular signaling and environmental cues such as nitric oxide in ovarian tumor angiogenesis (Trinh et al. 2015. Mol Cancer) and inflammatory signaling in peritoneal spread of ovarian tumor cells (Haria, Trinh et al. 2015. Am J Pathol. co-first author), and 4) Erroneous DNA repair pathway in drug resistance of breast and ovarian cancer (Trinh et al. 2013. Cancer Res).

University of Texas Graduate School of Biomedical Science, Houston, TX

- **Graduate Research Assistant** 08/2004 - 05/2011

Ph.D dissertation: Defining the role and mechanisms of homeobox gene *DLX4* in TGF-β resistance in cancer (Trinh et al. 2009. Oncogene; Schissler Foundation Fellowship in the Genetics of Human Disease; Vietnam Education Foundation Fellowship)

Institute of Biotechnology, Vietnam Academy of Science and Technology, Hanoi, Vietnam

- Research staff 06/2002 - 07/2004
- Undergraduate research assistant 01/2002 - 05/2002

Projects: 1) Generated recombinant proteins and developed diagnostic kits for infectious diseases, 2) Typing and diagnosis of disease causative agents (Yellow head, Dengue and, Bursal disease viruses), and 3) Detected

gene mutations (BRCA1 and BRCA2) in cancer samples by Real-Time PCR (3 papers, Vietnam Ministry of Education & Training Scholarship).

AWARDS AND HONORS

- **Abstract winner,** Research from Early Career Highlights (REACH) featuring studies of instructors and assistant professors, Beth Israel Deaconess Medical Center 2020
- **Team Award** of pitch competition, Harvard Healthcare Innovation and Commercialization (HIC) 2019
- Annual Meeting **Abstract Achievement Award**, American Society of Hematology 2018
- **NCI Mentored Research Scientist Development Award** (K01), National Cancer Institute (NCI) 2017
- Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship (F32), National Heart, Lung, and Blood Institute (NHLBI) (declined in order to accept another funding opportunity) 2017
- Scholar Award Finalist, American Society of Hematology 2014
- AMGEN Award in Basic Science Research Finalist, Trainee Research Day, UT MD Anderson Cancer Center 2014
- Scientific Award Nominee, Annual Conference, Vietnam Education Foundation 2012
- Best Poster Award, Annual Conference, Vietnam Education Foundation 2011
- Research Fellowship in the Genetics of Human Disease, Schissler Foundation 2010
- Best Poster Award, Annual Conference, Vietnam Education Foundation 2009
- Trainee Excellence Award, UT MD Anderson Cancer Center 2009
- Trainee Research Day Poster Finalist Award, UT MD Anderson Cancer Center 2009
- International Meeting Travel Award, UT Graduate School of Biomedical Sciences 2009
- International Meeting Travel Award, Vietnam Education Foundation 2009
- Chairman honor roll for Excellent Academic Performance, Vietnam Education Foundation 2008
- Professional Development Grant, Vietnam Education Foundation 2006-2008
- Research Day-Student Presentation Award, UT Health Sciences Center 2008
- Graduate Teaching Assistant Award, Graduate school of Biomedical Sciences 2007
- Best Research Presentation Award, Annual Conference, Vietnam Education Foundation 2005
- Fellowship for Graduate Studies in U.S Universities, Vietnam Education Foundation 2004
- Fellowship for Graduate Studies in Greifswald University, Joint Education and Training Centre (JETC) (declined in order to accept another opportunity) 2004
- B.S. in Biotechnology first-class honour, Vietnam National University 2002
- Tokyo-Mitsubishi Bank Scholarship, Bank of Tokyo-Mitsubishi 2001
- Undergraduate Scholarship, Vietnam Ministry of Education & Training Scholarship 1998-2002

FUNDED AND PENDING PROJECTS

- **K01 Mentored Research Scientist Development Award**, K01CA222707, NCI 2017 - 2022
  Title: Enhancer RNA-mediated Tumor Suppressor Gene Expression in Normal and Malignant Hematopoiesis
  Role: PI
  Direct cost: $527,935
  Major goals: To investigate the mechanism by which enhancer RNAs regulate tumor suppressor gene expression, and the significance of this regulation in normal hematopoiesis and Acute Myeloid Leukemia.

