Synthetic Biology

OMAR AKBARI



Omar Akbari

Current Position. Senior Postdoctoral Fellow, Division of Biology and Biological Engineering at California Institute of Technology. Advisor: Bruce A. Hay.

Education. PhD, Cellular and Molecular Biology at University of Nevada, Reno. Advisor: Robert A. Drewell. Combined BS/MS in Biotechnology at University of Nevada, Reno. Advisor: Robert A. Drewell.

Nonscientific Interests. I enjoy traveling, exploring new cultures, and everything outdoors—camping, biking, swimming, hiking, cycling.

My research predominantly focuses on the basic genetics and physiology of mosquitoes with the overall goal of developing innovative, novel, creative, synthetic biology inspired genetic control technologies for reducing the burden of mosquito borne vector diseases on humans. The underlying hypothesis inspiring this work is that the introduction and spread of genes that prevent mosquitoes to transmit pathogens should in theory lead to less transmission of these pathogens, resulting in decreases of human infections and/or death. To test this hypothesis, first we need a broad understanding of the biology of the mosquito to develop gene-based strategies for engineering mosquitoes that are resistant to pathogens; second, we need to develop tools to rapidly "drive" these laboratory developed genes into wild mosquito populations. This paper represents a significant step in that second direction, by demonstrating that engineering "gene drive" systems is possible. (Read Akbari's article; DOI: 10.1021/ sb300079h).

NICHOLE DARINGER



Current Position. Postdoctoral associate, Institute for Medical Engineering and Science, Massachusetts Institute of Technology. Advisor: Dr. Jim Collins.

Education. PhD Chemical and Biological Engineering, Northwestern University (2014). Advisor: Dr. Joshua Leonard. BSE Chemical and Biochemical Engineering, University of Iowa (2008).

Nonscientific Interests. Cycling, hiking, reading, playing the piano.

My doctoral research focused on using synthetic biology as a tool to develop cell-based biosensors that detect and respond to extracellular protein ligands in mammalian cells. I am particularly interested in utilization of these biosensors for therapeutic applications including modulation of immune responses. This article lays the groundwork for the development and characterization of this cell-based biosensor platform. (Read Daringer's article; DOI: 10.1021/sb400128g).

RACHEL M. DUDEK



Rachel M. Dudek

Current Position. PhD Candidate in Chemical and Biological Engineering, Northwestern University. Advisor: Dr. Joshua Leonard.

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ACS Synthetic Biology

AMAR GHODASARA

Education. BSE Chemical Engineering, University of Michigan (2008). **Nonscientific Interests.** Singing, playing the guitar, running,

baking, and watching Food Network.

My scientific interests largely comprise the engineering of mammalian cells to make "smart" cell therapeutics and diagnostics. An important bottleneck in this long-term vision, and the focus of my doctoral research and this paper, is the development of biosensor modalities that would enable these mammalian smart cell devices to sense extracellular cues in their environment and respond appropriately. We have therefore developed a biosensor platform technology that operates on the synthetic biology principles of orthogonality and modularity. This platform technology is not only a new tool in the mammalian synthetic biology biosensor toolbox but also a probe to elucidate the design criteria and constraints in the design space of extracellular biosensing in mammalian cells and to improve our ability to engineer in this space. (Read Dudek's article; DOI: 10.1021/sb400128g).

KEI FUJIWARA



Kei Fujiwara

Current Position. Assistant professor at Department of Biosciences and Informatics, Keio University.

Education. Postdoctoral fellow: Department Bioengineering and Robotics, School of Engineering, Tohoku University. Advisor: Dr. Shin-ichiro M. Nomura. PhD: Department of Medical Genome Sciences, Graduate School of Frontier Sciences, the University of Tokyo. Advisor: Dr. Hideki Taguchi. BS and MS: Department of Biotechnology, Graduate School of Agricultural and Life Sciences, the University of Tokyo. Advisor: Dr. Makoto Nishiyama.

Nonscientific Interests. Playing the violin (over 25 years of experience). I love to play Fritz Kreisler's pieces.

My major research interest is finding a way to construct biomimetic artificial cells that replicate themselves following their genetic information as living cells do. Recent progress in artificial cell engineering and bottom-up synthetic biology has revealed that artificial cells with reconstituted biological systems behave just as those in living cells. However, it is still challenging to construct replicative artificial cells using mixtures of biomolecules. To address this challenge, we are trying to construct mimics of living cells made from biomolecules, which would pave a path to understanding the inherent differences between life and materials. We have developed methods for reconstitution of intracellular environments in artificial cells, especially focusing on concentrations of macromolecules inside living cells (Read Fujiwara's article; DOI: 10.1021/sb4001917).



