BIOGRAPHICAL SKETCH

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NAME: Tin Tin Su

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

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

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 and regeneration 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. My lab is currently funded an NIH R35 MIRA award 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, two grants from the Department of Defense cancer research programs, grants from the State of Colorado Bioscience Discovery and Evaluation Program and the Colorado Center for Drug Discovery, generated three issued patents and one start-up company (SuviCa, Inc. Boulder). SuviCa has completed two phase I and two phase 2 NCI SBIR contracts; I was a PI on one phase I and one Phase II contracts.

Projects I led have resulted in the following notable publications/patents:

1. Colon Plaza S, **Su TT**. (2024) Ionizing radiation induces cells with past caspase activity that contribute to the adult organ in Drosophila and show reduced Loss of Heterozygosity. Cell Death Discov. Jan 5;10(1):6. PMC10770159.
2. Gomes NP, Frederick B, Jacobsen JR, Chapnick D, **Su TT**. (2023) A high throughput screen with a clonogenic endpoint to identify radiation modulators of cancer. Radiation Research, 2023 199(2):132-147. PMC10000021.
3. 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 Genet. 2022;18(1):e1009989. PMC8769364.
4. US Patent Office Issued Patent No. 9452215 & 10259846. Bourvadin derivatives and therapeutic uses thereof. Inventors: **Tin Tin Su** (lead inventor), Mara N. Gladstone, Gan Zhang, Tarek Sammakia.

Additional evidence of my leadership abilities includes my current role as the interim Chair of my department and as a Co-Program Leader for the Molecular and Cellular Oncology Program (69 labs on three campuses) of the University of Colorado Cancer Center. At the national level, I served as the elected President of the *Drosophila* Board (2021-2022) and as the past-President (2022-2024). I currently serve on the Board of the Genetics Society of America, was elected Treasurer and began my 3-year term in January 2023. I am honored

to have been asked to chair six different NIH study sessions (2 standing, 3 special emphasis and 1 declined due to conflict) that span in focus from genetics and cell signaling to SBIR projects. In total, I have served on 10 different NIH study sections with multiple years of service on 2 of them; as editor or guest editor for 5 journals; and organized national meetings and reviewed multiple manuscripts per year. More information on my service activities can be found later in this document.

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, 04/01/2019-03/31/2029).

I am collaborating with Dr. Jimeno on three cancer-focused projects.

1. Targeting Protein Translation Elongation to Treat Cancer Patients. The goal is to complete IND-enabling studies on SVC112, a drug that came out of our *Drosophila* research, and assess it on human cancer patients in a phase I clinical trial. Funded by a Anschutz Acceleration Initiative grant (multi-PI: Jimeno and Su, 2024-2028)
2. 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) and comprehensively identify targets of SVC112 in SGC by ribosome profiling and proteomics. As an Other Significant Contributor, I am providing reagents, advice, and data analysis support. Funded by NIH R01DE030683 (PI: Jimeno, 03/08/2021-03/07/2026).
3. 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.

For two decades, I have been dedicating time and effort to increase diversity and inclusiveness at all levels (undergrad to faculty) in the STEM fields at my home institution and beyond. Examples of my activities are:

1. I was a co-PI on an NSF ADVANCE grant whose goal was to increase faculty diversity in the STEM fields. I chose aspects of the program to make permanent after the ADVANCE grant expired.
2. I have been a faculty mentor to Summer Multicultural Access to Research Training (SMART) program at CU Boulder since 2001 and have supervised several summer undergraduate researchers. I was honored to be chosen to accept the 2007 Mentor Award from Leadership Alliance on behalf of our SMART program.
3. I recruited a 2018 SMART student to our graduate program (the first ever to join our department!) and she is now a PharmD/PhD student in my lab, funded by F31 GM149184.
4. As the Director of the Graduate Program in my home department (2019-2022), I partnered with diversity efforts on campus to improve the recruitment and retention of graduate students from under-served populations.
5. As an External Advisory Board member of the NIH IDeA Networks for Biomedical Research Excellence Program in Wyoming, I am helping the University of Wyoming facilitate access to lab research for students at all seven Community Colleges in the state.