- ***R21 Exploratory/Developmental Research Grant****,* PAR-21-061, NCI under review
  Title: The role of long noncoding RNAs in t(8;21) Leukemia
  Role: PI
  Major goals: To investigate molecular mechanisms and therapeutics potential of long noncoding RNAs in t(8;21) Leukemia.

- ***R21 Small Grant****,* PAR-19-222, NIDDK under review
  Title: lncRNA-mediated chromatin architecture in hematopoietic lineage specification
  Role: PI

Major goals: To investigate how lncRNA-mediated chromatin architecture affect productions of blood cell lineages.

- **F32 Kirschstein-NRSA postdoctoral fellowship**, 32HL139088, NHLBI 2018 - 2021
  Title: Long noncoding RNA-mediated long-range gene regulation in hematopoiesis
  Role: PI
  Direct cost: $197,070
  Major goals: To determine the role of long-range gene regulation mediated by long noncoding RNA in blood development (declined the offer to accept K01 award)

- **Research Fellowship** in the Genetics of Human Disease, Schissler Foundation 2009 - 2010
  Title: Novel function of homeobox gene DLX4 in regulating tumor angiogenesis
  Role: PI
  Direct cost: $33,800
  Major goals: To determine the mechanism underlying DLX4-mediated tumor angiogenesis.

PUBLICATIONS

Journal articles (published)

- Umarino S, Bassal M, Zhang Y, Joe A, Kobayashi IS, Borchiellini M, **Trinh BQ**, Ebralidze AK, Kobayashi SS, Di Ruscio A. NAD modulates DNA methylation and cell differentiation. *Cells*. Accepted.
- **Trinh BQ***, Ummarino S, Zhang Y, Ebralidze AK, Bassal MA, Nguyen TM, Heller G, Coffey R, Tenen DE, van der Kouwe E, Fabiani E, Gurnari C, Wu CS, Angarica VE, Yang H, Chen S, Zhang H, Thurm AR, Marchi F, Levantini E, Staber PB, Zhang P, Voso TM, Pandolfi PP, Kobayashi SS, Chai L, Di Ruscio A & Tenen DG*. Myeloid lncRNA *LOUP* Mediates Opposing Regulatory Effects of RUNX1 and RUNX1-ETO in t(8;21) AML. ***Blood journal***. 2021. PMID: 33971010 (*corresponding authors)
- van der Kouwe E, Heller G, Czibere A, Agreiter C, Castilla LH, Delwel R, Di Ruscio A, Ebralidze AK, Forte M, Grebien F, Heyes E, Kazianka L, Klinger J, Kornauth C, Le T, Lind K, Barbosa MA, Pemovska T, Pichler A, Pulikkan JA, Schmolke AS, Schweicker C, Sill H, Sperr W, Spittler A, Surapally S, **Trinh BQ**, Valent P, Vanura K, Welner RS, Zuber J, Tenen DG, Staber BP. Core binding factor leukemias hijack T-cell prone PU.1 antisense promoter. ***Blood journal***. 2021. PMID: 34010414
- **Trinh BQ**, Barengo N, Kim SB, Lee JS, Naora H. The homeobox gene DLX4 regulates erythro-megakaryocytic differentiation by stimulating IL-1β and NF-κB signaling. ***Journal of Cell Science*** 128(16):3055-67. 2015. PMID: 26208636
- Haria D*, **Trinh BQ***, Ko SY, Barengo N, Liu JS & Naora H. The homeoprotein DLX4 stimulates NF-κB activation and CD44-mediated tumor-mesothelial cell interactions in ovarian cancer. *American Journal of Pathology* 185(8):2298-308. 2015. PMID: 26067154 (*equal contribution)
- **Trinh BQ**, Ko SY, Haria D, Barengo N, & Naora H. The homeoprotein DLX4 controls ovarian tumor angiogenesis by regulating expression of inducible nitric oxide synthase. *Molecular* Cancer Apr 30;14(1):97. 2015. PMID: 25924901
- **Trinh BQ**, Ko SY, Barengo N, Lin SY, Naora H. Dual functions of the homeoprotein DLX4 in modulating responsiveness of tumor cells to topoisomerase II-targeting drugs. *Cancer Research* 73:1000-10. 2013. PMID: 23222298
- **Trinh BQ**, Barengo N, Naora H. Homeodomain protein DLX4 counteracts key transcriptional control mechanisms of the TGF-β cytostatic program and blocks the anti-proliferative effect of TGF-β. *Oncogene* 30: 2718-2729. 2011. PMID: 21297662
- Xie X, Hsu JL, Choi MG, Xia W, Yamaguchi H, Chen CT, **Trinh BQ**, Lu Z, Ueno NT, Wolf JK, Bast RC Jr, Hung MC. A novel hTERT promoter-driven E1A therapeutic for ovarian cancer. *Molecular Cancer Therapeutics* Aug;8(8):2375-82. 2009. PMID: 19671744
- Vu B, Nguyen DK, **Trinh BQ**, Bach Q, Dinh KD, Dinh VT. Detection and quantification of yellow head virus load in shrimp using Real-Time PCR with SYBR Green. *Journal of Science* (Hanoi National University). 21(2): 59-65. 2005
- Le C, Dai BD, Hoang CM, Nguyen VV, Le DT, Dinh KD, Bach Q, **Trinh BQ**, Duong QH, Nguyen HH, Nguyen DT, Nguyen DB. Detection of BRCA1 and BRCA2 mutations in breast cancer patients by Real-Time PCR.