Amar Ghodasara

Current Position. PhD Candidate, Department of Biological Engineering, MIT. Advisor: Christopher A. Voigt.

Education. BS in Biomedical Engineering at the University of California, Davis.

Nonscientific Interests. I enjoy cooking, playing basketball, outdoor activities, and traveling. I always have multiple projects going on in my apartment which can vary from making home-made yogurt to building electronic gadgets.

I am interested in developing tools to enable the engineering of complex biological systems. Mechanistic insights into diseases, the deciphering of the human and plant microbiome, and the whole-genome sequencing of diverse organisms are paving the way and providing the fuel for synthetic biology applications. My research focuses on precisely controlling gene expression at the post-transcriptional level in prokaryotes using engineered small RNAs that can downregulate and buffer fluctuations gene expression. Precise control of gene expression in an engineered system can improve functionality, predictability, and reduce failure. Ultimately, my goal is to apply this toolkit to complex circuits and metabolic pathways to engineer plant microbes to improve agriculture and to produce high value molecules, including therapeutics. (Read Ghodasara's article; DOI: 10.1021/sb5002856).

GEORGE A. KHOURY



Current Position. Wallace Memorial Fellow in Engineering and Ph.D. Candidate, Department of Chemical and Biological Engineering, Princeton University. Advisor: Prof. Christodoulos A. Floudas. Education. MA (2012) in Chemical and Biological Engineering, Princeton University. Advisor: Prof. Christodoulos A. Floudas; BS (2009) and MS (2010) in Chemical Engineering, Penn State University. Advisor: Prof. Costas D. Maranas.

Nonscientific Interests. My leadership roles have strongly influenced my nonscientific interests by being elected to and serving on the Priorities Committee and as President of the Graduate Engineering Council at Princeton and as President of the Council of Commonwealth Student Governments at Penn State. In these roles, I have represented students to a variety of administrative bodies, raised funds, and organized events. At Penn State, I interfaced with the University Registrar and a committee of developers, administrators, and students to advocate for and launch real-time course scheduling. Additionally, I have played electric guitar for 15 years and have opened for several well-known national artists.

Through my Ph.D. research, several major advances and tools have been introduced for protein engineering, design, simulations, and folding with modified and natural amino acids combining and applying principles from optimization, thermodynamics, and quantum chemistry. I have applied the tools I developed to design new lead compounds; one that physically blocks a critical step in HIV fusion and another that inhibits Complement activation. My research has led to the creation of 6 web interfaces that have been utilized over 10 000 times by both academic and industrial researchers at Fortune 500 companies. In this work, Force field NCAA enables the atomistic modeling, simulation, and design of protein-based compounds containing 147 unnatural amino acids. The parameters accurately reproduce the quantum mechanically derived electrostatic potential and are capable of distinguishing between active and inactive analogs of the complement inhibitor compstatin. (Read Khoury's article; DOI: 10.1021/sb400168u).

JOSHUA LEONARD



Jim Prisching

Current Position. Assistant Professor of Chemical and Biological Engineering, Northwestern University.

Education. Postdoctoral fellow, National Cancer Institute (NIH), advisor: David M. Segal; PhD, University of California Berkeley, Chemical Engineering. Advisor: David V. Schaffer. BS, Stanford University, Chemical Engineering.

Nonscientific Interests. Edible chemistry, amateur polyglottery, feats of endurance, and challenging fiction.

My group seeks to enable the emerging paradigm of designdriven medicine by integrating synthetic biology with systems biology to address pressing challenges in medicine and biotechnology. This manuscript describes an important advance in these efforts. In general, while our field has made substantial advances in engineering custom mammalian cell functions using sensors and circuits that utilize and modulate intracellular information, to date, our ability to couple engineered cells to external physiological systems is more limited. To help meet this need, the MESA platform we describe here enables one to engineer novel cell-surface receptors that sense exclusively extracellular species and relay the information that sensing has occurred to the nucleus, without relying upon any native receptors or signal transduction pathways. This self-contained, modular, and orthogonal technology will enable the construction of new cell-based devices that robustly interface with human physiology. (Read Leonard's article; DOI: 10.1021/sb400128g).

JOHN M. MARSHALL



Current Position. Assistant Professor, University of California, Berkeley (Division of Biostatistics, School of Public Health).

