BIOGRAPHICAL SKETCH

NAME: Sharma, Dr. Saurabh

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

POSITION TITLE: Post-Doctoral Scholar

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)	END DATE MM/YYYY	FIELD OF STUDY
Manipal Academy of Higher Education, Pharmacy, Manipal, Karnataka	B.Pharm	05/2013	Pharmacy
Gujarat Technological University, Pharmaceutics, Ahmedabad, Gujarat	M.Pharm	05/2015	Pharmaceutics
Birla Institute of Technology & Science Pilani, Pharmaceutical Science, Pilani, Rajasthan	Ph.D.	12/2020	Pharmaceutical Science
Terasaki Foundation, Terasaki Institute For Biomedical Innovation, Los Angeles, California	Postdoctoral Fellow	11/2022	Brain Targeted Nanoparticles mediated Immunotherapy for Cancer Treatment
Department of General and Vascular Surgery, School of Medicine, Stanford University, Stanford, Palo Alto, California	Postdoctoral Fellow	present	Nanoparticles mediated combination Immunotherapy for Melanoma-Brain-Metastasis Treatment

A. Personal Statement

In advanced pre-clinical research, I developed the expertise and training to design innovative nanoparticles to treat metastatic cancer. I worked on nano-drug engineering, synthesis, and delivery for cancer treatment during my Ph.D. degree at Birla Institute of Science and Technology (BITS-PILANI) in India. I designed and synthesized targeted microRNA, siRNA and chemotherapeutic containing nanoparticles medicines for various tumors and delivered them through cellular and subcellular biological barriers using a unique multifunctional cationic drug delivery nanoplatform. As a postdoctoral chemist and pharmacologist as my first postdoctoral research, I worked under the mentorship of Chief Executive Officer, Founding Director, Paul I. Terasaki Distinguished Professor **Prof. Ali Khademhosseini** and **Prof. Eggehard Holler** at Terasaki Institute for Biomedical Innovation, Los Angeles, California.

I develop strategies to transport immunotherapeutic molecules across the blood-brain barrier for imaging and treating brain cancer. Currently, under the mentorship of **Dr. Amanda Kirane**, I have continued my work in cancer-targeted nanotechnology as a post-doctoral researcher at General and Vascular Surgery, School of Medicine, Stanford University, Stanford, California, USA for the treatment of melanoma brain metastases. Immunotherapy, gene therapy, and chemotherapy are my specialties. I design innovative nanomedicines, such as nanoparticles, for preclinical and clinical use and open new modalities and methods for nanodrug manufacturing and systemic delivery to melanoma brain metastases and recipient immune cells. We work in an excellent multidisciplinary team of melanoma oncologists, chemists, pharmacologists, cell and cancer biologists and immunologists with complementary competence to cover all programmatic areas. I'm excited to be the project's PI and convinced that my skills will enable this unique nano-immune therapy concept for these grants and fellowship and seed grant Awards.

Peer-reviewed National Abstracts:

1. Brain Targeted Combinational Aurigene-012 Polymeric Nano-conjugates Specialized for Checkpoint-refractory Melanoma Brain Metastasis, Society for Melanoma Research (SMR) 20th International Congress, 2023, Philadelphia, PA.
2. AXL-targeted macrophage phenotype switching mediates immunotherapy-resistance in melanoma, SITC 2023 Annual Meeting, San Diego, CA.
3. Blood Brain Barrier (BBB) targeted NP-12-Polycefin™ Nanoconjugate as an Immunotherapeutic Agent Against Glioblastoma Multiforme, 8th Nano Today Conference 2023, San Diego, CA.

4. Immune Phenotype and iFRET Functional Analysis are biomarkers of response to Neoadjuvant Intralesional Therapy for High Risk Stage II Melanoma, Society for Melanoma Research (SMR) 20th International Congress, 2023, Philadelphia, PA.

