BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Tin Tin Su

eRA COMMONS USER NAME (credential, e.g., agency login): tintinsu

POSITION TITLE: Professor (with Tenure); CSO, SuviCa; Co-Program Leader, University of Colorado Cancer Center

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Mt. Holyoke College, MA	B.A.	05/1984	Biochemistry
Carnegie-Mellon University, PA	Ph. D.	12/1991	*E.coli* transcription (advisor; Will McClure)
University of California, San Francisco, CA	Post-doc	08/1998	*Drosophila* cell cycle regulation (advisor; Patrick O'Farrell)

A. Personal Statement

I have led an independent research program in radiation biology of *Drosophila* and human cancer models since 1998. Areas of research in my lab include DNA repair, apoptosis, signaling by apoptotic cells, and cell fate plasticity during regeneration after radiation damage. Basic research in my lab has been funded by federal and private grants from sources that include the NIH, the American Cancer Society, and the Department of Defense. Current funding for the lab is through an NIH R35 MIRA grant on which I am the sole PI.

Since 2005, I have been leveraging my basic research findings into discovery and development of new anti-cancer drugs. These efforts, funded by two R21 grants from the NIH and two grants from the Department of Defense cancer research programs generated three issued patents and one start-up company, SuviCa, Inc. SuviCa is a women-owned business. I recruited all key personnel to SuviCa including a world-class CEO (co-founder and former COO of Pharmion) and serve as the Chief Scientific Officer. SuviCa has successfully completed two phase I and two phase II NCI SBIR contracts.

For the last two decades, I have dedicated my time to increase diversity and inclusiveness at all levels (undergrad to faculty) in the STEM fields. Examples of my activities in this regard are:

1. As Assistant Vice Chancellor for Faculty Affairs at the University of Colorado, Boulder, I worked to institutionalize a faculty diversity program funded by an NSF ADVANCE grant on which I was co-PI. The goal of this program is to increase faculty diversity in STEM fields. I chose aspects of the program to make permanent as part of the Office of Faculty Affairs after ADVANCE grant expired.
2. As a member of the External Advisory Board of the NIH IDeA Networks for Biomedical Research Excellence (INBRE) Program in Wyoming, I help facilitate access to research of students at all seven Community Colleges in the state, in partnership with University of Wyoming.
3. As the Director of the Graduate Program in my home department, I partner with diversity efforts on campus to improve the recruitment and retention of graduate students from under-served populations.
4. As a faculty mentor to Summer Multicultural Access to Research Training program since 2001, I have supervised several summer undergraduate research projects on CU Boulder campus.

Besides research and diversity efforts, I am also interested in improving undergraduate instruction through innovative use of technology and peer discussion. I have published original peer-reviewed research articles as senior author in this field (Smith et al., Science, 2009, PMID: 19119232; Smith et al., CBE Life Sci Educ, 2011, PMID: 21364096).

I have held leadership positions as a Co-Program Leader for the Molecular and Cellular Oncology Program of the University of Colorado Cancer Center (in my 5th year in the role), Associate Chair for three

years and Interim Chair for one year for my home department, President of the Drosophila Board, Chair of the organizing committee for an annual Genetics Society of America conference, Chair of five different NIH study sections named in the Service to Profession section below, and above-mentioned leadership roles in biotech.

Currently, I am leading an NIH-funded research project:

Cellular Plasticity and Regeneration after Radiation Damage in Drosophila We are identifying positive and negative regulators of regenerative behavior after exposure to ionizing radiation (IR) and characterize the mechanisms by which signals from dying cells and other external factors regulate stem cell-like behavior. This project is funded by R35 GM130374 (PI: Su). It began on 01/01/2019 and will end on 12/31/2023.

I am also collaborating on two NIH-funded research projects.

1. Targeting oncogenic Myb fusions in salivary gland cancer with the elongation inhibitor SVC112. The goal is to study novel fusions in salivary gland cancer (SGC); comprehensively identify targets of SVC112 in SGC by ribosome profiling and proteomics; and identify predictive biomarkers. As an Other Significant Contributor, I am providing reagents, advice and data analysis support. This project is funded by NIH R01 DE030683 to Dr. Jimeno for 03/08/2021 to 03/07/2026. This proposal on SGC does not overlap with the current proposal in HNSCC.
2. Targeting protein translation elongation in head and neck cancer. This is project #3 in the Colorado Head and Neck Cancer SPORE (P50CA261605). Major goals of this project are to assess SVC112, particularly its ability to immune-modulate in HNSCC. My contribution (10% effort) will be to oversee proteomics analyses to address the selectivity of SVC112 in protein depletion in HNSCC, with an emphasis on the immune response (distinct from the current proposal).

