CURRICULUM VITAE

Yangzom Doma Bhutia, DVM, PhD

Office Address

Texas Tech University Health Sciences Center Department of Cell Biology and Biochemistry 3601 4th St Stop 6540 Lubbock, TX 79430 Phone: (806) 743-1282 Fax: (806) 743-2990 E-mail: <u>yangzom.d.bhutia@ttuhsc.edu</u>

US Visa Status: US Citizen

2004-2008	PhD in Veterinary Medicine, Adviser: Dr. Devendra Swarup Indian Veterinary Research Institute, Izatnagar, Uttar Pradesh, India
2001-2004	MVSc, Master's in Clinical Veterinary Medicine Adviser: Dr. D.S. Tirumala Rao Acharya N.G. Ranga Agricultural University, Andhra Pradesh, India
1996-2001	DVM, Veterinary Science Marathwada Agricultural University, Parbhani, Maharashtra, India
Positions	
	Associate Professor (Tenured), Texas Tech University Health Sciences Center, Lubbock, TX 79430
2022-2023	Associate Professor (Tenure Track), Texas Tech University Health Sciences Center, Lubbock, TX 79430
2017-2022	Assistant Professor (Tenure Track), Texas Tech University Health Sciences Center, Lubbock, TX 79430
2015-2017	Assistant Professor (Non-tenure Track), Texas Tech University Health Sciences Center, Lubbock, TX 79430
2014-2015	Assistant Professor (Research Track), Texas Tech University Health Sciences Center, Lubbock, TX 79430
2013-2014	Assistant Research Scientist, Georgia Regents University, Augusta GA 30912
2011-2013	Postdoctoral Fellow with Dr. Vadivel Ganapathy, Georgia Regents University, Augusta GA 30912

- 2009-2011 **Postdoctoral Fellow** with Dr. Rajgopal Govindarajan, University of Georgia, School of Pharmacy, Athens, GA 30602
- 2008-2009 **Research Assistant** with Dr. Devendra Swarup, Central Zoo Authority, Ministry of Environment, Indian Veterinary Research Institute, Izatnagar, Uttar Pradesh, India

Professional Memberships

- 2021-present Member of the TTUHSC Cancer Center, Texas Tech University Health Sciences Center, School of Medicine, Lubbock, TX
- 2020-present Member of the Biochemistry, Cellular, and Molecular Biology program, Graduate School of Biomedical Sciences, Texas Tech University Health Sciences Center, Lubbock, TX
- 2019 Life Member of American Association of Indian Scientists in Cancer Research (AAISCR)
- 2018-present Member of the Center for Membrane Protein Research, Texas Tech University Health Sciences Center, Lubbock, TX
- 2016-present Member of the Biotechnology program, Graduate School of Biomedical Sciences, Texas Tech University Health Sciences Center, Lubbock, TX
- 2010-present Member of the American Association for Cancer Research (AACR)
- 2010-present Member of the American Association of Pharmaceutical Scientists (AAPS)
- 2001 Life Member of Indian Society of Veterinary Medicine (ISVM)
- 2001 Life Member of Veterinary Council of India (VCI)
- 2001 Life Member of Sikkim Veterinary Council (SVC)

Honors and Awards

Dates	Honors
2024	NIH R01 grant highlighted in the Office of Research & Innovation 2023 Annual Report Magazine in Targeted Disease Breakthroughs "Stalking a silent killer: NIH grant to aid Bhutia's quest to treat pancreatic cancer."
2023	Research highlighted at the American Cancer Society's Cattle Barons Ball, Lubbock TX; Saturday July 29 th , 2023
2023	NIH R01 grant highlighted at TTUHSC Daily Dose (<i>Stalking a silent killer</i>); https://dailydose.ttuhsc.edu/2023/august/nih-grant-bhutia-pancreatic-cancer.aspx
2023	NIH R01 grant highlighted at <i>EurekAlert (Stalking a silent killer</i>); https://www.eurekalert.org/news-releases/997402

2022	Cover Photo Discharging Lawred
2022	Cover Photo, Biochemical Journal
2021	President's Early Career Investigator Award
2021	Cover Photo, Biochemical Journal
2019	Podium Presentation Award on Biomedical Transporters Conference at Lucerne, Switzerland, August 2019
2019	Received Dean Berk's 'Apple Pin' for effective Physiology lectures in Major Organ Systems to Medical Students
2017	Cover Photo, Biochemical Journal
2017	Research highlighted in a commentary in Biochemical Journal
2017	Research highlighted in <i>Medical News Today, www.medicalnewstoday.com</i> https://www.medicalnewstoday.com/articles/319578.php
2017	Research highlighted in TTUHSC Daily dose,
0047	https://dailydose.ttuhsc.edu/2017/september/lub-pancreaticcancer.aspx
2017	Research highlighted in <i>Parkinson's News Today</i> <u>https://parkinsonsnewstoday.com/2017/10/06/parkinsons-disease-drug-shows-</u> anti-cancer-effects/
2017	Research highlighted in European Pharmaceutical
	https://www.europeanpharmaceuticalreview.com/news/67495/parkinsons-
	<u>carbidopa-anticancer/</u>
2017	Research highlighted in Outlook The News Scroll
	https://www.outlookindia.com/newsscroll/this-parkinsons-disease-drug-shows- anticancer-effects-study/1156955
2011	Research highlighted in Breaking Advances Highlights from Recent Cancer
2011	Literature in Cancer Research Literature in Cancer Research
	https://cancerres.aacrjournals.org/content/canres/71/9/3173.full.pdf
2011	AAPS Exceptional Abstract & Podium Presentation Award, AAPS Workshop on
	Drug Transporters, Washington DC
2008	Qualified Indian Council of Agricultural Research (ICAR)- National Eligibility Test (ICAR-NET) as an eligibility for teaching Life Sciences
2004-	Awarded Senior Research Fellowship (SRF) at the Indian Veterinary Research
2008	Institute for the Doctoral program
2001-	Awarded Junior Research Fellowship (JRF) by the Indian Council of Agricultural
2004	Research (ICAR) for the Master's program
1996-	Awarded Indian Council of Agricultural Research (ICAR) State Education
2001	Fellowship for the Bachelor's program

Editor or Member of editorial boards (e.g. Circulation Research)

• Associate Editor in Frontiers in Molecular Biosciences [IF. 6.113]

Manuscript Reviews for Journals

- EBioMedicine
- Clinical Science
- Cellular Physiology and Biochemistry
- Bioscience Reports

- Biomedicine and Pharmacotherapy
- Cells

Grant Reviewer

Ad hoc Reviewer for NIH Digestive and Nutrient Physiology and Diseases (DNPD) Study Section since October 2023

TEACHING (35 % effort)

Teaching and Training Experience

I started teaching in the Graduate School of Biomedical Sciences (GSBS) since 2017 and the School of Medicine (SOM) since 2018. I teach a total of 8 hours to the graduate students and a total of 27 hours (including reviews) to the medical students. My teaching evaluations have been consistently good and in fact, in 2019, I received Dean Berk's '*Apple Pin*' for effective delivery of Physiology lectures in Major Organ Systems for the medical students. Apart from the lectures, I have mentored 4 Postdoctoral fellows, 5 PhD students, 3 Master's students, 3 undergraduate students, and also served as a committee member to 12 PhD students (4 MD/PhD and 8 PhD). Additionally, I have also mentored 5 first year medical students for the Medical Students Summer Research Program (MSSRP), and 3 volunteers (1 MD from TTUHSC Family Medicine, 1 DDS from Kathmandu Nepal, and 1 undergraduate (virtual mentoring due to COVID-19) from South Plains College).

Name of Institution	Course Number	Course Name	Topic (s) of Instruction	Years of Instruction
TTUHSC, SOM	MSC1 5103	Structure and Function of Major Organ System, GI Section	Salivary, Gastric, and Pancreatic Secretions	2018- present
	MS1 P3-1, Small Group, Facilitator			2021- present
	MS2 P3-2, Small Group Facilitator			2022- present
TTUHSC, GSBS	GBCM 6333	Advanced Protein Biochemistry	SLC transporters: Classification, function and relevance to health and disease	2017- present
	GSBS	Core II: Cells	Introduction to Cancer	2017-2019

Scheduled lectures:

5372			
GBTC	Biology of Cancer	The Biology of	2020-
5340		Pancreatic Cancer	2021
GBTC	Biotechnology Lab	Transporter Assay	2020-
5020	Methods		present

Current and Past Trainees: Postdoctoral Fellows & Research Associates: Past

<u>Toshihiro Sato, Ph.D.</u>, Postdoctoral Research Associate from 2017-2018. His research focus was pancreatic and prostate cancer wherein he was trying to understand the role of excess iron in tumorigenesis and induction of epithelial-mesenchymal transition. Further, he was also involved in the development of mouse models of pancreatic cancer. He is a co-author in *Asian Journal of Pharmaceutical Sciences* published in 2020. Currently, he is an Assistant Professor at the Tohoko University Hospital, Japan.