Patents and Publications:

a. A Lipid-Polymer Hybrid Nanoparticle. D Chitkara, SS Pukale, AK Singh, A Mittal, **S Sharma,** US Patent App. 17/284,155
b. A Drug Conjugate and Method Of Preparation Thereof. Chitkara D, Sahel D, **Sharma S,** Italiya K, Mittal A. IN Patent 201,911,018,304
c. **Sharma S**, Italiya K, Mittal A, Chitkara D. New strategies for cancer management: how can temozolomide carrier modifications improve its delivery?. Ther Deliv. 2017 Jul;8(7):475-477. PubMed PMID: 28633588.
d. Harsha P, Thotakura N, Kumar M, **Sharma S**, Mittal A, Khurana R, Singh B, Negi P, Raza K. A novel PEGylated carbon nanotube conjugated mangiferin: An explorative nanomedicine for brain cancer cells. Journal of Drug Delivery Science and Technology. 2019 October; 53:101186-. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1773224718315983 DOI: 10.1016/j.jddst.2019.101186
e. Kawakita S, Mandal K, Mou L, Mecwan MM, Zhu Y, Li S, **Sharma S**, Hernandez AL, Nguyen HT, Maity S, de Barros NR, Nakayama A, Bandaru P, Ahadian S, Kim HJ, Herculano RD, Holler E, Jucaud V, Dokmeci MR, Khademhosseini A. Organ-On-A-Chip Models of the Blood-Brain Barrier: Recent Advances and Future Prospects. Small. 2022 Sep;18(39):e2201401. PubMed Central PMCID: PMC9529899.
f. Sahel DK, Vora LK, Saraswat A, **Sharma S**, Monpara J, D'Souza AA, Mishra D, Tryphena KP, Kawakita S, Khan S, Azhar M. CRISPR/Cas9 Genome Editing for Tissue-Specific In Vivo Targeting: Nanomaterials and Translational Perspective. Advanced Science. 2023 May 11:2207512
g. **Sharma S**, Mazumdar S, Italiya KS, Date T, Mahato RI, Mittal A, Chitkara D. Cholesterol and Morpholine Grafted Cationic Amphiphilic Copolymers for miRNA-34a Delivery. Mol Pharm. 2018 Jun 4;15(6):2391-2402. PubMed PMID: 29747513.
h. **Sharma S**, Pukale S, Sahel DK, Singh P, Mittal A, Chitkara D. Folate targeted hybrid lipo-polymeric nanoplexes containing docetaxel and miRNA-34a for breast cancer treatment. Mater Sci Eng C Mater Biol Appl. 2021 Sep;128:112305. PubMed PMID: 34474856.
i. **Sharma S**, Mazumdar S, Italiya KS, Date T, Mahato RI, Mittal A, Chitkara D. Cholesterol and Morpholine Grafted Cationic Amphiphilic Copolymers for miRNA-34a Delivery. Mol Pharm. 2018 Jun 4;15(6):2391-2402. PubMed PMID: 29747513.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2022 - Current	Post-doctoral Researcher, Department of General and Vascular Surgery, School of Medicine, Stanford University, Stanford, Palo Alto, CA
2022 - Current	Affiliated Scientist, Terasaki Institute for Biomedical Innovation, Los Angeles, CA
2021 - 2022	Postdoctoral Chemist/Pharmacologist, Terasaki Foundation, Terasaki Institute For Biomedical Innovation, Los Angeles, California
2020 - 2021	Assistant Professor (Pharmaceutics), University of Petroleum and Energy Studies, School of Health Sciences, Department of Pharmaceutical Sciences, Dehradun, Uttarakhand

Honors

2023-present	**Best New Technology Award** at SITC-Sparkathon-2023 Workshop on Brain Targeted Nano-Immunotherapy
2023-present	Society For Melanoma Research (SMR) Travel Award on Brain Targeted Nano-Immunotherapy
2023-present	SITC-Sparkathon-2023 Award on Brain Targeted Nano-Immunotherapy
2023-present	Expert Research Chapter talk on "Synthetic and Nature-derived Non-toxic Actively Targeted Nanomedicine Platform technology for Cancer treatments" at Institute of Biomaterials, Tribocorrosion, Nano and Regenerative Medicine, Vellore Institute of Technology (VIT), Vellore, India
2021-2022	Expert guest speaker on Carrier Mediated Nucleic Acid and small molecule drug delivery at Parul University, Gujarat, India

2020 - 2021 Expert guest speaker in nucleic acid drug delivery, Trend in Life Sciences

2018 - 2020 SRF Award, CSIR-Senior Research Fellowship by Council of Scientific & Industrial Research (CSIR), India.