Proceeding of the National Conference on Basic Research. Institute of Military Medicine. 372-376. October 28, 2004

- **Trinh BQ**, Nguyen BH, Truong NU, Le M, Nguyen H, Dinh KD. 2003. Cloning and expression the region encoding Premembrane and envelope proteins of dengue virus type 4. *Journal of Biotechnology* 1(1): 33-38. 2003

Journal articles (under review)

- Ebralidze AK, Angarica VE, Ummarino S, Liu Y, Kappei D, Tenen DE, Monteleone E, Coffey R, Magallanes RT, Wanet A, Bassal M, **Trinh BQ**, Sheen MR, Poli V, Benoukraf T, Crane-Robinson C, Di Ruscio A, & Tenen DG. Formation of an active epigenetic mark is mediated by cell cycle-specific RNAs. *Nat Genet*. Under revision.
- Umarino S, Ebralidze AK, Monteleone E, Zhang Y, **Trinh BQ**, Di Ruscio A, Tenen DG. S-phase induced RNAs initiate formation of DNA replication origin. Bioarchive doi: https://doi.org/10.1101/2021.10.19.465050

Technological innovations

- Compositions and methods for targeting tumor associated transcription factors. US Patent Application Number: 63/054,531. Jointly developed with D. Tenen. This patent application was filed on 07/21/20.

Book chapter (invited)

- **Trinh BQ**, Naora H. Homeobox genes and theirs functional significance in ovarian tumorigenesis, Ovarian Cancer / Book 1, ISBN 978-953-307-812-0, 2012

Conference presentations (selected)

- Noncoding RNA Coordinates with Transcription Factor to Drive Long-Range Transcription Activation of Lineage Gene. Poster of a selected Abstract/First-author presentation. *Gene Regulation: From Mechanisms to Disease, Keystone Symposia Conference*, Keystone, CO. 2020
- Long Noncoding RNA *LOUP* Interacts with Runx1 and Regulates Long-Range Transcription of PU.1 in Acute Myeloid Leukemia. Poster of a selected Abstract/First-author presentation. *The American Society of Hematology Annual Meeting*, San Diego, CA. 2018
- The homeobox gene DLX4 stimulates inducible nitric oxide synthase-mediated angiogenesis in ovarian cancer. Poster of a selected Abstract/First-author presentation. *106th Annual Meeting of the American Association for Cancer Research,* Philadelphia PA. 2015
- The homeoprotein DLX4 induces topoisomerase IIα expression but reduces sensitivity of tumor cells to topoisomerase II poisons. Poster of a selected Abstract/First-author presentation. *104th Annual Meeting of the American Association for Cancer Research*, Washington DC. 2013
- The homeobox patterning gene DLX4 confers resistance to transforming growth factor-β signaling in tumors. Poster of a selected Abstract/First-author presentation. *2nd AACR International Conference on Frontiers in Basic Cancer Research*, San Francisco CA. 2011
- Novel function of homeobox gene DLX4 in regulating tumor angiogenesis/Poster of a selected Abstract/First-author presentation. *100th Annual Meeting of the American Association for Cancer Research*, Denver, CO. 2009
- Novel function of homeobox gene DLX4 in regulating tumor angiogenesis/Poster of a selected Abstract/First-author presentation. *2nd World Cancer Congress*, Beijing, China. 2009