<u>Ksenija Rorac, Ph.D;</u> Research Associate from January 2023- June 2023. Her research was focused on understanding how Carbidopa, an FDA-approved drug for Parkinson's disease inhibits SLC6A14 expression. She is currently working as a NIH T32 Postdoctoral Fellow at the University of Wisconsin, Madison.

Postdoctoral Fellows: Current

<u>Devaraja Rajasekaran, Ph.D</u>., Senior Research Associate from 2018-present. He primarily works on pancreatic cancer with a special focus on developing SLC6A14 as a drug target for pancreatic cancer. He uses PDAC organoids, orthotopic mouse models as well as *KPC* spontaneous mouse models of PDAC to achieve this. He is also actively involved in understanding the cross-talk between the pancreatic stellate cells (PSCs) and the tumor cells in the tumor microenvironment (TME) in regulating SLC6A14 via the Wnt/*b*-catenin signaling pathway. Furthermore, he is studying the role of micro-RNAs in SLC6A14 regulation. He is a co-author in an article published in *Asian Journal of Pharmaceutical Sciences* in 2020 and a coauthor in four other articles published in *Biochemical Journal and Scientific Reports* since 2021 and 2023. He has already completed the work on metformin and alpha-methyl-L-tryptophan (*a*-MLT) as an anticancer agent to treat pancreatic cancer, and the manuscript is in preparation.

<u>Souad Sennoune, Ph.D</u>; Senior Research Associate from March 2023-present. She is studying to understand the role of SLC38A5 in mitochondria and how its knockout impacts the oxidative phosphorylation and glycolysis in pancreatic cancer.

Major Advisor for Graduate Student (Past)

<u>Bradley Schniers (2018-2022)</u>: Bradley graduated with a Ph.D. in Biochemistry and Cell and Molecular Biology (BCMB), TTUHSC in May 2022. He is first author on two original papers published in *Biochemical Journal* and is also a co-author in an original paper published in *Asian Journal of Pharmaceutical Sciences*. He presented his work at the AACR Annual meeting 2019, in Atlanta GA as well as at the TTUHSC Annual Student Research Week 2019, 2020, and 2021. At the Annual Student Research Week 2019, his abstract was selected for the *Student Select Talk* and won the third prize for his poster presentation. He was also awarded the *Distinguished graduate student of the Biochemistry Cell and Molecular Biology (BCMB) concentration.* He also won the first prize in the Bioss AB's greatest stain contest for IHC and is currently working as a Vaccine Research Scientist at Bimeda Biologicals at San Angelo, Texas.

<u>Ksenija Korac (2019-2022)</u>: Ksenija graduated with a Ph.D. in Biochemistry and Cell and Molecular Biology (BCMB), TTUHSC in May 2023. In her research, Ksenija focused on SLC6A14, an amino acid transporter and indoleamine dioxygenase 1 (IDO1), a tryptophan catabolizing enzyme as drug targets for pancreatic cancer. She finds that Carbidopa, an FDA-approved drug for Parkinson's disease, inhibits both SLC6A14 and IDO1 at the transcriptional level in pancreatic cancer cells leading to attenuation of tumor growth in xenograft mouse models. She presented her work at the TTUHSC Annual Student Research Week 2020, and 2021 and at the 2021 CMPR (Center for Membrane Protein Research) annual meeting at TTUHSC wherein her work was awarded. She was also awarded the *Distinguished graduate student of the Biochemistry Cell and Molecular Biology (BCMB) concentration.* She is the first author on an original article published in *Biochemical Journal*. She co-authored two original papers published in *Biochemical Journal*. She co-authored two original papers published in *Biochemical Journal*. She co-authored two original papers published in *Biochemical Journal*. She co-authored two original papers published in *Biochemical Journal*. She co-authored two original papers published in *Biochemical Journal*. She co-authored two original papers published in *Biochemical Journal*.

Tyler Sniegowski (2020-2023): Tyler graduated with a Ph.D. in Biochemistry and Cell and Molecular Biology (BCMB), TTUHSC in May 2024. In his research Tyler focused on SLC38A5, which is an amino acid transporter and its relevance to pancreatic cancer. He finds that SLC38A5 (SN2/SNAT5), a neutral amino acid transporter is highly upregulated and functional in PDAC cells. Using CRISPR/Cas9-mediated knockout of SLC38A5, he shows its tumor promoting role in an *in vitro* cell line model as well as in a subcutaneous xenograft mouse model. He presented his work at the TTUHSC Annual Student Research Week as well as several symposiums and AACR meetings. He is the first author on an original article published in *Scientific Reports* and a review article in *Pharmaceuticals* as well as co-authored four original papers in *Biochemical Journal*. He was also awarded the *Distinguished graduate student of the Biochemistry Cell and Molecular Biology (BCMB) concentration.*

Major Advisor for Graduate Students (Current)

<u>Mosharaf Mahmud-Syed</u>: Mosharaf is a 3rd year PhD graduate student in my laboratory. He started rotating through my lab in January of 2022 and officially joined my group in May 2022. Mosharaf works on pancreatic cancer wherein the focus is to understand whether inhibition of SLC6A14, an amino acid transporter and a tumor promoter induces autophagy and macropinocytosis, both of which are nutrient scavenging mechanisms and thereby partly compensate for the loss of SLC6A14 function. If this is true, Mosharaf's research will show whether inhibiting both SLC6A14 and autophagy/macropinocytosis will lead to a better therapeutic outcome in pancreatic cancer.

Tanima Sharker: Tanima is a second year PhD graduate student in my laboratory. She started rotating through my laboratory from January of 2023 and officially joined in April 2023. Tanima's project involves generation of pancreatic cancer organoids and its molecular characterization with a special focus on amino acid transporters that are tumor promoters viz., SLC7A5 and SLC6A14.

Advisor and Co-Advisor for Biotechnology students: Past

<u>Suchithra Raveendar (2015-2016)</u>: Suchithra was a Biotechnology Master's student from the Texas Tech University. I co-mentored her for her project that involved the molecular analysis of the placenta and retina of Mfsd2a-null mice, which is a model for omega-3 fatty acid deficiency. MFSD2A (Major Facilitator Superfamily Domain Containing 2A) is a transmembrane protein coding gene, also called sodium-dependent lysophosphatidylcholine (LPC) symporter that plays an essential role in the formation and function of the blood brain barrier. She is currently working as a high throughput Biologist at GSK in London, England.

<u>Anagha Tapaswi (2017-2018)</u>: Anagha was a Biotechnology Master's student from TTUHSC. I was a co-mentor for her project that involved the use of Carbidopa, an FDA-approved drug for Parkinson's disease for treatment of both androgen-sensitive and androgen-refractory prostate cancer via multiple modes of action. She is currently working as a Research Associate at the University of Michigan School of Public Health, Ann Arbor, Michigan.

<u>Varsha Ravi (2019-2020)</u>: Varsha was a Biotechnology Master's student from Texas Tech University. She joined my laboratory for her internship programme and her area of research was to elucidate the molecular mechanism of SLC6A14 upregulation in pancreatic cancer with a special focus on pancreatic stellate cells (PSCs). She is currently working as a Research Associate at Caribou Biosciences at Berkeley, California.

Graduate Student Thesis Committee Member (10 Ph.D. & 5 M.D./Ph.D.)

Bojana Ristic, 2016-2020: Dissertation Committee Member, Cell Biology and Biochemistry.

Mohd. Omar Sikder, 2016-2020: Dissertation Committee Member, Cell Biology and

Biochemistry. He is currently working as a Postdoctoral Fellow at NCI, Bethesda MD.

<u>Timothy Brown, 2017-2020</u>: Dissertation Committee Member, Cell Biology and Biochemistry. He is currently continuing his Radiology Residency at TTUHSC.