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

2024 August 1-Dec 31: interim Chair, MCD Biology Department
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, MCD Biology 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
2024, 2015, 2017, Recipient, Arts and Sciences Fund for Excellence, University of Colorado, Boulder
2023, Elected Treasurer, Genetics Society of America
2023, Invited to chair the Cell Death section, AACR annual meeting, 2024
2021, Elected President of the *Drosophila* Board
2021, Elected Senior Member, National Academy of Inventors
Chaired five different NIH Study Sections (dates of service are provided in the next section):
Cell Signaling and Regulatory Systems (CSRS)
Molecular Genetics B (MGB)
ZRG1 ETTN-U (82) SEP for DoD-USU-High Priority Research Grant Applications
ZRG1 CB-K (55) R, to review R35 MIRA proposals for established investigators
NCI ZCA1-TCRB-J-C1 for SBIR contracts
2021, Undergraduate Research Opportunities Program, Outstanding Mentor Award; Honorable Mention
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.
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 (listing activities for the past 10 years only)
2023-2026, Treasurer and Board Member, Genetics Society of America
President (2021-2022) and member (2022-2024) of the *Drosophila* Board
2016-present, Editorial Board member, British Royal Society's Open Biology
2024, Reviewing Editor, eLIFE
2005-2023, Editorial Board member, Current Biology (Cell Press)
2023, 2019, 2015, Guest Editor, PLoS Genetics
2013, Guest Editor, Annual Reviews of Genetics
Grant/Contract/Institute Reviews (listing only national/international activities)
2020-2021 (member), 2021-2023 (Chair) NIH Cellular Signaling and Regulatory Systems study section
2022, Chair NIH ZRG1 ETTN-U (82) SEP for DoD-USU High Priority Research Grant Applications

2020, member, NIH ZRG1 CB-E 55 R, special panel to review MIRA proposals
2019, Chair, NIH ZRG1 CB-K 55 R, special panel to review MIRA proposals
2019, member, NIH ZAI1 JA-I (J1) SEP, Centers for Medical Countermeasures Against Radiation Consortium
2018-2019, Invited reviewer, NIH CSR Anonymization study
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 'Drugs to Exploit the Immune Response Generated by Radiation Therapy' study section for SBIR contracts
2016-2017, member, NIH Special Emphasis Panel for F05-U (3 meetings, trainee fellowships)
2017, External reviewer, Linda Crnic Institute for Down Syndrome Research
2015, member, NIH special study section for shared instrument (S10) proposals
2015- invited evaluator, NIH study section, Genes, Genomes, and Genetics Integrated Review Group
2010-2014 (member), 2014-2015 (Chair), NIH Molecular Genetics B study section
2013, 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 over 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, surviving cells regenerated to allow larval survival.

1. B. Jaklevic and **Su TT**, 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. NIHMSID:1901779.
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. PMC1698627.
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. PMC1502560.
4. Wichmann, A.,L. Uyetake and **Su TT**. (2010) E2F1 and E2F2 have opposite effects on radiation-induced p53-independent apoptosis in *Drosophila*, Dev Biol. 346(1):80-9. PMC1502560.

The finding that Chk1 is dispensable for larval survival so long as surviving cells could regenerate led us to shift our focus from DDR to recovery and regeneration. Notable findings since then include a novel phenomenon in which dying cells send signals to protect the neighbors from radiation-induced cell death, 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 14(9):e1002536. PMC5008734. *The journal considered 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;14(11):e1007659. PMC6248896. *The journal considered 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;16(10):e1009056. PMC7595702.
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 Genet. 2022;18(1):e1009989. PMC8769364.

To translate our basic research findings into potential therapies, we screened for small molecule modulators of tissue regeneration after radiation damage. Such molecules have the potential to inhibit tumor regrowth and stem cell activity. These efforts led to a proprietary screen for chemical inhibitors of tissue regeneration after radiation damage using *Drosophila* mutants and 3 issued patents. Hits from this screen are being developed for cancer, with funding from SBIR contracts from the NCI to a start-up company I co-founded (www.suvica.com). Proprietary small molecule SVC112, a product of these efforts, was accepted into the NCI Experimental Therapeutics (NExT) program in March 2023 for development towards the clinic.

5. Stickel SA, Gomes NP, Frederick B, Raben D, **Su TT**. (2015) Bouvardin Is a Radiation Modulator with a Novel Mechanism of Action. Radiation Research, 184:392-403. PMC4643058.
6. 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. PMC7056512.
7. Gomes NP, Frederick B, Jacobsen JR, Chapnick D, **Su TT**. (2023) A high throughput screen with a clonogenic endpoint to identify radiation modulators of cancer. Radiation Research, 2023 199(2):132-147. PMC10000021.
8. US Issued Patents 9452215 and 10259846. Bouvardin derivatives and therapeutic uses thereof. **Su TT,** lead inventor.

Additional publications may be found at

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