INVITED PRESENTATIONS (selected)

- Harvard Science Research Showcase, Faculty of Arts and Sciences – Harvard University 2020
  Noncoding RNAs in normal and malignant myelopoiesis
- Research from Early Career Highlights (REACH), Beth Israel Deaconess Medical Center 2020
  Myeloid lncRNA modulation of transcription factor and derived oncogenic fusion in acute myeloid leukemia
- Hematopoiesis Supergroup meeting, Division of Hematology/Oncology Boston Children's Hospital 2018
  Long noncoding RNA LOUP promotes long-range regulation of PU.1 expression in myeloid development
- Center for Life Sciences, Harvard Medical School 2016
  Transcriptional and Post-Transcriptional Functions of Homeoprotein DLX4 in Hematopoiesis and Cancer

- Department of Leukemia, UT MD Anderson Cancer Center 2016
  Molecular Controls of Cytokine Signaling and DNA Repair Pathways in Erythro-Megakaryopoieis and Chemo-Drug Sensitivity
- Department of Cell Biology, Albert Einstein College of Medicine 2015
  Transcription and Non-transcriptional Functions of Homeobox Protein DLX-4 (DLX4) in Cancer and Hematopoiesis
- Sylvestor Comprehensive Cancer Center, University of Miami Miller School of Medicine 2015
  Multifunctional Roles of the Homeoprotein DLX4 in Blood Cell Development and Cancer

TEACHING AND MENTORING EXPERIENCE

Harvard Medical School, Boston, MA

Co-supervisor: supervising and teaching intern students, visiting scholar and junior laboratory members for methods and concepts.

- Miguel Fuentes, Undergraduate Student, Harvard University 2021
- Madeline Hughes, Undergraduate Student, Brown University 2020
- Abby R. Thurm, Undergraduate Student, The University of California, Los Angeles 2018

UT MD Anderson Cancer Center, Houston, TX

Seminar in Health Care, School of Health Professions, UT MD Anderson Cancer Center 2016

Guest lecturer**:** 1-hour lecture on Transcriptional controls in myeloid cell development and abnormalities in myeloid malignancies for Undergraduate and Graduate students.

Co-supervisor: supervising graduate students and junior laboratory members for methods and concepts.

- Dhwani Haria, MS student, UT Graduate school of Biomedical Sciences 2012 - 2014
- Hiep Khong, PhD student, UT Graduate school of Biomedical Sciences 2011

University of Texas Graduate School of Biomedical Science, Houston, TX

Graduate Teaching Assistant, Graduate course in Cancer cell signalling 01/07-06/07

Mentored by Dr. Gary Gallick. *Developed and gave lectures* on Transcription regulation (topics: promoters, polymerases, basal transcription machinery, transcription regulators, chromosome remodelling, transcription factors, transcription regulations and cancer). Contributed to exams. Provided assistance to students having difficulty with the course. Helped in the evaluation of students enrolled in the course.

Institute of Biotechnology, Vietnam Academy of Science and Technology, Hanoi, Vietnam

Co-supervisor: supervising undergraduate students and junior laboratory members for methods and concepts.

- Sinh T. Nguyen, B.S. Program, Hanoi Open University 2003 - 2004
- Tuan M. Pham, Honor BS Program, Vietnam National University 2003 - 2004
- Bang H. Nguyen, Honor BS Program, Vietnam National University 2003 - 2004
- Khoa Truong Nguyen, BS Program, Hanoi Open University 2002 - 2003

Teaching certifications: STEM Education Solutions (2018), Vietnam National School of Education (2002)

SERVICE ACTIVITIES

Journal review: Journal of Oncology (2021), Journal of Data Mining in Genomics & Proteomics (2021), Tumour Biology (2015)

Award and fellowship review: Schissler Foundation (2011), Vietnam Education Foundation Fellow Association (2012), Vietnam Education Foundation 2.0 (2021)

Meeting organizing/leadership: Graduate school of Biomedical Sciences Leadership Development Academy Workshop (2008); Co-organizer, Research Exchange forum (2008); Chair, Biology Scientific Session, 4th Vietnam Education Foundation Annual Conference (2007).