<u>Jonathan Koppel, 2018-2021</u>: Dissertation Committee Member, Cell Biology and Biochemistry. He is currently continuing his MD program at TTUHSC.

<u>Josue Enriquez, 2018-2022</u>: Dissertation Committee Member, Immunology and Molecular Microbiology. He is currently working as a Postdoctoral fellow at Netherlands.

Kevin Bass, 2019-present: Dissertation Committee Member, Cell Biology and Biochemistry.

<u>Sayanika Dutta, 2021-present</u>: Dissertation Committee Member, Cell Biology and Biochemistry.

<u>Marilyn Mathew, 2022-present</u>: Dissertation Committee Member, Cell Biology and Biochemistry.

<u>Tasmin Omy, 2022-present:</u> Dissertation Committee Member, Cell Biology and Biochemistry.

<u>Geetha Priya Boligala, 2022-present:</u> Dissertation Committee Member, Cell Biology and Biochemistry.

Ganesh Acharya, 2023-: Dissertation Committee Member, Cell Biology and Biochemistry.

Iffat Jahan, 2023-: Dissertation Committee Member, Cell Biology and Biochemistry.

Nhi Nguyen, 2023-: Dissertation Committee Member, Cell Biology and Biochemistry.

Nghi Tran, 2023-: Dissertation Committee Member, Cell Biology and Biochemistry.

<u>Caezaan Keshvani, 2023-:</u> Dissertation Committee Member, Translational Neuroscience and Pharmacology.

Undergraduate Students

Logan Smoot, 2018-2019: Logan was an undergraduate student from Texas Tech University Honors College, who worked in my laboratory from May 2018 to July 2019. He came from the Undergraduate Research Scholars (URS) program and in his research he was focusing on the micro-RNA regulation of SLC6A14. He presented his work in the form of poster at the TTU Undergraduate Research Conference and is also a co-author in an original article published in *Asian Journal of Pharmaceutical Sciences*.

<u>Nhu On, 2018-2019</u>: Nhu was a TTU CISER Scholar who joined my laboratory for an undergradute research. I also mentored her for her Research Credit (BIOL 4300). In her research, Nhu used metformin, which is an FDA-approved drug for Type 2 diabetes to target SLC6A14 in pancreatic cancer. She made significant progress in her project and we are currently getting the manuscript ready to submit to *Biochemical Journal* with her as the first author. She presented her work at the 10th Texas Tech Annual Biological Sciences Symposium at Texas Tech University, Lubbock TX. April 26-27, 2019 and also at the TTU Undergraduate Research Conference. She is also a co-author in an original article published in *Asian Journal of Pharmaceutical Sciences*. She is currently working as a Research Technician II at UT Southwestern Medical Center at Dallas, TX and is also applying to medical schools for the MD program.

<u>Andrew Ibrahim, 2021-2022:</u> Andrew is an undergraduate Cell and Molecular Biology student from Texas Tech University Honors College. He started working in my laboratory from March, 2021. His aim in the research work was to elucidate the molecular mechanism of transcriptional inhibition of SLC6A14 following metformin treatment in pancreatic cancer cells with a special focus on certain miRNAs that are the predicted targets for SLC6A14.

SOM Student Summer Research

<u>Elise Shen, 2015</u>: Elise was an MD student who had registered for the Medical Student Summer Research Program (MSSRP). Since her project was focused on prostate cancer, I was responsible for teaching her cell culture techniques, RNA isolation, cDNA synthesis, Real-time PCR, and data analysis. I also helped her with immunofluorescence and phase contrast microscopy and also guided her to prepare the poster for the TTUHSC Annual Student Research Week 2016.

<u>Nita Kuttikandathil, 2016</u>: Nita was an MD student who had registered for the Medical Student Summer Research Program (MSSRP). Since her project was focused on prostate cancer, I was responsible for teaching her cell culture techniques, especially handling of cancer cell lines, molecular biology techniques like RNA isolation, cDNA synthesis, Real-time PCR, immunofluorescence and also data analysis. She is currently pursuing her Anesthesiology Resident at UT Health, San Antonio, TX.

<u>Prisca Pungwe, 2018</u>: Prisca was an MD student who joined my lab in June 2018 for the Medical Student Summer Research Program (MSSRP). Her research focus was to characterize the expression profile of PEPT1/SLC15A1 in pancreatic cancer cells. I taught her to culture pancreatic cancer cell lines, to prepare cell lysates from these cell lines, estimate protein concentration using BCA assay, prepare SDS-PAGE gels, to run Western blotting, and also to develop and analyse them. She is currently pursuing her Internal Medicine Resident at Baylor College of Medicine, Houston, TX.

<u>Justin Malin, 2021:</u> Justin is an MD student who joined my lab for the Medical Student Summer Research Program (MSSRP). In his project, he focused on the role of pancreatic stellate cells (PSCs) in pancreatic cancer progression and growth. As his summer research mentor, my responsibility was to guide him by giving a thorough explanation of the project

that he was working on, designing experiments and troubleshooting and also help in analyzing the data. He is currently continuing his MD program here at TTUHSC.

<u>Richard Zhu, 2022:</u> Richard is a first year MD student who joined my lab for the Medical Student Summer Research Program (MSSRP). In his project, Richard focused on studying whether blockade of SLC6A14 induces macropinocytosis in pancreatic cancer cells and if yes, whether targeting both SLC6A14 and macropinocytosis will lead to a better therapeutic outcome in pancreatic cancer. As his MSSRP mentor, my responsibility included giving a thorough explanation of the project that he was working on, designing experiments and troubleshooting and also help in analyzing the data. He is currently continuing his MD program here at TTUHSC.

Volunteers

<u>Abhilash Perisetti, 2016:</u> Abhilash was a resident from the Family Medicine at TTUHSC, Lubbock TX. He was interested in checking the expression of OCTN1 in Sirt3/WT vs. Sirt3/KO mice. He also wanted to know the effects of excess iron on hepatocytes. Therefore, my role was to teach him to culture and maintain cancer cell lines and also to teach him drug treatment. He also learned RNA isolation, cDNA synthesis, and Realtime PCR, Western blotting and data analysis under my guidance. He is currently working at the department of Gastroenterology and Hepatogy, at the University of Arkansas, Little Rock, AR.

<u>Yangjee Sherpa, 2019-2020</u>: Yangjee is a DDS from Kathmandu, Nepal and since her goal was to apply for dental school in the United States, she wanted to gain some research experience. She volunteered in my lab from for about a year and learned several techiques like culturing cancer cells, isolating RNA, running Real-time PCR, and preparing SDS-PAGE gels. She is currently pursuing her dental degree at University of Buffalo, Dental School at New York.

<u>Kate Jurek, 2022</u>: Kate is a third year MD student here at TTUHSC. Since she is interested to pursue her residency in neonatal gastroenterology, she is volunteering in my laboratory to gain a hands-on experience in research using pancreatic cancer cell lines.

Rotation Students

- 2023 Nghi Nyguen
- 2023 Tanima Sharker
- 2021 Mosharaf Mahmud-Syed
- 2021 Geetha Priya Boligala
- 2019 Tyler Sniegowski
- 2018 Bradley Schniers

ACADEMICALLY-RELATED PUBLIC SERVICE (10% effort)

TTUHSC Committees

2023-	Adhoc member, Tenure and Promotion committee
2022- 2024	Texas Tech University Health Sciences Center Faculty Appointments Committee
2022-2023	Texas Tech University Health Sciences Center Graduate Council Member
2019-2023	Texas Tech university Health Sciences Center Institutional Animal Care and Use Committee (TTUHSC IACUC) scientific voting member
2019-present	Cell Biology and Biochemistry, Faculty Recruitment Committee (Kayla Weitlauf Endowed Professor)
2018- present	GSBS Biotech Student Selection Committee Member, TTUHSC-SOM Committee Member
2022- present	GSBS PhD Student Selection Committee Member, TTUHSC-SOM Committee Member

