BIOGRAPHICAL SKETCH

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NAME: **Arash Hatefi**

eRA COMMONS USER NAME: **ahatefi**

POSITION TITLE: **Professor of Pharmaceutical Sciences**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
University of Alberta, Alberta, Canada	PhD	01/1998-09/2002	Pharmaceutical Sciences
University of Maryland, Center for Cellular Delivery and Nanomedicine, Maryland, USA	Postdoc	08/2003-08/2006	Cellular and Biomolecular Engineering

A. Personal Statement

I am a Professor of Pharmaceutical Sciences and an investigator at the Cancer Institute of New Jersey (CINJ). My research is focused on the development of genetically engineered stem cells, immune cells, and antibodies for targeted therapy of cancer. My laboratory is among the leaders in enzyme/prodrug therapy of cancer, where our publications in this field have been cited and reviewed by many research groups. We have freely shared our engineered cells, vectors, and enzyme/prodrug systems with various research teams across the US and Europe for targeted cancer therapy. As my publication records show, I have experience in molecular biology and biochemical techniques, stem cell genetic modification, stable cell production, live cell imaging and analysis, enzyme/prodrug therapy, xenograft tumor models (ectopic and orthotopic) in mice, immunogenicity studies in immune-competent mice, and quantitative analysis of tumor response to therapy by Bioluminescence Imaging (BLI) and Magnetic Resonance Imaging (MRI).

My research team has recently engineered a novel bispecific killer cell engager (BiKE) with high affinity and specificity/selectivity toward CD16a receptor on natural killer (NK) cells and HER2 on cancer cells for cancer immunotherapy. This patented BiKE technology, shown as BiKE:HER2/CD16a, has specificity, affinity, and anticancer efficacy superior than the best-in-class FDA-approved anti-HER2 antibody Trazimera™ (trastuzumab). A patent has been filed and the results of this research are published:

a. Nikkhoi SK, Li G, Eleya S, Yang G, Vandavasi VG, **Hatefi A**. Bispecific killer cell engager with high affinity and specificity toward CD16a on NK cells for cancer immunotherapy. *Front Immunol*. **2023** Jan 6;13:1039969. doi: 10.3389/fimmu.2022.1039969. PMID: 36685519, PMC: In progress

b. **Hatefi A**, Nikkhoi SK. Single-domain High Affinity Antibodies and Methods of Use Thereof. **2021**, Provisional Patent Application# 63294,664

In addition, my lab was the first to show the utility of mesenchymal stem cells as a cell-based platform for screening and comparative evaluation of the efficacy of different enzyme-prodrug systems (PMID: 25575867). Recently, my lab pioneered and successfully demonstrated the possibility of using adipose-derived stem cells (ASCs) to generate high concentrations of anticancer drug SN-38 within ovarian tumors and overcome drug resistance (PMID: 31499084). Furthermore, we have shown that our engineered ASCs can make drug-resistant cancer stem-like cells vulnerable to natural killer cells. These translational works are currently funded by the NIH/NCI and DoD:

- NCI (1R01CA251438) (PI: Hatefi) 04/01/2021-03/31/2026
  Title: Stem Cell-based Platform for Targeted Enzyme/Prodrug Therapy of Ovarian Cancer
  Objective: The objective of this research is "to develop a non-surgical, targeted and clinically translatable stem cell-based platform that can overcome drug resistance in metastatic ovarian cancer.

- DoD Ovarian Cancer Program (HT9425-23-1-0191) (PI: Hatefi) 4/1/2023-3/31/2026
  Title: Targeted Chemoimmunotherapy of Drug-Resistant Ovarian Cancer
  Objective: The objective of this research is to combine stem cell-directed targeted chemotherapy with natural killer (NK) cell-based immunotherapy to prevent cancer recurrence in ovarian cancer.

I have worked on gene therapy of cancer for more than a decade and have a significant publication record in this field. As a member of CINJ, I have access to its core facilities, including Biospecimen Repository Core, Biostatistics Core, Cell and Gene Therapy Good Manufacturing Practice Facility, and Clinical Trial Planning and Execution. As PI, I have directed a range of federally (NIH and DOD) and foundation-funded grants, collaborated with other national and international researchers, and published the results of my work in various reputable journals. Some examples of my past funding sources for research projects are highlighted below:

- NCI (R01CA175318) (PI: Hatefi) 04/01/2015-03/30/2021
  Title: A Nanotechnology Platform for Suicide Gene Therapy of Recurring Ovarian Cancer
  Objective: The objective of this research was to develop a targeted nanotechnology that can effectively treat primary ovarian tumors and demonstrate their effective eradication.

- New Jersey Health Foundation (PC95-20) (PI: Hatefi) 02/15/2020-02/14/2021
  Title: Stem Cell-assisted Natural Killer Cell-based Ovarian Cancer Immunotherapy.
  Objective: The objective of this research is to genetically engineer mesenchymal stem cells that secrete a bifunctional nanobody to activate the natural killer cells and kill the ovarian cancer cells.

