BIOGRAPHICAL SKETCH

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NAME: Antonina Mitrofanova

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

POSITION TITLE: **Associate Dean for Research and Associate Professor**

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Bogomolets National Medical University (Ukraine)	M.D. student	06/1999	Internal Medicine
Brooklyn College (New York, USA)	B.S. (Honors)	01/2004	Computer Science
New York University, NYU (New York, USA)	Ph.D. (Honors)	09/2009	Computer Science
Columbia University (New York, USA)	Postdoctoral training	10/2015	Computational Oncology

A. Personal Statement

My main interests are in developing novel computational algorithms and models to elucidate molecular mechanisms that govern cancer progression and response to therapies and translating our discoveries to clinic. Our algorithms integrate statistical modeling, network inference, and machine learning to uncover a complex interplay in genomic, transcriptomic, and epigenomic mechanisms implicated in cancer initiation, progression, and therapeutic resistance. We have extensively tested our algorithms in experimental and clinical setting and have demonstrated that they accurately capture response to a variety of treatment regimens (*Nature Communications* 2018, *EBiomedicine* 2018, *Nature Communications Biology* 2019, *Nature Cancer 2020*, *Computational and Structural Biotechnology* 2022 etc.). We have filed seven provisional and/or permanent patents on these discoveries and methodologies and are aiming for their short-term translation into clinic. Such advances provide the foundation for our long-term goal to develop an adaptable cost-effective multi-modal clinical decision support system that will utilize patients' clinical and molecular profiles to assist on patient's personalized therapeutic strategies, improving quality of life and outcomes.

Role: XXXX

Prostate cancer publications most relevant for this grant application (chronological order):

1. Epsi, N.J., Panja, S., Pine, S.R., and **Mitrofanova, A.** †. (2019)
   PathCHEMO: Uncovering transcriptomic and epigenomic pathways of chemoresistance in lung adenocarcinoma.
   Nature Communications Biology (by Nature), 2:334, PMCID: PMC6731276.

2. Rahem, S.M., Epsi, N.J., Coffman, F.D., **Mitrofanova, A.†** (2020)
   Genome-wide analysis of therapeutic response uncovers molecular pathways governing tamoxifen resistance in ER+ breast cancer.
   EBioMedicine (by THE LANCET). PMCID: PMC7585053.

3. Arriaga, J.M., Panja, S., Alshalalfa, M., Zhao, J., Zou, M., Giacobbe, A., Madubata, C.J., Kim, J.Y., Rodriguez, A., Coleman, I., Virk, R.K., Hibshoosh, H., Ertunc, O., Ozbek, B., Fountain, J., Karnes, R.J., Luo, J., Antonarakis, E.S., Nelson, P.S., Feng, F.Y., Rubin, M.A., De Marzo, A.M., Rabadan, R., Sims, P.A., **Mitrofanova, A.**†, and Abate-Shen, C†. (2020)
   A MYC and RAS co-activation signature in localized prostate cancer drives bone metastasis and castration resistance.

Nature Cancer (by Nature), 1(11):1082-1096, PMCID: PMC8171279.
†Co-senior co-corresponding author.

4. Bohannan, Z., Coffman, F., and **Mitrofanova, A.**† (2022)
Random survival forest model identifies novel biomarkers of event-free survival in high-risk pediatric acute lymphoblastic leukemia.
Computational and Structural Biotechnology Journal, 20: 583-597. PMCID: PMC8777142

I would like to highlight the following grants, important for this application:

R01 LM013236-01A1 Mitrofanova (PI) 09/2020 – 08/2024
NIH/NLM
Title: *Generalizable biomedical informatics strategies for predictive modeling of treatment response*
The major goal of this project is to develop generalizable machine learning computational paradigm to elucidate mechanisms of treatment resistance, using prostate cancer and AML as a proof of concept
Role: Principal Investigator