Faculty Development Activities Attended

- 2022-2023 School of Medicine, Lessons, Life and Leadership faculty development course September 16, 2022, TTUHSC, Lubbock, TX
- 2022-2023 School of Medicine, Lessons, Life and Leadership faculty development course December 2, 2022, TTUHSC, Lubbock, TX
- 2022-2023 School of Medicine, Lessons, Life and Leadership faculty development course January 10, 2023, TTUHSC, Lubbock, TX
- 2019- 2020 School of Medicine, Lessons, Life and Leadership faculty development course June 8, 2020, TTUHSC, Lubbock, TX
- 2019-2020 School of Medicine, Lessons, Life and Leadership Seminar Series (L3) Faculty development course July 27, 2020, TTUHSC, Lubbock, TX
- 2019-2020 Lessons, Life and Leadership Seminar Series for Women Faculty in Academic Medicine, TTUHSC, Lubbock, TX

SCHOLARSHIP (55% effort)

Peer-reviewed publications (total of 57) (* indicates corresponding author) Google Scholar *h*-index: 29

- 1. Mallela, M.K., *Bhutia, Y.D., Suryanarayana, C., Rajni, V. and Reddy, M.C.S. (2006) Efficacy of conservative therapy in managing chronic renal failure in dogs. *Indian J Vet Med* **26**, 89-92.
- 2. ***Bhutia**, **Y. D.** (2007) Diagnosis, therapy and control of milk fever and ketosis in dairy animals. *Intas Polivet* **8**, 343-52.
- 3. *Bhutia, Y. D., and Rao, D. S. (2008) Clinicopathological study and therapeutic management of critically ill gastrointestinal tract emergencies in canine. *Indian J Vet Med* 28, 87-90.
- 4. **Bhutia**, **Y.D.**, Saini, M., Sharma, A.K., Sharma, B. and Swarup, D. (2009) Efficacy of Curcuma Longa extract against DMBA induced skin cancer in rats. *J App Animal Res* **36**, 291-296.
- Kang, N., Jun, A. H., Bhutia, Y. D., Kannan, N., Unadkat, J. D., and Govindarajan, R. (2010) Human equilibrative nucleoside transporter-3 (hENT3) spectrum disorder mutations impair nucleoside transport, protein localization, and stability. *J Biol Chem* 285, 28343-28352.
- 6. **Bhutia, Y. D.,** Hung, S. W., Patel, B., Lovin, D., and Govindarajan, R. (2011) CNT1 expression influences proliferation and chemosensitivity in drug-resistant pancreatic cancer cells. *Cancer Res* **71**, 1825-1835.
- Bhutia, Y. D., Hung, S. W., Krentz, M., Patel, D., Lovin, D., Manoharan, R., Thomson, J. M., and Govindarajan, R. (2013) Differential processing of let-7a precursors influences RRM2 expression and chemosensitivity in pancreatic cancer: role of LIN-28 and SET oncoprotein. *PLoS One* 8, e53436.
- Hung, S. W., Mody, H., Marrache, S., Bhutia, Y. D., Davis, F., Cho, J. H., Zastre, J., Dhar, S., Chu, C. K., and Govindarajan, R. (2013) Pharmacological reversal of histone methylation presensitizes pancreatic cancer cells to nucleoside drugs: in vitro optimization and novel nanoparticle delivery studies. *PLoS One* 8, e71196.
- 9. Ananth, S., Gnana-Prakasam, J. P., **Bhutia, Y. D.,** Veeranan-Karmegam, R., Martin, P. M., Smith, S. B., and Ganapathy, V. (2014) Regulation of the cholesterol efflux transporters ABCA1 and ABCG1 in retina in hemochromatosis and by the endogenous siderophore 2,5-dihydroxybenzoic acid. *Biochim Biophys Acta* **1842**, 603-612.
- 10. *Bhutia, Y. D., Babu, E., and Ganapathy, V. (2015) Interferon-gamma induces a tryptophan-selective amino acid transporter in human colonic epithelial cells and mouse dendritic cells. *Biochim Biophys Acta* **1848**, 453-462.

- Gopal, E., Babu, E., Ramachandran, S., Bhutia, Y. D., Prasad, P. D., and Ganapathy, V. (2015) Species-specific influence of lithium on the activity of SLC13A5 (NaCT): lithium-induced activation is specific for the transporter in primates. *J Pharmacol Exp Ther* 353, 17-26.
- Hung, S. W., Marrache, S., Cummins, S., Bhutia, Y. D., Mody, H., Hooks, S. B., Dhar, S., and Govindarajan, R. (2015) Defective hCNT1 transport contributes to gemcitabine chemoresistance in ovarian cancer subtypes: overcoming transport defects using a nanoparticle approach. *Cancer Lett* 359, 233-240.
- 13. **Bhutia, Y. D.,** Babu, E., Ramachandran, S., and Ganapathy, V. (2015). Amino Acid transporters in cancer and their relevance to "glutamine addiction": novel targets for the design of a new class of anticancer drugs. *Cancer Res* **75**, 1782-1788.
- 14. Bardhan, K., Paschall, A. V., Yang, D., Chen, M. R., Simon, P. S., Bhutia, Y. D., Martin, P. M., Thangaraju, M., Browning, D. D., Ganapathy, V., et al. (2015) IFNgamma Induces DNA Methylation-Silenced GPR109A Expression via pSTAT1/p300 and H3K18 Acetylation in Colon Cancer. *Cancer Immunol Res* 3, 795-805.
- 15. Babu, E., Bhutia, Y. D., Ramachandran, S., Gnanaprakasam, J. P., Prasad, P. D., Thangaraju, M., and Ganapathy, V. (2015) Deletion of the amino acid transporter Slc6a14 suppresses tumour growth in spontaneous mouse models of breast cancer. *Biochem J* 469, 17-23.
- 16. Gurav, A., Sivaprakasam, S., Bhutia, Y. D., Boettger, T., Singh, N., and Ganapathy, V. (2015) SIc5a8, a Na⁺-coupled high-affinity transporter for short-chain fatty acids, is a conditional tumour suppressor in colon that protects against colitis and colon cancer under low-fibre dietary conditions. *Biochem J* 469, 267-278.
- 17. **Bhutia, Y. D.,** and Ganapathy, V. (2015) Short, but smart: SCFAs train T cells in the gut to fight autoimmunity in the brain. *Immunity* **43**, 629-631.
- 18. Arjunan, P., Gnanaprakasam, J. P., Ananth, S., Romej, M. A., Rajalakshmi, V. K., Prasad, P. D., Martin, P. M., Gurusamy, M., Thangaraju, M., Bhutia, Y. D., and Ganapathy, V. (2016) Increased retinal expression of the pro-angiogenic receptor GPR91 via BMP6 in a mouse model of juvenile hemochromatosis. *Invest Ophthalmol Vis Sci* 57, 1612-1619.
- 19. Bhutia, Y. D., Babu, E., Ramachandran, S., Yang, S., Thangaraju, M., and Ganapathy, V. (2016) SLC transporters as a novel class of tumour suppressors: identity, function and molecular mechanisms. *Biochem J* **473**, 1113-1124.
- 20. **Bhutia**, **Y. D.**, Babu, E., and Ganapathy, V. (2016) Re-programming tumour cell metabolism to treat cancer: no lone target for lonidamine. *Biochem J* **473**, 1503-1506.
- 21. Bhutia, Y. D., and Ganapathy, V. (2016) Glutamine transporters in mammalian cells

and their functions in physiology and cancer. Biochim Biophys Acta 1863, 2531-2539.

- 22. Coothankandaswamy, V., Cao, S., Xu, Y., Prasad, P. D., Singh, P. K., Reynolds, C. P., Yang, S., Ogura, J., Ganapathy, V., and *Bhutia, Y. D. (2016) Amino acid transporter SLC6A14 is a novel and effective drug target for pancreatic cancer. *Br J Pharmacol* 173, 3292-3306.
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List of published work in My Bibliography

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Abstracts:

- Zhu, R., Rajasekaran, D. and Bhutia, Y.D. SLC6A14 blockade induces micropinocytosis as a compensatory mechanism for amino acid acquisition in pancreatic cancer cells. 35th Annual Student Research Week 2023, Texas Tech University Health Sciences Center, Lubbock TX. February 28-March 3, 2023.
- Mahmud Syed, M., Rajasekaran, D., Sniegowski, T. and Bhutia, Y.D. Studying the compensatory mechanism associated with SLC6A14 blockade in pancreatic cancer. 35th Annual Student Research Week 2023, Texas Tech University Health Sciences Center, Lubbock TX. February 28-March 3, 2023.
- 3. Sniegowski, T., Ganapathy, V. and **Bhutia, Y.D.** Investigating the tumor promoting role of SLC38A5 in pancreatic ductal adenocarcinoma. 35th Annual Student Research Week 2023, Texas Tech University Health Sciences Center, Lubbock TX. February 28-March 3, 2023.
- Korac, K., Rajasekaran, D., and Bhutia, Y.D. Carbidopa, an activator of aryl hydrocarbon receptor, suppresses IDO1 expression in pancreatic cancer and decreases tumor growth. [abstract]. In: Proceedings of the AACR Special Conference: Precision Prevention, Early Detection, and Interception of Cancer; 2022 Nov 17-19; Austin, TX. Philadelphia (PA): AACR; Can Prev Res 2023;16(1 Suppl): Abstract nr P052.
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- Sniegowski, T., Ganapathy, V., and Bhutia, Y.D. SLC38A5 characterization and its tumor promoting role in pancreatic ductal adenocarcinoma. [abstract]. In: Proceedings of the AACR Special Conference: Precision Prevention, Early Detection, and Interception of Cancer; 2022 Nov 17-19; Austin, TX. Philadelphia (PA): AACR; Can Prev Res 2023;16(1 Suppl): Abstract nr P005.
- 7. Sniegowski, T., Ganapathy, V., and **Bhutia, Y.D.** SLC38A5 characterization and its tumor promoting role in pancreatic ductal adenocarcinoma. In: Fifth Annual Abilene Interdisciplinary Symposium on Cancer and Biomedical Research; September 9, 2022.
- 8. Sniegowski, T. and **Bhutia, Y.D.** Tumor promoting role of SLC38A5 in pancreatic ductal adenocarcinoma. 34th Annual Student Research Week 2022, Texas Tech University Health Sciences Center, Lubbock TX. March 8-11, 2022.
- Korac, K. and Bhutia, Y.D. Carbidopa, an activator of aryl hydrocarbon receptor, suppresses IDO1 expression in pancreatic cancer and decreases tumor growth. 34th Annual Student Research Week 2022, Texas Tech University Health Sciences Center, Lubbock TX. March 8-11, 2022.

- 10. Schniers, B.K. and **Bhutia, Y.D.** PEPT1 is essential for the growth of pancreatic cancer cells: A viable drug target. 34th Annual Student Research Week2022
- Sniegowski T, and Bhutia YD. (2021). Expression profile and functional characterization of SLC38A5 in pancreatic ductal adenocarcinoma. 33rd Annual Student Research Week 2021, Texas Tech University Health Sciences Center, Lubbock TX. March 9-12, 2021.
- 12. Korac K, and **Bhutia YD.** (2021). Carbidopa as a novel and targeted single agent chemo-immunotherapy for pancreatic cancer.33rd Annual Student Research Week 2021, Texas Tech University Health Sciences Center, Lubbock TX. March 9-12, 2021.
- Schniers BK, and Bhutia YD. (2021). PepT1: tumor promoter and novel drug target treat pancreatic cancer. 33rd Annual Student Research Week 2021, Texas Tech University Health Sciences Center, Lubbock TX. March 9-12, 2021.
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- 15. Korac K, and **Bhutia YD.** (2020). Carbidopa as a novel and targeted single agent chemo-immunotherapy for pancreatic cancer. 32nd Annual Student Research Week 2020, Texas Tech University Health Sciences Center, Lubbock TX. March 10-13, 2020.
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- Bhutia YD, Ellappan B, Singh PK, Ganapathy V. (2015). Amino acid-based prodrugs of gemcitabine - a therapeutic option to overcome chemoresistance in pancreatic cancer. [abstract]. In: Proceedings of the 106th Annual Meeting of the American Association for Cancer Research; 2015 Apr 18-22; Philadelphia, PA. Philadelphia (PA): AACR; Cancer Res 2015;75(15 Suppl):Abstract nr 348.
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- 32. **Bhutia YD**, Patel B, Hung SW, Lovin D, and Govindarajan R. (2010). CNT1 expression influences proliferation and chemosensitivity in drug-resistant pancreatic cancer cells. AAPS workshop on drug transporters in ADME: From the bench to bedside, Bethesda, MD, March 14- March 16.
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- 34. **Bhutia YD**, Patel B, Hung SW, Lovin D, and Govindarajan R. (2010). Human concentrative nucleoside transporter-1 (hCNT1) regulates pancreatic cancer cell proliferation and improves gemcitabine efficacy. 2010 AAPS Annual meeting and exposition /FIP pharmaceutical sciences world congress, New Orleans, Louisiana, November 14- November 18.
- 35. Kent JM, **Bhutia YD**, Govindarajan R. (2009). Profiling, localization and function of nucleoside transporter expression in pancreatic cancer. 2009 AAPS Annual meeting and exposition, Los Angeles, California, November 8- November 12 (Abst. #R6103).
- 36. Cummins S, Patel B, **Bhutia YD**, and Govindarajan R. (2009). Diminution of concentrative nucleoside transporter 1 (CNT1) activity in human ovarian cancer cells: subtype-dependent gemcitabine response to exogenously expressed hCNT1. UGA conference on drug discovery, November 5, 2009.
- 37. Bhutia YD, Patel B, and Govindarajan R. (2009). Cell cycle dependent expression of

nucleoside transporters regulates gemcitabine transport in human pancreatic cancer cells. UGA conference on drug discovery, November 5, 2009.

Poster Presentations:

- 1. University of Georgia conference on Drug Discovery, November 2009, Athens GA
- 2. AAPS Annual meeting and exposition, November 2009, Los Angeles, California
- American Association of Pharmaceutical Sciences (AAPS) Annual meeting and exposition /FIP pharmaceutical sciences world congress, November 2010, New Orleans, Louisiana
- 4. American Association of Pharmaceutical Sciences (AAPS) workshop on drug transporters in ADME: From the bench to bedside, March 2011, Bethesda, MD
- 5. American Association for Cancer Research (AACR) Annual Meeting April 2012, Chicago, IL
- 6. American Association for Cancer Research (AACR) Annual Meeting April 2012, Washington, DC
- 7. American Association for Cancer Research (AACR) Annual Meeting April 2014, San Diego, California
- 8. AAPS Annual meeting and exposition, Denver, CO November 13- November 17, 2016
- 9. American Association for Cancer Research (AACR) Annual Meeting March 29-April 3, 2019, Atlanta, GA
- 10. Biomedical Transporters Conference 2019, Lucerne, Switzerland. August 4-8, 2019.
- 11. 31st Annual Student Research Week 2019, Texas Tech University Health Sciences Center, Lubbock TX. March 19-22, 2019.
- 12. 32nd Annual Student Research Week 2020, Texas Tech University Health Sciences Center, Lubbock TX. March 10-13, 2020
- 13. 33rd Annual Student Research Week 2021, Texas Tech University Health Sciences Center, Lubbock TX. March 9-12, 2021.
- 14. 34th Annual Student Research Week 2022, Texas Tech University Health Sciences Center, Lubbock TX. March 8-11, 2022.
- 15. 35th Annual Student Research Week 2023, Texas Tech University Health Sciences Center, Lubbock TX. February 28- March 3, 2023.

Invited Seminars and talks:

- 1. Amino acid transporter SLC6A14 is a unique drug target for pancreatic cancer. Cell Biology and Biochemistry, Texas Tech University Health Sciences Center, Lubbock TX. September 21, 2022.
- 2 Cell cycle dependent expression of nucleoside transporters regulates gemcitabine transport in human pancreatic cancer cells. University of Georgia, School of Pharmacy, Athens, GA. November 5, 2010.
- 3. CNT1 expression influences proliferation and chemosensitivity in drug-resistant pancreatic cancer cells. AAPS workshop on drug transporters in ADME: From the bench to bedside, Bethesda, MD, March 14- March 16, 2010. *Invited Podium*

Presentation.