- NIH/NIBIB (R21EB016792) (PI: Hatefi) 05/01/2014-04/30/2016
  Title: Bioengineering a Safe and Efficient Vector Technology for Stem Cell Transfection
  Objective: The objective of this research is to develop a non-genotoxic/non-oncogenic vector that could transfect stem cells with high efficiency while preserving their viability and tumor tropism.

The following publications are examples that demonstrate the cancer-related expertise in my laboratory:

c. Nouri FS, Wang X, **Hatefi A.** Genetically engineered theranostic mesenchymal stem cells for the evaluation of the anticancer efficacy of enzyme/prodrug systems. *J Control Release*. **2015** Feb 28;200:179-87. PMID: 25575867; PMCID: PMC4758350.
d. Malekshah OM, Sarkar S, Nomani A, Patel N, Javidian P, Goedken M, Polunas M, Louro P, **Hatefi A**. Bioengineered adipose-derived stem cells for targeted enzyme-prodrug therapy of ovarian cancer intraperitoneal metastasis. *J Control Release*. **2019**. doi: 10.1016/j.jconrel.2019.09.006. PMID: 31499084. PMCID: PMC6884134.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2002-2003	R&D Scientist: Patheon Inc., Toronto, Ontario, Canada
2006-2010	Graduate Faculty: NIH Protein Biotechnology Training Program (T-32), Washington State University, WA, USA
2006-2010	Assistant Professor of Pharmaceutical Sciences, Washington State University, WA, USA
2010-2016	Assistant Professor, Ernest Mario School of Pharmacy, Rutgers University, NJ, USA
2010-present	Investigator and full member of Cancer Pharmacology program, Cancer Institute of New Jersey, NJ, USA
2016-2022	Associate Professor (with tenure), Ernest Mario School of Pharmacy, Rutgers University, NJ, USA

2022-present Professor (with tenure), Ernest Mario School of Pharmacy, Rutgers University, NJ, USA
2022-present Executive member, Drug Delivery Advisory Committee, *Phrma* Foundation, Washington DC, USA

Grant Reviewer/ Panel Member

2009 National Science Foundation (NSF), Grant reviewer for Nanobiological Applications Panel (SBIR/STTR) with focus on Nanotechnology and Advanced Materials
2011 United States-Israel Binational Science Foundation, Grant reviewer for Nanotechnology.
2012 Department of Defense Peer Reviewed Medical Research Program (PRMRP), Nanomedicine for Drug Delivery Science topic area, Reviewer for Technology/Therapeutic Development Award
2015 Italian Ministry of Health, Grant Reviewer for Drug Delivery and Nanotechnology
2015 American Association of Colleges of Pharmacy (AACP), New Investigator Award program
2015 National Institutes of Health, NCI, Special Emphasis Panels ZCA1 RPRB-C (O2), ZCA1 TCRB-T (O2), and ZCA1 TCRB-T (J1) S
2016 National Institutes of Health, NCI, Special Emphasis Panels ZCA1 TCRB-Q (M3) S, and ZCA1 TCRB-6 (O1) S
2017 National Institutes of Health, NCI, Special Emphasis Panel, (IGDD) ZRG1 SBIB-F (58) R, and SCORE
2018 National Institutes of Health, NCI, Special Emphasis Panels (IGDD) ZRG1 SBIB-Q (58) SEP, ZRG1 OTC-Y (56), NANO Study Section, and IGIS study section
2019 National Institutes of Health, IGIS study section
2020 National Institutes of Health, IGIS study section
2021 National Institutes of Health, DT study section
2022 National Institutes of Health, NCI Special Emphasis Panel (R03/R21), *Phrma* Foundation, Drug Delivery Study Section

Other Professional Activities

Since 2007 Associate Editor, Journal of Bioactive and Compatible Polymers
2010 Theme Editor, Journal of Advanced Drug Delivery Reviews
2012 Theme Editor, Journal of Drug Delivery and Translational Research
2012 Program Chair and Organizer, 10th International Nanomedicine and Drug Delivery (NanoDDS'12) Symposium, Atlantic City, NJ, USA
Since 2013 Editorial board member, Journal of Pharmaceutics & Pharmacology
2014 Session Chair, 12th International Nanomedicine and Drug Delivery (NanoDDS'14) Symposium, Chapel Hill, NC, USA
2016 Session Chair, 14th International Nanomedicine and Drug Delivery (NanoDDS'16) Symposium,
Since 2016 Associate Editor, Journal of Nanomedicine: Nanotechnology, Biology and Medicine