B. Positions, Scientific Appointments, and Honors

Academic Positions

Professor (2011-now), Associate Professor (2005-2011), Assistant Professor (1998-2005)
all in Dept. Molecular, Cellular & Developmental Biology, Univ. Colorado, Boulder

2012, Visiting Professor (sabbatical), Institute for Biomedical Research, Barcelona, Spain
2005, Visiting Professor (sabbatical), Dept. Radiation Oncology, Univ. Colorado Cancer Center

Administrative positions

2018 July- present: Co-Program Leader, Molecular and Cellular Oncology, Univ. Colorado Cancer Center
2010- present: Co-founder and Chief Scientific Officer, SuviCa, Inc.
2016 August-2017 August: Interim Chair, MCDB Department, Univ. Colorado, Boulder.
2009-2011, 2015-2016 August: Associate Chair & Head of the Executive Committee, MCDB Department, Univ. Colorado, Boulder.
2006-2007: Assistant Vice Chancellor, Faculty Affairs, Univ. Colorado, Boulder *(a 1-yr faculty internship that lets faculty try out an administrator position)*

Honors, Awards and other Recognitions

Invitation to Chair 5 different NIH study sections (details in Service to the Profession section below)
2021-2022, President of the Drosophila Board, a representative group of working scientists world-wide who use Drosophila as their primary model organism
2021, Elected Senior Member, National Academy of Inventors
2021, Undergraduate Research Opportunities Program, Outstanding Mentor Award; Honorable Mention
2018-2019, Invited reviewer, NIH CSR Anonymization study
2018, Invited consultant, United Nations-Internal Atomic Energy Agency, Vienna, Austria. Member of a 7-person panel to harmonize methods to test the effect of radiation on human cells.
2017, 2015, Recipient, Arts and Sciences Fund for Excellence, University of Colorado
2016, Invited participant, *Rethinking Cancer* workshop organized by The Company of Biologists (Publishers), Wiston House, Steyning, Britain
2015- invited evaluator, NIH study section, Genes, Genomes, and Genetics Integrated Review Group
2015, Outstanding Undergraduate Research Mentor Award (student-nominated), U. Colorado, Boulder
2013, Invited participant, *Provocative Questions* Workshop, National Cancer Institute

2012, 2008, 2006, 2004 & 2002 Recipient, The Dean's Fund for Excellence, University of Colorado
2011, Inducted as an Honorary Member, The Genetics Society of Mexico
2008, The Laura and Arthur Colwin Endowed Summer Faculty Research Fellowship, Woods Hole Marine Biology Lab
2007, Mentor Award, The Leadership Alliance (for increasing underrepresented students in academia)
2006, Travel Award from Gulbenkian Foundation, Portugal
2002, Residence Life Academic Teaching Award (student-nominated), University of Colorado
1999-2002, American Cancer Society Research Scholar Grant
1999, Recipient, Junior Faculty Development Award, University of Colorado
1997-1998, Herbert W. Boyer Postdoctoral Fellowship, UCSF
1992-1995, NIH Postdoctoral Fellowship
1984 Graduated magna cum laude in Biochemistry, Mount Holyoke College, and Elected to Sigma Xi
1981-1984 Mount Holyoke Scholarship
1983, Elizabeth M. Boyd Scholarship, Mount Holyoke College
1983, Abby Howe Turner Award in Biology, Mount Holyoke College