ACS RSG-21-023-01-TBG Mitrofanova (PI) 07/2021 – 06/2025
American Cancer Society (ACS) Research Scholar grant
Title: *Systems analysis of drug resistance in prostate cancer*
The major goal of this project is to develop computational methods to identify optimal drug combinations for prostate cancer patients that failed standard-of-care androgen deprivation
Role: Principal Investigator

COCR21RBG003 Mitrofanova (PI) 05/2021 – 04/2023
NJCCR
Title: *Scalable generalizable framework for predicting treatment response in prostate cancer*
The major goal of this project is to develop computational algorithms to elucidate a cross talk between alternative splicing and long-non-coding RNAs as mechanisms of treatment resistance to second-generation androgen targeting in prostate cancer
Role: Principal Investigator

B. Positions, Scientific Appointments, and Honors

Positions and Employment:

05/22-present	Associate Dean for Research, Rutgers School of Health Professions (SHP), Rutgers Biomedical and Health Sciences (RBHS), Rutgers University
07/21-present	Associate Professor, Department of Health Informatics, School of Health Professions (SHP), Rutgers Biomedical and Health Sciences (RBHS), Rutgers University
08/16-present	Full Member, Rutgers Cancer Institute of New Jersey (Rutgers CINJ), Clinical Investigations and Precision Therapeutics Program
10/15-06/21	Assistant Professor, Department of Health Informatics, School of Health Professions (SHP), Rutgers Biomedical and Health Sciences (RBHS), Rutgers University
10/09-09/15	Postdoctoral Fellow, Columbia University, *Mentor: Andrea Califano*

Fellowships and Scholarships:

2009 – 2011	National Science Foundation (NSF)/Computing Research Association (CRA)/Computer Community Consortium (CCC) Computing Innovation (CI) Postdoctoral Fellowship
2007 – 2010	Henry M. MacCracken PhD Fellowship, New York University
2002 – 2003	Stewart M. Monchik Memorial Scholarship in Computer and Information Science, Brooklyn College, awarded to a student majoring in computer and information science who has demonstrated achievement and potential for work in the field
1995 – 1999	Bogomolets National Medical University Scholarship, Ukraine, granted for GPA above 3.75

Academic Awards:

2022	Presidential Fellowship for Teaching Excellence, Rutgers University
2018	Excellence in Research, Rutgers SHP
2010	Janet Fabri (Most Outstanding PhD Dissertation) Award, Department of Computer Science, Courant Institute of Mathematical Sciences, New York University
2010	Henning Biermann Prize (for outstanding contributions to education and service), Department of Computer Science, New York University
2009	Sandra Bleistein Prize, Courant Institute of Mathematical Sciences, New York University
2004	Jack Wolfe Award in Computer and Information Science, Brooklyn College

C. Contributions to Science

1. My early work focused on the development of computational algorithms for analysis of biological network behavior. I studied a range of problems that arise in protein-protein interaction networks, where experimental noise or poorly characterized neighborhood can mislabel structural and functional relationships in the network, with the aim to improve functional classification for proteins, especially those isolated or poorly connected in their own networks. Furthermore, using temporal changes in gene expression patterns of Malaria parasite during its intra-erythrocytic developmental cycle, I discovered a significant shift in assignment of functions to un-annotated Malaria proteins, including novel potential targets for vaccine and drug discovery. This work was paralleled by the study of the copy number variations in human genome where I designed a computational simulation model, suitable not only for physiological, but also for pathological (i.e., cancer) evolutionary processes. This work collectively constituted a base for my PhD dissertation, for which I received Sandra Bleistein prize for significant contribution to applied mathematics and computer science and Most Outstanding PhD Dissertation from NYU.

a. **Mitrofanova, A.,** Farach-Colton, M., and Mishra, B. (2009)
Efficient and robust prediction algorithms for protein complexes using Gomory-Hu trees.
Pacific Symposium on Biocomputing. 2009: 215-226. PMID: 19209703.

b. **Mitrofanova, A.,** Pavlovic, V., and Mishra, B. (2010)
Prediction of protein functions with gene ontology and inter-species protein homology data.
IEEE/ACM Transactions on Computational Biology and Bioinformatics Journal. ISSN 1545-5963. PMID: 21393654.