- 4. Cell cycle dependent expression of nucleoside transporters regulates gemcitabine transport in human pancreatic cancer cells. Medical College of Georgia, Department of Biochemistry and Molecular Biology, Augusta GA. December 5, 2010. Host: Dr. V. Ganapathy. *Invited talk*, December 5, 2010.
- 5. SLC6A14 for pancreatic cancer for chemotherapy and drug delivery. Department of Cell Biology and Biochemistry, Texas Tech University Health Sciences Center, Lubbock, TX, February 8, 2016.
- 6. SLC6A14 as a tumor promoter for pancreatic cancer. Department of Immunology and Molecular Microbiology, Texas Tech University Health Sciences Center, Lubbock, TX, February 8, 2016. Host: Dr. Robert Bright. *Invited talk*, December 12, 2018.
- 7. SLC6A14 as a molecular target for metformin and its relevance to the therapeutic potential of the drug for pancreatic cancer. Biomedical Transporters Conference 2019, Lucerne, Switzerland. August 4-8, 2019. *Invited Podium Presentation.*
- 8. SLC6A14 as a unique drug target for pancreatic cancer treatment. Ritsumeiken University, Graduate School of Pharmaceutical Sciences, Nojihigashi, Kasatsu, Shiga, Japan. *Invited talk*, June 11, 2020 (Cancelled due to COVID-19).
- 9. SLC6A14 is a tumor promoter and a novel drug target for pancreatic cancer. Center for Membrane Protein Research, Texas Tech University Health Sciences Center, Lubbock TX. *Invited talk*, October 28-29, 2021.
- 10. Validation of the amino acid transporter SLC6A14 as an actionable drug target for pancreatic cancer. Cell Biology and Biochemistry, Texas Tech University Health Sciences Center, Lubbock TX. September 9, 2021.

Highlights of my Professional Achievement

- 1. The first seminal discovery that I made in the field of pancreatic cancer was the involvement of the concentrative nucleoside transporter CNT1 in susceptibility and resistance to the anticancer drug gemcitabine. Nucleoside transporters are critical for the efficacy of nucleoside derivatives (e.g., gemcitabine) for treatment of pancreatic cancer because these transporters deliver these drugs into cancer cells. Decreased expression of these transporters renders pancreatic cancer resistant to such drugs. Until recently, only the equilibrative nucleoside transporter ENT1 has been implicated in gemcitabine resistance. My research discovered that the concentrative nucleoside transporter CNT1 also plays a critical role in this phenomenon. This work on the relationship between expression of CNT1 and chemosensitivity in pancreatic cancer cells was published in *Cancer Research*; this publication caught significant attention from cancer biologists as evident from its selection in *Cancer Research* for *Breaking Advances: Highlights from Recent Cancer Literature*.
- 2 Next, I examined the relevance of miRNAs in chemoresistance in pancreatic cancer.

In addition to the nucleoside transporters, intracellular enzymes that activate gemcitabine or the enzymes that are targets for gemcitabine also play a role in gemcitabine resistance. Ribonucleotide reductase as a target for the triphosphate derivative of gemcitabine underlies the anticancer effect of gemcitabine in pancreatic cancer. I discovered that miRNA *Let-7a* targets the modulatory subunit of ribonucleotide reductase and contributes to gemcitabine resistance. This work was published in *PLoS One*.

- 3. I further discovered that SLC6A14, an amino acid transporter with a broad substrate selectivity is significantly upregulated in human pancreatic cancer and blocking its function with alpha methyl-L-tryptophan (*a*-MLT) leads to amino acid deprivation and inhibition of mTORC1 signaling pathway in tumor cells. The paper highlighting the role of SLC6A14 as a potential drug target for treatment of pancreatic cancer was published in *British Journal of Pharmacology*. My laboratory has made significant progress in terms of SLCA614 as a drug target for pancreatic cancer. Our recent findings show that genetic deletion or pharmacological blockade of SLC6A14 in *LSL-Kras*^{G12D/+}; *LSL-p53*^{R172H/+}; *Pdx-1 Cre* (KPC) mouse, a spontaneous mouse model of pancreatic cancer significantly improves their survival and also delays tumor growth. Based on our study, SLC6A14 is definitely a unique drug target for cancer therapy.
- 4. Tryptophan is not only an essential amino acid but also an effective signaling molecule as an indicator of amino acid sufficiency. It is catabolized by indoleamine 2,3dioxygenase 1 (IDO1) with kynurenine as one of the final end products. IDO1 induced in one cell type can impact on a neighboring cell type through rapid degradation of tryptophan in IDO1-positive cells thereby causing depletion of extracellular tryptophan. This is the mechanism responsible for the ability of IDO1- expressing antigenpresenting immune cells to suppress proliferation of effector T cells. Antigenpresenting immune cells in tumor-draining lymph nodes express high levels of IDO1 because of the signaling cues from the tumor cells themselves. In fact, pharmacological inhibitors of IDO1 (e.g., 1-methyltryptophan) are in clinical trials in cancer immunotherapy. An often-overlooked component of this mechanism is the transport process in the plasma membrane of IDO1-positive cells that delivers extracellular tryptophan to the intracellular IDO1. I have been focusing on this particular aspect of tumor immunology as well and was successful in discovering the existence of a transporter selective for tryptophan (TrpT) in dendritic cells at the functional level. This work was published in Biochim Biophys Acta.
- 5. Repurposing FDA-approved drugs as an anticancer agent is a very attractive strategy. If the drug possesses anticancer property translating them into clinics will be lot easier since the PK/PD and the toxicity test has already been done. With this quest, I was able to identify Carbidopa, an FDA-approved drug for Parkinson's disease as a potential anticancer agent. Carbidopa has the ability to kill pancreatic cancer cells by activating aryl hydrocarbon receptor (AhR). This work was selected for a *commentary* by the *Biochemical Journal* and also formed a *Cover Photo* in the journal. In fact, this worked received a lot of attention and therefore was press released.
- 6. One of the highlights of my professional achievement is the establishment of the LSL-

Kras^{G12D/+}; *LSL-p53*^{R172H/+}; *Pdx-1 Cre* (KPC) mouse, a spontaneous mouse model of pancreatic cancer in Slc6a14 knockout background. Using the KPC mice in both Slc6a14 wildtype and knockout backgrounds, we have recently shown that deletion of Slc6a14 in this mouse attenuates pancreatic cancer growth, decreases the metastatic spread of the tumor, reduces ascites fluid accumulation, and improves overall survival. At the molecular level, we show lower proliferation index and reduced desmoplastic reaction following Slc6a14 deletion. This work was published in *Biochemical Journal* and also formed a *Cover Photo* in the journal.

7. Our latest finding includes identification of SLC38A5 as a tumor promoter in pancreatic cancer. This amino acid transporter with a narrow substrate selectivity is highly upregulated in pancreatic cancer. Using CRISPR-Cas9 mediated knockout, we have demonstrated that the loss of SLC38A5 significantly impacts tumor growth in athymic nude mice. More interestingly, we find that the loss of SLC38A5 impacts oxidative phosphorylation and glycolysis in the pancreatic cancer cells. This work was published in *Scientific Reports*.

Research Funding

Completed and Current Support:

a. Local but not from TTUHSC

- 1. School of Medicine Research Collaboration Fund on January 15, 2024. Guan (Principal Investigator) and **Bhutia (Co-Principal Investigator)**; Development of novel tools for analyzing cancer-related molecules. Funded; \$10,000 for 1 year.
- 2. The <u>CH</u> Foundation; January 2022 December 2022, **Bhutia YD** (Principal Investigator) Repurposing metformin as a novel chemotherapeutic agent to treat pancreatic cancer, 30% effort, \$75,000.
- Laura W. Bush Institute for Women's Health and UMC Health System, Women's Health Seed Grant, January 2021 – December 2021, **Bhutia YD (Principal Investigator)** Role of HPV16 Protein, E6/E7 in regulating SLC6A14 expression in cervical cancer, 30% effort, \$20,000.
- Laura W. Bush Institute for Women's Health and UMC Health System, Women's Health Seed Grant, January 2018 – December 2018, Bhutia YD (Principal Investigator); Nair A (Co-Investigator) SLC6A14 and GPR81 in the pap smear derived cells as predictive biomarker for early detection of cervical dysplasia/cancer, 30% effort, \$20,000.
- 5. The <u>CH</u> Foundation; January 2017 December 2017, **Bhutia YD** (**Principal Investigator**) Therapeutic potential of Carbidopa for treatment of pancreatic cancer as a single-agent for chemotherapy, 30% effort, \$75,000.
- South Plains Foundation (SPF), September 2016 August 2017, Bhutia YD (Principal Investigator) Therapeutic potential of Carbidopa for treatment of pancreatic cancer as a single-agent for chemotherapy, 100% effort, \$15,000.

b. <u>State and/or regional</u>

1. CPRIT-TREC 2021 with Dr. Reynolds (Program Director), August 2021- July 2023, **Bhutia YD (Principal Investigator for a subproject)** Alpha-methyl-L-tryptophan as a novel agent to treat pancreatic cancer, 40% effort, \$310,000/2 years.