Service to the Profession (partial listing)
Editorial Board member, Current Biology (Cell Press), 2005-present
Editorial Board member, British Royal Society's Open Biology, 2016-present
Guest Editor, PLoS Genetics, 2019, 2015
Guest Editor, Annual Reviews of Genetics, 2013
Grant/Contract/Institute Reviews (listing only national/international activities
- 2021 July-2023 June, Chair, NIH Cellular Signaling and Regulatory Systems study section
- 2022, Chair NIH special study section for DoD-USU-High Priority Research Grant Applications
- 2020-June 2021, member, NIH Cellular Signaling and Regulatory Systems study section
- 2020, ZRG1 CB-E 55 R, member, special panel to review MIRA proposals
- 2019, Chair, ZRG1 CB-K 55 R, special panel to review MIRA proposals
- 2019, ZAI1 JA-I (J1), member, special panel, NIH Centers for Medical Countermeasures Against Radiation Consortium
- 2018-2019, Member, Special Emphasis Panel, NCI's Provocative Questions (PQ12) (2 meetings)
- 2019, *ad hoc* member, NIH Cellular Signaling and Regulatory Systems study section
- 2018, member, ZRG1-GGG-D-90 special emphasis study section to review proposals by NIH reviewers
- 2018, Chair, NCI ZCA1-TCRB-J-C1 SBIR contracts for 'Drugs to Exploit the Immune Response Generated by Radiation Therapy' study section
- 2016-2017, NIH Special Emphasis Panel for F05-U (3 meetings, trainee fellowships)
- 2017, External reviewer, Linda Crnic Institute for Down Syndrome Research
- 2015, NIH special study section for shared instrument (S10) proposals
- 2015, Invited evaluator of NIH study sections, Genes, Genomes, and Genetics IRG
- 2014-2015, Chair, NIH Molecular Genetics B study section
- 2010-2014, regular member, NIH Molecular Genetics B study section
- 2013, 2012 & 2009, National Research Fund, Qatar

Meeting Organizer
- 2018, Chair, Organization Committee for the Genetics Society of America, Annual *Drosophila* Research Conference, Philadelphia, PA
- 2014, 2011 & 2010-Co-organizer and Co-Chair, workshop on "Chemical Genetics and Drug Screening in *Drosophila*", Genetics Society of America, annual *Drosophila* meeting
- 2007**,** 2005, 2004 & 2002-Co-organizer and Co-Chair, workshop on "Cell Cycle Checkpoints", Genetics Society of America, annual *Drosophila* meeting
- 2006-Co-organizer, 3rd International Workshop on *Drosophila* Cell Division Cycle, Porto, Portugal
- 2003-Chair and Organizer, "Cell Cycle" session, Annual meeting of the American Society for Molecular Biology and Biochemistry
- 2003-Co-Chair, "Cell Cycle" Session, Genetics Society of America annual *Drosophila* meeting

Manuscript reviewer for (partial listing in alphabetical order, several manuscripts per journal):
Biochemistry, Cancer Research, Cell Cycle, Cell Death & Differentiation, Chromosoma, Current Biology, Development, Developmental Biology, Developmental Cell, Disease Models and Mechanisms, Genes & Development, Genetics, J. Biological Chem, J. Cell Biology, J. Cell Science, Mechanisms of Development, Molecular Biology of the Cell, Molecular Cancer Research, Molecular Cell, Mutation Research, Nature Cell Biology, Nature Communications, Nature Genetics, Oncogene, PLoS Biology, PLoS Genetics, PLoS ONE, PNAS, Radiation Research, Science, Science Signaling.

C. Contributions to Science

I started my lab about 2 decades ago, to study DNA Damage Responses (DDR). While DDR was an active research topic, most of the field used single cell systems such as yeast and cultured mammalian cells. I set out to study DDR in the context of profound cellular reprograming that happens during *Drosophila* development. We found that cells and multicellular organisms have common as well as different DDR mechanisms. The most notable was our finding that Chk1 kinase (Grapes in *Drosophila*) is required for the survival of irradiated cells but not for the survival of irradiated larvae. The reason, we discovered, was that although more cells die in Chk1 mutant larvae, as long as the survivors could regenerate, larvae survives. This led to a new research direction, to study regeneration after radiation damage and to identify chemical modulators of this process, which has been the focus of my lab for the past 10 years as described in the sections that follow.

