BIOGRAPHICAL SKETCH

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NAME: Abou Donia, Mohamed Samir

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

POSITION TITLE: Associate Professor of Molecular Biology

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
Suez Canal University (Ismailia, Egypt)	B.Sc.	06/2004	Pharmacy
University of Utah (Salt Lake City, USA)	Ph.D.	08/2010	Chemistry and Metagenomics of Marine Invertebrate Symbionts
University of California, San Francisco	Postdoctoral	09/2014	Chemistry and Metagenomics of the Human Microbiota

A. Personal Statement

The goal of my laboratory is to understand the role of the human microbiome in human health, disease, and response to therapy. We study the role of small molecules synthesized by the human microbiome, or of enzymatic activities encoded by the microbiome in mediating microbe-microbe and microbe-host interactions that are important for human health. We develop systematic screens to identify these interactions, which integrate large-scale computational analyses, molecular and biochemical investigations, and mouse studies. My record highlights my experience in studying the human microbiome and its encoded bioactive enzymes and molecules, and demonstrates my ability to plan and successfully execute experiments in this area of research.

Ongoing and recently completed projects that I would like to highlight include:

NIH Director's New Innovator Award Program (DP2) ID: 1DP2AI124441-01
Donia (PI)
09/30/15-06/30/20
Uncultivated bacterial symbionts of humans: an untapped resource for drug discovery

The Pew Charitable Trusts (Pew Scholars Program in the Biomedical Sciences) Award #: 00030608
Donia (PI)
08/01/17-07/31/22
Endogenous production of an antidiabetic drug by yet-uncultivated members of the human microbiome

Pershing Square Sohn Cancer Research Alliance Award Award #: N/A
Donia (PI)
07/01/2020-06/30/2024
Systematic characterization of microbiome-derived small molecules in colorectal cancer

National Institute of Health ID: 1R01AI172144-01
Donia (PI)
6/2022-5/2027
Systematic characterization of bioactive molecules from the human microbiome

Citations:

1. Balaich JN, **Donia MS. (2020).** Microbial Chemical Ecology in the Human Microbiome. in Comprehensive Natural Products III: Chemistry and Biology. PMID: *In progress*
2. **Donia MS** and Fischbach MA. (2015). Small molecules from the human microbiota. *Science* 349, 1254766, doi:10.1126/science.1254766 PMCID: PMC4641445
3. **Donia MS**. (2015). A toolbox for microbiome engineering. *Cell Syst*, 29;1(1). PMID: 27135687 DOI: 10.1016/j.cels.2015.07.003

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2019-2022	Member, Scientific Advisory Board, VastBiome Therapeutics
2020-present	Associate Professor, Department of Molecular Biology, Princeton University
2019-2022	Member, Scientific Advisory Board, DeepBiome Therapeutics
2014-2020	Assistant Professor, Department of Molecular Biology, Princeton University
2013	Participant, The Gladstone Institutes, University of California, San Francisco; workshop on scientific leadership and laboratory management
2012	Participant, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA; workshop on synthetic biology and natural products
2010-2014	Postdoctoral Scholar, University of California, San Francisco
2009-Present	Member, The American Society of Pharmacognosy (ASP)
2009-Present	Member, International Symbiosis Society (ISS)
2009	Participant, Institute for Genome Science (IGS), Department of Microbiology and Immunology, University of Maryland School of Medicine, University of Maryland, USA; workshop on metagenomics
2005-2010	Ph.D. student, Dr. Eric Schmidt, Department of Medicinal Chemistry, School of Pharmacy, University of Utah
2005	Participant, The Institute for Genomic Research (TIGR), Rockville, Maryland, USA; workshop on annotation of bacterial genomes
2004	Teaching Assistant, Department of Pharmacognosy and Phytochemistry, Misr International University, Cairo, Egypt
2004	Participant, Bolak El-Dakrour General Hospital, Guiza, Egypt; workshop on clinical pharmacology
2003	Participant, Toxicology and Micro-analytical Research Unit, Faculty of Science, Suez Canal University, Ismailia, Egypt; workshop on chromatography and water analysis

Honors

2022	Blavatnik National Awards Finalist, Life Sciences, the Blavatnik Family Foundation and the New York Academy of Sciences
2021	National Institute of Health Director's Transformative Research Award
2021	The Vilcek Prize for Creative Promise in Biomedical Science
2020	The Pershing Square Sohn Prize for Young Investigators in Cancer Research
2020	Theobald Smith Society Young Investigator Award, New Jersey Chapter of the American Society of Microbiology
2020	Symbiosis in Aquatic Systems Investigator Award, Gordon and Betty Moore Foundation
2018	ASPIRE Award (Advancing Science Through Pfizer Investigator Research Exchange Research Awards), Pfizer
2018	Dean for Research Innovation Award for New Ideas in the Natural Sciences, Princeton University
2017	Kenneth Rainin Foundation Phase III Award
2017	Pew Scholar in the Biomedical Sciences
2016	Kenneth Rainin Foundation Breakthrough Award

2015 Molecular Biology Department Innovator Award (Princeton University)
2015 Kenneth Rainin Foundation Innovator Award
2015 National Institute of Health Director's New Innovator Award
2009 Kilmer Price For Outstanding Research In Natural Products, American Society of Pharmacognosy and the American Pharmacist's Association
2004 Excellence with Honor Degree award from the Faculty of Pharmacy, Suez Canal University, Egypt