c. National and/or international

- 1. 1 R01 CA262420-01A1; 05/12/2023-04/30/2028, **Bhutia (Principal Investigator);** Sharma (Co-Investigator); Yang (Co-Investigator) SLC6A14 as a unique drug target to treat pancreatic cancer, 40% effort, \$1,760,323.
- 2. 1 R21 CA277140-01; 12/16/2022-11/30/2024, **Bhutia (Co-Investigator);** Ganapathy (Principal Investigator). Amino acid transporter SLC38A5 as a drug target for TNBC: Evaluation with genetic and pharmacologic approaches.
- 3. National Institutes of Health (NIH), 1 R03 CA223271-01A1, January 2018 December 2020, **Bhutia YD (Principal Investigator)** Carbidopa as an inhibitor of the Trp/(IDO1) functional complex: A novel immunotherapy agent, 25% effort, \$153,000.
- Abbot Nutrition; May 2017 December 2017, Ganapathy V (Principal); Bhutia YD (Co-Investigator) Transport mechanisms for 3-hydroxy-3-methylbutyrate in mammalian cells, 30% effort, \$46,000.
- Abbot Nutrition; May 2016 December 2016, Bhutia YD (Principal Investigator) Identification of transporters for 3-hydroxy-3-methylbutyrate (HMB) Part 2, 30% effort, \$43,550.

Grants submitted and pending approval

1. Grant submitted to CPRIT-HIHR on January 5, 2024. Guan (Principal Investigator) and **Bhutia (Co-Investigator)**; Development of novel tools for analyzing cancer-related molecules. \$45,000 for 2 years.

Grants submitted but not funded Full Applications:

- National Institute of Health; NIH R21CA201654-01; submitted on 02/18/2015, Bhutia YD (Principal Investigator); Babu E (Co-Investigator) Strategic use of transporters to reverse gemcitabine resistance in pancreatic cancer. 40% effort, \$275,000. <u>Impact score:</u> <u>40 & Percentile: 31.</u>
- National Institute of Health; NIH R15 CA202046-01; submitted on 02/19/2015, Bhutia YD (Principal Investigator); Babu E (Co-Investigator) Carbidopa as a novel single-agent chemo-immunotherapy drug for pancreatic cancer. 30% effort, \$300,000. <u>Impact score:</u> <u>31.</u>
- 3. Department of Defense, DoD Breakthrough Award Funding Level 3 PC150537; submitted

on 06/25/2015, Ganapathy V (Principal Investigator), **Bhutia YD (Co-Investigator)** Chronic exposure to excess iron in prostate cancer drives tumor growth. 20% effort, \$573,750. <u>Overall Evaluation Score: 2.3.</u>

- Department of Defense; DoD Concept Award LC150581, submitted on 06/26/2015, Bhutia YD (Principal Investigator) Chronic exposure to excess iron promotes lung cancer and metastasis via heme-dependent suppression of p53. 50% effort, \$153,000. <u>Score: 1.5.</u>
- National Institute of Health; NIH R21 CA205490-01, submitted on 06/26/2015, Bhutia YD (Principal Investigator); Ganapathy V (Co-Investigator); Wachtel M (Co-Investigator) Hemochromatosis in pancreatic cancer suppresses p53 and induces drug resistance. 20% effort, \$275,000. <u>Not Discussed.</u>
- CPRIT HIHR RP160754, submitted on 10/08/2015, Bhutia YD (Principal Investigator); Ganapathy V (Co-Investigator); Wachtel M (Co-Investigator), The amino acid transporter SLC6A14 drives pancreatic cancer and represents a novel selective drug for this difficultto-treat cancer. 20% effort, \$275,000. <u>Overall Evaluation Score: 6.0.</u>
- National Institute of Health; NIH R21 CA201654-01A1, submitted on 11/05/2015, Bhutia YD (Principal Investigator); Babu E (Co-investigator) Strategic use of transporters to reverse gemcitabine resistance in pancreatic cancer. 50% effort, \$275,000. <u>Not</u> <u>Discussed.</u>
- Department of Defense, DoD Breakthrough Award Funding Level 3 BC151170; submitted on 12/23/2015, Ganapathy V (Principal Investigator), Bhutia YD (Co-Investigator) A novel and effective dual-target chemo-immunotherapy agent for breast cancer. 20% effort, \$3,742,005. <u>Overall Evaluation Score: 2.3.</u>
- National Institute of Health; NIH 1 R21 TR001724-01, submitted on 01/11/2016, Bhutia YD (Principal Investigator); Babu E (Co-investigator) Carbidopa as a single-agent, dualtarget chemo-immunotherapy drug for pancreatic cancer. 40% effort, \$275,000. <u>Impact</u> <u>Score: 40.</u>
- 10. American Association of Pharmaceutical Scientists; AAPS Foundation New Investigator Grant, submitted on 03/21/2016, **Bhutia YD (Principal Investigator)** Alpha-methyl-L-DOPA, an FDA-approved drug, as a novel agent for pancreatic cancer. 40% effort, \$40,000. <u>Not Funded.</u>
- Department of Defense, DoD Breakthrough Award Funding Level 1 BC160532; submitted on 05/05/2016, Ganapathy V (Principal Investigator), Bhutia YD (Co-Investigator) BCRP guards against breast cancer via promotion of p53 function and ferroptosis. 20% effort, \$573,750. <u>Overall Evaluation Score: 1.6.</u>
- 12. CPRIT HIHR RP170758; submitted on 01/13/2017, **Bhutia YD (Principal Investigator)**, Filleur S (Co-investigator) Hemochromatosis drives prostate cancer: A golden opportunity for cancer prevention. 30% effort, \$200,000. <u>Overall Evaluation Score: 5.0.</u>

- National Institute of Health; NIH 1 R03 CA223271-01; submitted on 02/21/2017, Bhutia YD (Principal Investigator) Carbidopa as an inhibitor of the TrpT/IDO1 complex: Potential for use as an immunotherapy agent? 15% effort, \$100,000. <u>Impact Score: 31.</u>
- 14. Presidents' Collaborative Research Initiative (PCRI); submitted on 06/23/2017, Bhutia YD (Principal Investigator); Masoud ZM (Co- investigator) Synergistic lethality of Carbidopa and Metformin in pancreatic cancer via metabolomics reprogramming. 15% effort, \$48,365.80. <u>Not Funded.</u>
- Pancreatic Cancer Action Network, Catalyst Grant, Proposal ID: 569328; submitted on 12/31/2017, Bhutia YD (Principal Investigator) SLC6A14 is a novel and effective drug target for pancreatic cancer. 40% effort, \$500,000. <u>Not Funded.</u>
- 16. CPRIT HIHR RP180799; submitted on 01/29/2018, Bhutia YD (Principal Investigator); Filleur S (Co-Investigator) Hemochromatosis drives prostate cancer: A golden opportunity for cancer prevention in a sizeable population. 30% effort, \$200,000. <u>Overall Evaluation</u> <u>Score: 4.3.</u>
- 17. CPRIT HIHR RP190572; submitted on 01/25/2019, **Bhutia YD (Principal Investigator)** Pancreatic organoids as models to identify novel and effective blockers of SLC6A14 to treat pancreatic cancer. 30% effort, \$250,000. <u>Overall Evaluation Score: 4.3.</u>
- 18. National Institute of Health; NIH 1R01 CA248153-01; submitted on 06/04/2019, Bhutia YD (Principal Investigator); Ganapathy V (Co-Investigator); Wachtel M (Co-Investigator) SLC6A14 as a unique drug target to treat pancreatic cancer. 40% effort, \$1,927,615. <u>Impact Score: 41; Percentile: 41.</u>
- 19. American Cancer Society Research Scholar Grants; Proposal ID:681379; submitted on 10/11/2019, **Bhutia YD (Principal Investigator)** SLC6A14 as a unique drug target to treat pancreatic cancer. 10% effort, \$789,066. *Not Funded*.
- 20. National Institute of Health; 1 R03 CA252257-01; submitted on 10/21/2019, Bhutia YD (Principal Investigator) Pancreatic organoids as models to identify novel and effective blockers of SLC6A14 to treat pancreatic cancer. 10% effort, \$100,000. <u>Impact Score: 35.</u>
- 21. National Institute of Health; 1 R01 CA248153-01A1; submitted on 03/03/2020, Bhutia YD (Principal Investigator); Yang S (Co-Investigator); Wachtel M (Co-Investigator) SLC6A14 as a unique drug target to treat pancreatic cancer. 40% effort, \$1,923,903. Impact Score:38 & Percentile: 29.
- 22. National Institutes of Health (NIH), R41; submitted on 04/06/2020, Bhutia YD (Principal Investigator) Alpha-methyl-L-tryptophan as an anti-obesity drug: Potential benefits of combination with Carbidopa. 15% effort, \$88,036. <u>Not Funded.</u>
- 23. National Institute of Health; 1 R03 CA252257-01A1; submitted on 06/24/2020, Bhutia YD (Principal Investigator) Pancreatic organoids as models to identify novel and effective blockers of SLC6A14 to treat pancreatic cancer. 10% effort, \$100,000. <u>Not Discussed.</u>