Honors/Awards

1999 Dorothy Whitman Award
2000 & 2001 Teaching-Research Award
2001 J. Gordin Kaplan Award
2004 National Cancer Center Postdoctoral Fellow
2009 DOD Prostate Cancer New Investigator Award
2016 GALLO Award for Scientific Excellence, Awarded by the Cancer Institute of New Jersey
2016 Rutgers University, The Board of Trustees Research Fellowship for Scholarly Excellence
2017 Research Excellence Award, New Jersey Pharmaceutical Association for Science and Technology (NJPhAST) Symposium, Whippany, NJ
2017 GALLO Award for Scientific Excellence, Awarded by the Cancer Institute of New Jersey
2018 Research Excellence Award, New Jersey Pharmaceutical Association for Science and Technology (NJPhAST) Symposium, Whippany, NJ
2019 GALLO Award for Scientific Excellence, Awarded by the Cancer Institute of New Jersey
2022 GALLO Award for Scientific Excellence, Awarded by the Cancer Institute of New Jersey

C. Contribution to Science

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/arash.hatefi.1/bibliography/public/

1. *Discovery of a bispecific killer cell engager (BiKE) for cancer immunotherapy.*

We have engineered a BiKE with high affinity (sub-nanomolar) toward CD16a antigen without cross-reactivity with CD16b-NA1 on neutrophils or CD32b on B cells. Our data show that the engineered BiKE activates NK cells to release cytokines much greater than best-in-class mAbs in the clinic. The cytotoxicity data also show that the developed BiKE induces higher ADCC to both ovarian and breast cancer cells in comparison to Trazimera™ (trastuzumab). Taken together, the data demonstrate the creation of a novel BiKE with high affinity and specificity toward CD16a on NK cells with the potential to elicit a superior therapeutic response in patients with HER2+ cancer than existing anti-HER2 mAbs.

a. Nikkhoi SK, Li G, Eleya S, Yang G, Vandavasi VG, **Hatefi A**. Bispecific killer cell engager with high affinity and specificity toward CD16a on NK cells for cancer immunotherapy. *Front Immunol*. **2023** Jan 6;13:1039969. doi: 10.3389/fimmu.2022.1039969. PMID: 36685519, PMC: In progress
b. **Hatefi A**, Nikkhoi SK. Single-domain High Affinity Antibodies and Methods of Use Thereof. **2021**, Provisional Patent Application# 63294,664

2. *Development of a stem cell-based system for evaluation of the efficacy of the enzyme/prodrug systems:*

Over the past decade, various enzyme/prodrug systems have been used for stem cell mediated suicide gene therapy of cancer. Yet, no study has been conducted to compare and demonstrate the advantages and disadvantages of using one system over another. Knowing that each enzyme/prodrug system has its own strengths and weaknesses, we engineered a theranostic mesenchymal stem cell-based system as a medium to perform for the first time a comparative study that illustrated the impact of subtle differences among these systems on the therapeutic outcome.

a. Nouri FS, Wang X, Hatefi A. Genetically engineered theranostic mesenchymal stem cells for the evaluation of the anticancer efficacy of enzyme/prodrug systems. J Control Release. 2015 Feb 28;200:179-87. PMID: 25575867; PMCID: PMC4758350.
b. Nouri FS, Banerjee D, **Hatefi A.** Practical Issues with the Use of Stem Cells for Cancer Gene Therapy. Stem Cell Rev. 2015 Oct;11(5):688-98. PMID: 26123358; PMCID: PMC4758683.
c. Malekshah OM, Sarkar S, Nomani A, Patel N, Javidian P, Goedken M, Polunas M, Louro P, Hatefi A. Bioengineered adipose-derived stem cells for targeted enzyme-prodrug therapy of ovarian cancer intraperitoneal metastasis. J Control Release. 2019 Oct;311-312:273-287 PMCID: PMC6884134.

3. *Development of a new class of non-viral vectors, termed Designer Biomimetic Vectors (DBVs):* We have used genetic engineering techniques to create novel fusion vectors suitable for targeted gene delivery to mammalian cells. The concept of engineering recombinant fusion vectors for gene delivery dates back to late 1990s. However, due to significant technical difficulties related to vector production and formulation of stable and efficient nanoparticles, recombinant fusion vectors remained inefficient for more than a decade. Since 2006, my laboratory has worked to overcome these challenges and through use of several innovative approaches have successfully created highly efficient receptor targeted fusion vectors for various gene delivery needs including targeting different cancer cell types or compartments inside the cells. My lab is currently the leader in recombinant fusion vector design. The developed vectors by my research team are the most advanced and efficient ones reported in the literature. The following publications from my lab show our most important contributions to the field of recombinant fusion vector design:

a. Hatefi A, Chen X, Nomani A. Gene Transfer Systems for Stem Cell Engineering. Publication Number US20200207834A1.
b. Hatefi A, Karjoo Z, Nomani A. Development of a Recombinant Multifunctional Biomacromolecule for Targeted Gene Transfer to Prostate Cancer Cells. Biomacromolecules. 2017 Sep 11;18(9):2799-2807. PMID: 28806522; PMCID: PMC5593778.
c. Chen X, Nomani A, Patel N, Nouri FS, Hatefi A. Bioengineering a non-genotoxic vector for genetic modification of mesenchymal stem cells. Biomaterials. 2018 Jan;152:1-14. PMCID: PMC5671363.