C. Contributions to Science

1. Developed computational and experimental methods to discover and study biologically active small molecules produced by the human microbiome. During my post-doctoral work, I developed a computational pipeline that identified small molecule biosynthetic gene clusters in the genomes of human-associated bacteria, and calculated their abundance and distribution in human samples. Using this pipeline, I identified several small molecule families that are widely distributed in healthy humans, and experimentally characterized one of them. As a result, I purified and solved the structure of a new potent antibiotic (lactocillin), produced by a prominent member of the human vaginal microbiome. This pioneering work was the first of its kind to show that the human microbiome is rich in its capacity to produce potent, drug-like, small molecules. In my own laboratory, we recently developed a novel strategy to discover and characterize microbiome-derived small molecules directly from human metagenomic sequencing data without the need to access bacterial isolates. This is based on an elaborate computational algorithm (*MetaBGC*) that operates on the metagenomic read level, and a multi-host synthetic biology strategy that allows for the heterologous expression of the discovered biosynthetic pathways. We discovered several new molecules, including derivatives of clinically used antibiotics and anticancer drugs.
   a. Sugimoto Y, Camacho FR, Wang S, Chankhamjon P, Odabas A, Jeffrey PD, **Donia MS**. (2019). A metagenomic strategy for harnessing the chemical repertoire of the human microbiome. Science, Dec 13;366(6471):eaax9176. PMID: 31582523; NIHMSID:NIHMS1626329
   b. **Donia MS**, Cimermancic P, Schulze C, Wieland Brown LC, Martin J, Mitreva M, Clardy J, Linington, R, Fischbach M. (2014). A systematic analysis of biosynthetic gene clusters in the human microbiome reveals a common family of antibiotics. Cell, 158, 6, 1402-1414. PMCID: PMC4164201
   c. Guo CJ, Chang FY, Wyche TP, Backus KM, Acker TM, Funabashi M, Taketani M, **Donia MS**, Nayfach S, Pollard KS, Craik CS, Cravatt BF, Clardy J, Voigt CA, Fischbach MA. (2017). Discovery of Reactive Microbiota-Derived Metabolites that Inhibit Host Proteases. Cell, 168(3). PMCID: PMC5302092

2. Developed a systematic approach for mapping the ability of the human gut microbiome to metabolize orally administered drugs. We developed a novel approach, Microbiome-Derived Metabolism Screen, or MDM-Screen, to study drug metabolism by the human microbiome. We developed a batch culturing approach to sustain the growth of complex, personalized, gut microbiome-derived microbial communities in an *ex vivo* setting, a biochemical / analytical chemistry drug screen to test the ability of these cultured communities to metabolize hundreds of orally administered small molecule drugs, genomic and metagenomic functional screens to identify the genes responsible for the observed metabolism, and microbiome-dependent pharmacokinetic assays in mice to test the *in vivo* consequences of the observed metabolism.
   a. Balaich, J.; Estrella, M.; Wu, G.; Jeffrey, P.D.; Biswas, A.; Zhao, L.; Korennykh, A., Donia, M.S.; The human microbiome encodes resistance to the antidiabetic drug acarbose. Nature, 600, 110–115 (2021). PMID: 34819672
   b. Javdan B, Lopez JG, Chankhamjon P, Lee, Y-C J, Hull R, Wu Q, Wang X, Chatterjee S, **Donia, MS**. (2020). Personalized Mapping of Drug Metabolism by the Human Gut Microbiome. Cell, Jun 25;181(7):1661-1679. PMID: 32526207; NIHMSID:NIHMS1603084

3. Discovered biosynthetic pathways that uncultivated symbiotic bacteria use to produce combinatorial libraries of heavily modified peptides with different biological activities in several marine symbiotic systems. During early work in my Ph.D., I was able to reveal and characterize a biosynthetic pathway in the genomes of an uncultivated symbiont of marine tunicates (*Prochloron didemni*) that is responsible for

synthesizing more than 60 natural products of various biological activities. I then used this knowledge to discover more biosynthetic pathways, and small molecules of this class – which we coined "cyanobactins". In addition, I succeeded in cloning, expressing, and genetically engineering this system in laboratory strains of *Escherichia coli*, which provided a renewable source of both rare natural molecules, and also engineered derivatives thereof. This work was the first of its kind, where biosynthetic pathways from uncultivated symbiotic bacteria are successfully expressed in the laboratory. In my own laboratory, we studied defensive peptides produced in marine sponges, algae, and mollusks. In *Haliclona* sponges, we discovered an intracellular bacterial symbiont (*Candidatus* Endohaliclona renieramycinifaciens) that produces the defensive toxins renieramycins, and showed that it resides in a new sponge cell type (which we named chemobacteriocytes). In *Bryopsis* sp. alga, we discovered an intracellular symbiont (*Candidatus* Endobryopsis kahalalidefaciens) that produces a library of >15 defensive lipopeptides (the kahalaides) that protect the algal host from predation. These peptides are then hijacked by a predatory mollusk (*Elysia rufescens*) and used for its own defense.

a. Zan J, Li Z, Tianero MD, Davis J, Hill RT, **Donia MS**. (2019). A microbial factory for defensive kahalalides in a tripartite marine symbiosis. Science, Jun 14;364(6445). PMID: 31196985; NIHMSID:NIHMS1626346
b. Tianero MD, Balaich JN, **Donia MS**. (2019). Localized production of defence chemicals by intracellular symbionts of *Haliclona* sponges. Nat. Microbiol, Jul;4(7):1149-1159. PMID: 30936484; NIHMSID:NIHMS1522097
c. **Donia MS**, Hathaway BJ, Sudek S, Haygood MG, Rosovitz MJ, Ravel J, Schmidt EW. (2006). Natural combinatorial peptide libraries in cyanobacterial symbionts of marine ascidians. Nature Chem Biol, 2, (12), 729-735. PMID: 17086177
d. **Donia MS**, Ravel J, Schmidt EW. (2008). A global assembly line for cyanobactins. Nature Chem Biol, 4, 6, 341-3. PMCID: PMC2862271.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/16usQygvDIC5e/bibliography/public/