- 24. Department of Defense (DoD), Idea Award CA200293; submitted on 08/27/2020, Ganapathy V (Principal Investigator); Bhutia YD (Co-Investigator) Synergism between citrate and iron shields liver cancer from ferroptosis: Evaluation of SLC13A5 as a novel drug target in a humanized mouse. 15% effort, \$765,000. <u>Score: 2.1</u>.
- 25. National Institute of Health; 1 R01 CA262420-01; submitted on 10/05/2020, **Bhutia** YD (**Principal Investigator**); Yang S (Co-Investigator); Wachtel M (Co-Investigator) SLC6A14 as a unique drug target to treat pancreatic cancer. 40% effort, \$1,923,903. Impact Score:43 & Percentile: 42.
- 26. RP210124-CPRIT-HIHR; submitted on January 2021, Bhutia YD (Principal Investigator); Pruitt K (Co-Investigator) Pancreatic stellate cells and Wnt/Beta-catenin pathway: A dynamic duo regulate SLC6A14 and promote pancreatic tumorigenesis, 20% effort, \$250,000. <u>Overall Evaluation Score: 4.7.</u>
- 27. National Institutes of Health (NIH), R21, 2020, **Bhutia (Co-Investigator)** A Na-coupled transporter for amyloid peptides: Role in brain clearance of Abeta in health and disease, 15% effort. *Not Discussed.*
- 28. National Institutes of Health (NIH), R21, 2020, **Bhutia (Co-Investigator)** Urinary citrate/sarcosine ratio: A logical and mechanistically based biomarker for metastatic prostate cancer in bone, 10% effort. *Impact Score: 40 & Percentile: 32.*
- 29. DoD PC190209, submitted on 09/19/2019, Ganapathy (Principal Investigator); Bhutia Y (Co-Investigator) Urinary citrate/sarcosine as a novel and mechanistically based biomarker for metastatic prostate cancer in bone. 10% effort. <u>Average Score: 2.3.</u>
- 30.RP220272 CPRIT-IIRA; submitted on June 2021, **Bhutia YD** (Principal Investigator); Grisham M (Co-Investigator); Bickel U (Co-Investigator) Alpha-methyl-L-tryptophan and Carbidopa as a novel and targeted dual-agent chemo-immunotherapy for pancreatic cancer treatment, 20% effort, \$914,510. <u>Overall Evaluation Score: 4.6.</u>
- 31.1 R01 CA269628-01; submitted on June 2021, Bhutia YD (Principal Investigator); Grisham M (Co-Investigator); Bickel U (Co-Investigator) Alpha-methyl-L-tryptophan and Carbidopa as a novel and targeted dual-agent chemo-immunotherapy for pancreatic cancer treatment, 40% effort, \$1,530,000. <u>Not discussed</u>.
- 32.1 R21 CA263116-01A1; SLC38A5, a glutamine/serine/glycine transporter and WNT/DVL1 target, selectively promotes TNBC, revised grant application submitted in June 2021, Ganapathy, V (Principal Investigator); Bhutia, YD (Co-Investigator with 10% effort). The original application received a priority score of 40 (Percentile, 29), \$275,000.
- 33.1 R01 DK132048-01; SLC6A14 deficiency and diet-induced obesity/fatty liver: Mechanism and treatment, submitted in June 2021, Ganapathy, V (Principal Investigator); Bhutia, YD (Co-Investigator with 20% effort), \$1,000,000.
- 34. Grant submitted to Hirshberg Foundation for Pancreatic Cancer Research on 08/15/2023. **Bhutia (Principal Investigator)**; Kai (Principal Investigator); Development

of SLC6A14 blockers for pancreatic ductal adenocarcinoma (PDAC) treatment. \$50,000 for 1 year.

Letter of Intent/Pre-applications:

- 35. Department of Defense; DoD Idea Award Pre-application CA150390, submitted on 08/25/2015, **Bhutia YD (Principal Investigator)** Impact of excess iron on the tumor suppressor p53 and on epigenetic:EL Kras/Hfe-/- mouse as an innovative model for pancreatic cancer. *Not Invited*.
- 36. Department of Defense; Idea Development Award DoD PC160692, submitted on 06/23/2016, Ganapathy (Principal Investigator); Bhutia YD (Co-Investigator) Carbidopa, an FDA-approved drug for Parkinson's disease as an effective dual-target, chemo-immunotherapy agent for pancreatic cancer. <u>Not Invited.</u>
- 37. DoD Idea Development Award Pre-application PC171041; submitted on 07/14/2017, Bhutia YD (Principal Investigator) Carbidopa for treatment of both androgen-sensitive and androgen-refractory prostate cancer via multiple modes of action. <u>Not Invited.</u>
- 38. AACR NextGen Grants for Transformative Cancer Research LOI; submitted on 09/22/2017, Bhutia YD (Principal Investigator) Carbidopa as a novel single agent, multi- target anticancer drug. <u>Not Invited.</u>
- 39. Department of Defense; Breakthrough Award DoD BC171024, submitted on 06/09/2017, Ganapathy V (Principal Investigator); Bhutia (Co-Investigator) Carbidopa for breast cancer: chemotherapy, immunotherapy and hormone therapy all in one drug. <u>Not Invited.</u>
- 40.REACH Grant program at Texas The University; submitted on 03/18/2019, **Bhutia YD** (**Principal Investigator**) α-Methyltryptophan as a novel single-agent chemoimmunotherapy drug for pancreatic cancer. <u>Not Invited</u>.
- 41. Juvenile Diabetes Research Foundation; JDRF LOI Submission Number:201307408; submitted on 08/05/2019 **Bhutia YD (Principal Investigator).** <u>Not Invited.</u>
- 42. DoD Preapplication PA200369 Translational Research Partnership Award; submitted on 08/25/2020, Bhutia YD (Principal Investigator); Rehman R (Co-Investigator); Chedella NKS (Partnering PI). Alpha-methyl-L-tryptophan as a novel therapeutic agent to treat pancreatic cancer. <u>Not Invited.</u>
- 43. DoD Preapplication PA200266 Idea Development Award; submitted on 08/25/2020, Bhutia YD (Principal Investigator) Pancreatic stellate cells and Wnt/Beta-catenin pathway: A dynamic duo regulate SLC6A14 and promote pancreatic tumorigenesis. <u>Not</u> <u>Invited.</u>
- 44. DoD Preapplication PA210310 Idea Development Award; submitted on 07/01/2021, Bhutia YD (Principal Investigator) Lactate in the tumor microenvironment as a signaling molecule for the induction of PEPT1 to drive pancreatic cancer growth and progression. <u>Not Invited.</u>

45. PA230205, submitted to DoD PCARP Pre-Application, **Bhutia (Principal Investigator)**; Kai, (Co-Investigator); Development of highly potent SLC6A14 blockers for pancreatic ductal adenocarcinoma (PDAC) treatment. Submitted on -07/10/2023. Status: Not Invited.

Patents:

- Patent No, US 10,064,834 B2, Carbidopa for the treatment of cancer. <u>Inventers</u>: Vadivel Ganapthy, Yangzom D. Bhutia, Babu Ellappan, Sabarish Ramchandran.
- 2. U.S. Provisional Patent Application No. 63/134,230. Alpha methyl-L-tryptophan as an orally active drug for weight loss and diet-induced diabetes, insulin resistance and metabolic syndrome. Assignors: Vadivel Ganapathy, Sathish Sivaprakasam, Yangzom D. Bhutia, and Sabarish Ramachandran.