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DEPARTMENT OF CHEMICAL AND
BIOLOGICAL ENGINEERING

CBE Seminar Series – Fall 2020

Dr. Karmella Haynes

Assistant Professor of Biomedical Engineering
Emory University

Seminar: Wednesday, November 11, 2020
12:00 p.m. (ONLINE)

WebEx link: https://rensselaer.webex.com/rensselaer/onstage/g.php?d=1207823066&t=h
Password: CBESeminar

"Epigenetic co-regulation of genes with engineered sensor-actuator proteins"

Abstract:

Mounting evidence from genome-wide comparisons of chromosome packaging and gene expression in healthy versus cancer cells suggests that epigenetic hyper-repression, rather than genetic mutation in many cases, supports cancer aggressiveness. Aberrant behavior of the chromatin system (genomic DNA, and nuclear RNA and proteins) has been implicated as a driver of metastasis and drug resistance. Since the early 1990's small compounds have been used to disrupt hyper-repressed chromatin to simultaneously activate sets of therapeutic genes in cancer cells. However, it is difficult to customize the biological activity of these small compound inhibitors, and they do not directly mediate RNA PolII activity at silenced tumor suppressor genes. To address these limitations, our lab has designed synthetic reader-actuator (SRA) fusion proteins that bind epigenetic marks within chromatin. The first SRA we have designed and tested in cancer cells, "Polycomb-based transcription factor" (PcTF), reads histone modifications through a protein-protein interaction between its N-terminal Polycomb chromodomain (PCD) motif and trimethylated lysine 27 of histone H3 (H3K27me3). The C-terminal VP64 domain of PcTF recruits endogenous activators to silenced targets. We identified a set of 104 genes that become consistently activated from 24 - 72 hours after PcTF-overexpression in a triple negative breast cancer cell line (BT-549). To enhance the activity of SRAs in cancer cells, we investigated tunable parameters. We discovered that enhancing the avidity of the H3K27me3 binding domain with tandem human wild-type PCDs increases target gene activation in a model cell line (HEK293). We are developing a miniaturized on-chip cell-free protein expression array to rapidly screen a library of PCD variants produced by site saturation mutagenesis. We believe that peptides that specifically interact with epigenetic marks are a key, complementary approach to overcome barriers to the advancement of epigenetic cancer therapy.

Biography:

Karmella Haynes is an Assistant Professor of Biomedical Engineering at Emory University. She earned her Ph.D. studying epigenetics and chromatin in Drosophila at Washington University, St. Louis. Postdoctoral fellowships at Davidson College and Harvard Medical School introduced her to synthetic biology. Her Davidson HHMI postdoc fellowship project on bacterial computers was recognized as "Publication of the Year" in 2008 by the Journal of Biological Engineering. Today, her research aims to apply the intrinsic properties of chromatin, the DNA-protein structure that packages eukaryotic genes, to engineer proteins and nucleic acids that control cell development. After Dr. Haynes joined the faculty at the Emory School of Medicine in 2019, she received an NIH R21 grant (2019) to develop new protein engineering and computational tools for cancer epigenetics, and launched the annual NSF-funded AfroBiotech conference. She is a founder and instructor of the Cold Spring Harbor Summer Course on Synthetic Biology, a member of the national Engineering Biology Research Consortium (EBRC), and Advisor and Judge Emeritus for the annual International Genetically Engineered Machines (iGEM) competition. She has been a featured guest on PBS NOVA (2020) and PRI's Science Friday (2016), and her work has been profiled in Forbes magazine (2020).

Due to COVID-19, no refreshments will be available for this seminar.
For more information, please contact Lisa Martin (swishl@rpi.edu) or Helen Zha (zhar@rpi.edu)