Education. Postdoctoral Fellow, University of California, Los Angeles (Society and Genetics, Advisor: Charles Taylor), California Institute of Technology (Biology and Biological Engineering, Advisor: Bruce Hay), Imperial College London (Infectious Disease Epidemiology, Advisor: Azra Ghani). MS, PhD (Biomathematics), University of California, Los Angeles, Advisor: Charles Taylor. BSc (Biological Sciences), BTech Hons (Optoelectronics), University of Auckland, New Zealand.

Nonscientific Interests. I enjoy discovering new music and cultures while conducting epidemiological field work. My coworkers are my DJ managers. I have a radio show on Berkeley's KALX 90.7 FM.

I enjoy the synergy of interdisciplinary collaboration and had a very productive time as a mathematician in Prof. Bruce Hay's molecular biology lab at Caltech. This paper documents a novel approach to engineering a self-ish genetic element called Medea using a toxin-antidote combination that leads to the element being preferentially inherited among offspring. I am interested in the population-level implications of these systems, and in this paper, the potential of Medea to spread and induce a population crash if linked to a gene inducing diapause-dependent female lethality. Together with members of the Hay lab, we have developed a series of systems for spreading genes into populations with exciting applications such as the potential to reduce and possibly eliminate devastating mosquito-borne diseases such as malaria and dengue fever on a wide scale. (Read Marshall's article; DOI: 10.1021/sb300079h).

TUSHAR PATEL



Tushar Patel

Current Position. Scientist at Bristol-Myers Squibb Company, Devens, MA.

Education. PhD (2014), MS (2011) in Chemical Engineering, Columbia University. Advisor: Dr. Scott Banta; BS (2009) in Chemical Engineering, Northeastern University.

Nonscientific Interests. I enjoy sports, cycling, and am an avid disc golfer.

My doctoral research was focused on the development and characterization of heterogeneous biocatalysts via enzyme immobilization. One such biocatalyst was a transport-limited whole-cell biocatalyst generated by recombinantly expressing carbonic anhydrase within the periplasm of *E. coli* cells. Following the initial characterization, we sought to employ synthetic biology tools to enhance this basic design. In this paper, we demonstrate an enhancement to the apparent activity of these biocatalysts. To do so, an α -helical protein, which oligomerizes into pentameric bundles that form nonspecific pores in the outer membrane of *E. coli* cells was recombinantly coexpressed with the periplasmic carbonic anhydrase. This modification to the cells enhanced the permeability of the outer membrane, which was quantified using principles of porous catalysis. This strategy demonstrated the ability to modify a heterogeneous biocatalyst in a modular fashion. (Read Patel's article; DOI: 10.1021/sb400202s).

KELLY SCHWARZ



Kelly Schwarz

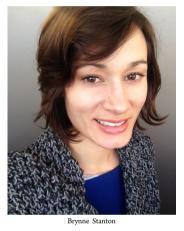
Current Position. PhD Candidate, Chemical and Biological Engineering Department, Northwestern University. Advisor: Dr. Joshua Leonard.

Education. BS, Johns Hopkins University, Chemical and Biomolecular Engineering.

Nonscientific Interests. Playing and watching sports, running, baking.

My research focuses on developing a technology that enables cells to sense and respond to their environment specifically through their interaction with extracellular cues. To accomplish this goal, we developed a synthetic protein receptor system for mammalian cells that allows for transduction of extracellular signals, such as an interaction with a protein, into intracellular events—a change in cell state or gene expression, for example. I am specifically interested in using this platform as a method for modulating the immune system for the treatment of diseases such as cancer; however, what is unique and exciting about our technology is that the system is composed of interchangeable parts, which can be readily adapted for other applications. (Read Schwarz's article; DOI: 10.1021/sb400128g).

BRYNNE STANTON



Current Position. Biological Engineer at Ginkgo BioWorks.

Education. Postdoctoral fellow at University of California, San Francisco and MIT. Advisor: Dr. Christopher Voigt; PhD, University of Wisconsin–Madison. Advisor: Dr. Christina Hull; BS, University of Oregon. Advisor: Dr. Diane Hawley.

Nonscientific Interests. Voracious reader, dog enthusiast, runner, and culinary experimentalist. I have a double major in French, and apart from living in France for one year, this skill is massively underutilized.

I'm particularly proud of this work because it represents a significant advancement of not only the number of transcription factors that can be used to control expression in mammalian cells but also because we are contributing an additional mammalian sensor that is both robust and reliable. Based on my experiences in industry thus far, it has become clear that these kinds of sensors and switches will be useful in engineering a variety of organisms for diverse applications. (Read Stanton's article; DOI: 10.1021/ sb5002856).