C. Contribution to Science (25 papers, 3 book chapter, 2 granted patents, H-index=11, i-10-index=12 > 267 citations).

1. Smart nanocarrier-based systemic drug delivery:

Many diagnosed breast cancers are HER2+ and ER- /PR- , or HER2- /ER- /PR triple-negative (TNBC) with poor prognosis. Therapeutic regimen employed in TNBC consist of chemotherapeutic agents, including taxanes (paclitaxel, docetaxel), anthracyclines (doxorubicin), 5-fluorouracil and cyclophosphamide. Among these, docetaxel has been explored widely due to its higher potency and better physico-chemical properties; however, it still offers several challenges in delivery that needs to be addressed. Several nanotechnology-based systems are in the clinical and preclinical investigation to enable the delivery of hydrophobic drugs while largely mitigating the toxicity of chemotherapeutic agents as well as the excipients. There have been several attempts to design novel formulations of docetaxel as well to overcome its side effects along with improvement in drug delivery to the target site. These carrier systems aim to provide *in vitro* and *in vivo* stability, prolonged drug release profile, high intracellular uptake, improved pharmacokinetic profile, enhanced permeability, and retention (EPR) at the tumor site, and target specificity to tumor cells. Further, literature evidence suggested that a combination of small molecules with RNA interference (RNAi) therapeutics such as microRNA (miRNA) could improve the therapeutic outcome. These miRNAs provide the advantage of targeting multiple oncogenic pathways, thus providing a rationale for combining them with chemotherapeutic agents. miRNA-34a (miR-34a) is a master tumor suppressor and can antagonize many oncogenic processes by regulating genes involved in the cell cycle (CDK4, CDK6), apoptosis (BCL2, Abstract xxi survivin), metastasis (JAG1, WNT1, NOTCH1), cancer cell stemness (CD44, NANOG, SOX2) and oncogenic transcription (E2F3, MYC). Literature evidence also suggested that combining DTX with miR-34a could improve the therapeutic outcome in cancer. However, these therapeutics pose challenges for the delivery because of their different physicochemical properties. miRNAs are high molecular weight, hydrophilic and negatively charged while DTX has poor aqueous solubility and the emergence of resistance that limits its optimal therapeutic use. Additionally, the carrier should deliver the payload at the desired site, could be efficiently uptaken by the cells, undergo endosomal escape and release the payload in the cytoplasm. The research work disclosed in the present work entitled “Development and Evaluation of Lipo-polymeric Nano-carriers Containing MicroRNA-34a and Docetaxel for the Treatment of Breast Cancer” systematically provides development of a nanocarrier for the delivery of DTX and miR-34a alone and in combination followed by in vitro and in vivo evaluation of the developed formulations.

a. Sharma S, Pukale S, Sahel DK, Singh P, Mittal A, Chitkara D. Folate targeted hybrid lipo-polymeric nanoplexes containing docetaxel and miRNA-34a for breast cancer treatment. Mater Sci Eng C Mater Biol Appl. 2021 Sep;128:112305. PubMed PMID: 34474856.
b. Sharma S, Pukale SS, Sahel DK, Agarwal DS, Dalela M, Mohanty S, Sakhuja R, Mittal A, Chitkara D. Folate-Targeted Cholesterol-Grafted Lipo-Polymeric Nanoparticles for Chemotherapeutic Agent Delivery. AAPS PharmSciTech. 2020 Oct 9;21(7):280. PubMed PMID: 33037506.
c. Sharma S, Mazumdar S, Italiya KS, Date T, Mahato RI, Mittal A, Chitkara D. Cholesterol and Morpholine Grafted Cationic Amphiphilic Copolymers for miRNA-34a Delivery. Mol Pharm. 2018 Jun 4;15(6):2391-2402. PubMed PMID: 29747513.

2. Passively Targeted Brain Cancer Drug Nanoconjugates Platform:

Glioblastoma multiforme (GBM) is the most prevalent and malignant primary brain tumor in adults, with an incidence of 3.2% per 100,000 people. Nonetheless, treatment remains difficult due to restrictions of drugs crossing the blood brain barrier (BBB). Temozolomide (TMZ), an imidazotetrazine, is a second-generation DNA alkylating drug used in the first-line therapy of glioblastoma multiforme (GBM). It was FDA-approved in 2005 and a blockbuster in 2008. TMZ has 100% oral bioavailability, penetrates the blood-brain barrier, and has a short half-life (1.8 h), quick metabolism, and low brain accumulation (10–20%). It also causes chemoresistance. To circumvent TMZ's limitations, improved delivery systems have been investigated.