c. **Mitrofanova, A.,** and Mishra, B. (2010)
On a novel coalescent model for genome-wide evolution of copy number variations.
International Journal of Data Mining and Bioinformatics. 4: 300-315. PMID: 20681481.

d. **Mitrofanova, A.,** Kleinberg, S., Carlton, J., Kasif, S., and Mishra, B. (2010)
Predicting malaria interactome classifications from time-course transcriptomic data along the intra-

erythrocytic developmental cycle.
Artificial Intelligence in Medicine Journal. 49: 167-176. PMID: 20580212.

2. During my postdoctoral fellowship at Columbia University, I developed computational network-inference-based algorithms to study transcriptional regulatory mechanisms involved in cancer initiation, progression, and metastasis. I have constructed and subsequently compared transcriptional regulatory networks for human and mouse prostate cancer to discover conserved regulatory drivers that can be studied in mice and then effectively translated to human patients. These analyses identified two conserved regulators, FOXM1 and CENPF, which act as synergistic drivers of prostate cancer and are biomarkers of the most aggressive form of this disease (*Cancer Cell*). Following the identification of key regulatory genes of cancer progression, I further developed computational algorithms to predict optimal therapeutic strategies to target these drivers of malignancy (*Cell Reports*). Finally, I developed a computational approach to identify NSD2 as a conserved driver of metastatic prostate cancer (*Nature Communications*). To pursue this work, I was awarded an NSF Computing Innovation Fellowship and Prostate Cancer Foundation Young Investigator Award.

a. Aytes, A.*, **Mitrofanova, A.*,** Lefebvre, C.*, Alvarez, M.J., Castillo-Martin, M., Zheng, T., Eastham, J.A., Gopalan, A., Pienta, K.J., Shen, M.M., Califano, A., and Abate-Shen, C. (2014)
Cross-species analysis of genome-wide regulatory networks identifies a synergistic interaction between FOXM1 and CENPF that drives prostate cancer malignancy.
Cancer Cell. 25(5):638-651. PMCID: PMC4051317 .
*Co-First author**.**

b. **Mitrofanova, A.*,** Aytes, A.*, Zou, M., Shen, M., Abate-Shen, C., and Califano, A. (2015)
Predicting drug response in human prostate cancer from preclinical analysis of in vivo mouse models.
Cell Reports. 12(12):2060-71. PMCID: PMC4591242.
*Co-First author.

c. Aytes, A.*, Giacobbe, A.*, **Mitrofanova, A.*,** Ruggero, K., Cyrta, J., Arriaga, J., Palomero, L., Farran-Matas, S., Rubin, M.A., Shen, M.M., Califano, A., and Abate-Shen, C. (2018)
NSD2 is a conserved driver of metastatic prostate cancer progression.
Nature Communications. 9(1):5201. PMCID: PMC6281610.
*Co-First author.

3. My interests in understanding cancer mechanisms resulted in development of the computational systems methods tailored for identification of drivers of cancer initiation, progression, and dissemination. This included a discovery of NKX3.1 in early-stage prostate cancer as a marker of response to response to 5a-reductase inhibition (*European Urology*) and MYC and RAS co-activation as a driver of bone metastasis and castration resistance in prostate cancer (*Nature Cancer*) in addition to major review work focusing on the emerging role of machine learning in predictive modeling of treatment response in cancer (*Current Genomics*) and on mechanism-centric approaches for biomarker detection in cancer (*Frontiers in Genetics*). To pursue this work, I received Dean's Research grant from Rutgers School of Health Professions and Bridge grant from NJCCR.