1. B. Jaklevic and T. T. Su, Relative contribution of DNA repair, cell cycle checkpoints and cell death to survival after DNA damage in *Drosophila* larvae. (2004) Current Biology, 14:23-32. PubMed ID:14711410
2. Jaklevic B, Uyetake L, Lemstra W, Chang J, Leary W, Edwards A, Vidwans SJ, Sibon O, Su TT. (2006) Contribution of Growth and Cell Cycle Checkpoints to Radiation Survival in *Drosophila*. Genetics. 174(4):1963-72. PMID 17028317
3. Wichmann, A., Jaklevic, B. and Su TT. (2006) Ionizing Radiation induces caspase-dependent but Chk2 and p53-independent cell death in *Drosophila melanogaster*. PNAS, 103; 9952-57. PMID: 16785441
4. Wichmann, A.,L. Uyetake and T. T. Su. (2010) E2F1 and E2F2 have opposite effects on radiation-induced p53-independent apoptosis in *Drosophila*, Dev Biol. 346(1):80-9. PubMed ID:20659447

We found that cell-cell communication makes profound contributions to how cells and tissues survive and regenerate after radiation damage. Notable findings from our lab include a novel phenomenon in which dying cells send signals to protect the neighbors from radiation-induced cell death, the identification of radiation-resistant epithelial cells that acquire regenerative properties after radiation damage, and mechanisms by which cells with broken chromosomes are culled.

1. Verghese, S. and Su TT. (2016) *Drosophila* Wnt and STAT Define Apoptosis-Resistant Epithelial Cells for Tissue Regeneration after Irradiation. PLoS Biology, 2016 Sep 1. PMID: 27584613

   The journal deems this work to be of sufficient importance and interest to issue a press release (phys.org/news/2016-09-cellular-hotspots-tumors-regeneration.html)
2. Verghese, S. and Su TT. (2018) Ionizing radiation induces stem cell-like properties in a caspase-dependent manner in *Drosophila*. PLoS Genetics, 2018 Nov 21;14(11):e1007659. PMID: 30462636

   The journal deems this work to be of sufficient importance and interest to commission an accompanying Prospective article, "The many fates of tissue regeneration" by RJ Duronio & C Abdullah.
3. Brown J, Bozon J, Bush I, and Su TT. (2020) Cells that acquire loss-of-heterozygosity after exposure to ionizing radiation in Drosophila are culled by p53-dependent and p53-independent mechanisms. PLoS Genetics, 2020 Oct 19;16(10):e1009056. PMID: 33075096

4. Ledru M, Clark C, Brown J, Verghese S, Ferrara S, Goodspeed A and Su TT. (2022) Differential gene expression analysis identified determinants of cell fate plasticity during radiation-induced regeneration in Drosophila. PLoS Genetics, 2022 Jan 6;18(1):e1009989. doi: 10.1371/journal.pgen.1009989.

In order to translate our basic research findings, we have been screening for small molecule modulators of tissue regeneration after radiation damage. Such molecules have the potential to improve the efficacy of radiation therapy of cancer. These efforts have been funded by two R21 grants from the NIH, two grants from the Department of Defense, and grants from the State of Colorado. We have two issued and one pending patent, including a proprietary patented screen for chemical inhibitors of tissue regeneration after radiation damage using *Drosophila* mutants. Hits from this screen are being developed to use as radiation enhancers in cancer, with funding from phase 1 and phase 2 SBIR contracts from the NCI to a start-up company I co-founded (www.suvica.com). Proprietary small molecule SVC112 is a product of these efforts.

1. Keysar SB, Gomes N, Miller B, Jackson BC, Le PN, Morton JJ, Reisinger J, Chimed TS, Gomez KE, Nieto C, Frederick B, Pronk GJ, Somerset HL, Tan AC, Wang XJ, Raben D, Su TT*, Jimeno A*. (*co-corresponding authors). (2020) Inhibiting translation elongation with SVC112 suppresses cancer stem cells and inhibits growth in head and neck squamous carcinoma. Cancer Res. 80(5):1183-1198. PMID: 31911553

2. Stickel SA, Gomes NP, Frederick B, Raben D, T. T. Su. (2015) Bouvardin Is a Radiation Modulator with a Novel Mechanism of Action. Radiation Research, 184:392-403. PMID:26414509

3. US Patent Office Issued Patent NO. 9452215. Bourvadin derivatives and therapeutic uses thereof. Inventors: Tin Tin Su (lead inventor), Mara N. Gladstone, Gan Zhang, Tarek Sammakia. September 27, 2016; patent extension to cover additional chemical structures issued April 16, 2019.

4. Gomes NP, Frederick B, Jacobsen JR, Chapnick D, Su TT. (2022) A high throughput screen with a clonogenic endpoint to identify radiation modulators of cancer. bioRxiv 2022.05.24.493331

Additional publications may be found at

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/44261907/?sort=date&direction=descending