Liposomes, SLNs, NLCs, and polymeric nanoparticles can improve circulation time, stability, tissue-specific accumulation, sustained release, and cellular uptake. TMZ's water solubility (>5 mg/mL) makes physical loading in these nanocarriers difficult. Conjugating TMZ to polymers or small compounds improves in vitro and in vivo results. Many medicinal compounds need physicochemical modifications to improve stability, cellular absorption, pharmacokinetics, and biodistribution. These APIs become more lipophilic and stable when conjugated with fatty acids. Conjugating a medication with a fatty acid boosted half-life, cellular uptake and retention, targeted tumor delivery, reduced cancer chemoresistance, and BBB penetration. These small compounds, peptides, and oligonucleotides conjugated with fatty acid and their conjugation techniques. Because to its controlled medication release, targeting, and reduced side effects, nano-system-based delivery is gaining popularity. The drug-fatty acid conjugate's lipophilicity increases the drug's affinity for these carriers, improving entrapment efficiency and formulation performance.

a. Kawakita S, Mandal K, Mou L, Mecwan MM, Zhu Y, Li S, Sharma S, Hernandez AL, Nguyen HT, Maity S, de Barros NR, Nakayama A, Bandaru P, Ahadian S, Kim HJ, Herculano RD, Holler E, Jucaud V, Dokmeci MR, Khademhosseini A. Organ-On-A-Chip Models of the Blood-Brain Barrier: Recent Advances and Future Prospects. Small. 2022 Sep;18(39):e2201401. PubMed Central PMCID: PMC9529899.
b. Harsha P, Thotakura N, Kumar M, Sharma S, Mittal A, Khurana R, Singh B, Negi P, Raza K. A novel PEGylated carbon nanotube conjugated mangiferin: An explorative nanomedicine for brain cancer cells. Journal of Drug Delivery Science and Technology. 2019 October; 53:101186-. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1773224718315983 DOI: 10.1016/j.jddst.2019.101186
c. Sharma S, Italiya K, Mittal A, Chitkara D. New strategies for cancer management: how can temozolomide carrier modifications improve its delivery?. Ther Deliv. 2017 Jul;8(7):475-477. PubMed PMID: 28633588.
d. Granted Patent: A drug conjugate and method of preparation thereof.

3. Actively Blood-Brain-Barrier Targeted Nanoconjugates Platform:

Our objective is to create a mini-nano drug that can penetrate the BBB and deliver nucleic acid (AON) and antibodies to reactivate the immune response specific to the tumor and enhance the efficacy of chemotherapy and host survival. We created polymeric nano imaging agents with easy platform modification capabilities to effectively identify the majority of the tumor intraoperatively and turn them into nanotherapies to eradicate invasive non-visible glioma cells. Nanodevice made of polycefin: I learned how to create a brand-new all-in-one covalent nanomedicine based on polymalic acid drom my mentor Prof. Eggehard Holler. The concept was developed for the treatment of preclinical tumors Prof. Holler, created PolycefinTM technology, a nanoscale delivery method for brain and other cancers. Polycefin has several devices for drug activation, distribution to tumor cells across the blood-brain barrier (BBB), release from endosome vesicles, degradation/ERS collection, and imaging. It also features a polymalic acid (PMLA) platform coupled to a prodrug.

a. Galstyan A, Markman JL, Shatalova ES, Chiechi A, Korman AJ, Patil R, Klymyshyn D, Tourtellotte WG, Israel LL, Braubach O, Ljubimov VA. Blood–brain barrier permeable nano immunoconjugates induce local immune responses for glioma therapy. Nature Communications. 2019 Aug 28;10(1):3850.

b. Sharma S, Italiya K, Mittal A, Chitkara D. New strategies for cancer management: how can temozolomide carrier modifications improve its delivery?. Ther Deliv. 2017 Jul;8(7):475-477. PubMed PMID: 28633588.

c. Sahel DK, Vora LK, Saraswat A, Sharma S, Monpara J, D'Souza AA, Mishra D, Tryphena KP, Kawakita S, Khan S, Azhar M. CRISPR/Cas9 Genome Editing for Tissue-Specific In Vivo Targeting: Nanomaterials and Translational Perspective. Advanced Science. 2023 May 11:2207512.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/dr.%20saurabh.sharma.1/bibliography/public/

Section D. Additional Information: Research Support and/or Scholastic Performance

Current Research Support:

11/27/2022 – Present Postdoctoral Researcher working on " AXL Molecular signature and Targeted therapy for Melanoma treatment" at General Surgery, Stanford Scholl of Medicine, Stanford University, CA, USA

Completed Research Support:

07/22/2021-11/26/2022. Postdoctoral Chemist/Pharmacologist working on NIH Funded Project Novel Brain targeted Nanoconjugate for Glioma Therapy. Terasaki Institute for Biomedical Innovation, Los Angeles, CA, USA