a. Dutta, A., Panja, S., Virk, R.V., Kim, J.Y., Zott, R., Cremers, S., Golombos, D.M., Liu, D., Mosquera, J.M., Mostaghel, E.A., Barbieri, C.E., **Mitrofanova, A.** †, and Abate-Shen, C.† (2017)
Co-clinical analysis of a genetically-engineered mouse model and human prostate cancer reveals significance of NKX3.1 expression for response to 5a-reductase inhibition.
European Urology. pii: S0302-2838(17)30252-X. PMCID:PMC5600823.
†Co-senior co-corresponding author.

b. Arriaga, J.M., Panja, S., Alshalalfa, M., Zhao, J., Zou, M., Giacobbe, A., Madubata, C.J., Kim, J.Y., Rodriguez, A., Coleman, I., Virk, R.K., Hibshoosh, H., Ertunc, O., Ozbek, B., Fountain, J., Karnes, R.J., Luo, J., Antonarakis, E.S., Nelson, P.S., Feng, F.Y., Rubin, M.A., De Marzo, A.M., Rabadan, R., Sims, P.A., **Mitrofanova, A.** †, and Abate-Shen, C†. (2020)
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Nature Cancer (published by Nature), 1(11):1082-1096, PMCID: PMC8171279.
†Co-senior co-corresponding author.

c. Panja, S., Rahem, S., Chua, C.J, **Mitrofanova, A.†** (2020)
Big Data to Knowledge: application of machine learning to predictive modeling of therapeutic response in cancer.
Current Genomics, 22(4):244-266, PMCID: PMC8822229.

d. Yu, Ch., **Mitrofanova, A.†** (2021).
Mechanism-centric approaches for biomarker detection and precision therapeutics in cancer.
Frontiers in Genetics, 12: 687813. PMCID: PMC8365516.

4. In my laboratory at Rutgers, I have established an independent research program that focuses on development of novel computational algorithms that effectively integrate statistical modeling, network inference, and machine learning that are applied to genomic, transcriptomic, and epigenomic profiles in cancer patients to uncover markers of drug response and resistance. In particular, my lab developed a statistical learning approach Epi2GenR which identified five (epi) genomic markers of resistance to androgen-deprivation in prostate cancer, used to predict patients with poor and favorable response to first-generation androgen-deprivation (*EBioMedicine*). Furthermore, we pioneered two pathway-centric computational algorithms: pathER, which uncovered molecular pathways altered on the transcriptomic level as markers of resistance to tamoxifen in ER+ breast cancer (*EBioMedicine*); and pathCHEMO, which uncovered molecular pathways altered on both transcriptomic and epigenomic levels as markers of resistance to specific chemotherapy combinations in lung and colorectal adenocarcinoma (*Nature Communications Biology*), alongside a novel machine learning model to identify genomic markers in pediatric ALL (*Computational and Structural Biotechnology Journal*). For this work, I received NIH NLM R01 and American Cancer Society (ACS) Research Scholar grant.

a. Panja, S., Hayati, S., Epsi, N., Parrott, J.S., **Mitrofanova, A** †. (2018)
Integrative (epi) genomic analysis to predict response to androgen-deprivation therapy in prostate cancer.
EBioMedicine (published by THE LANCET). 31:110-121, PMCID: PMC6013754.

b. Epsi, N.J., Panja, S., Pine, S.R., and **Mitrofanova, A.** †. (2019)
PathCHEMO: Uncovering transcriptomic and epigenomic pathways of chemoresistance in lung adenocarcinoma.
Nature Communications Biology (published by Nature), 2:334, PMCID: PMC6731276.

c. Rahem, S.M., Epsi, N.J., Coffman, F.D., **Mitrofanova, A.†** (2020)
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EBioMedicine (published by THE LANCET). PMCID: PMC7585053.

d. Bohannan, Z., Coffman, F., and **Mitrofanova, A.†** (2022)
Random survival forest model identifies novel biomarkers of event-free survival in high-risk pediatric acute lymphoblastic leukemia.
Computational and Structural Biotechnology Journal, 20: 583-597. PMCID: PMC8777142

Complete List of Published Work:
https://www.ncbi.nlm.nih.gov/myncbi/antonina.mitrofanova.1/bibliography/public/