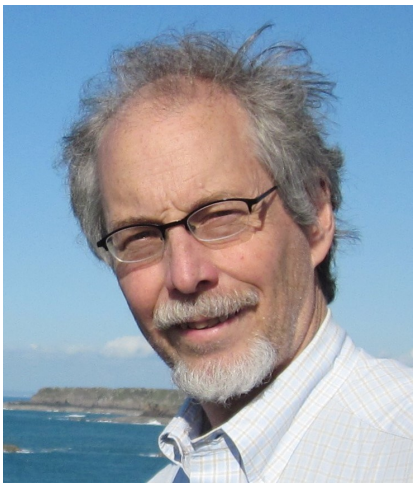
Department of Biochemistry



Fall 2016 Seminar Series
Beach Distinguished Lectures

Presented by

Jef Boeke

Director, Institute for Systems Genetics
Professor, Department of Biochemistry and
Molecular Pharmacology
NYU Langone Medical Center

Tuesday and Wednesday, September 20 & 21 at 3:30

Deans Auditorium (PFEN 241)

Genome Writing

Rapid advances in DNA synthesis techniques have made it possible to engineer viruses, biochemical pathways and assemble bacterial genomes. They have also enabled the construction of novel genetic pathways and genomic elements, furthering our understanding of systems-level phenomena. The synthetic yeast genome project, Sc2.0, is well on its way with several of the first synthetic Saccharomyces cerevisiae chromosomes completed. Undergraduate students provide a workforce for synthesis and assembly for some of these chromosomes, although a wide variety of assembly schemes are employed by the various groups worldwide building chromosomes. The synthetic genome features several systemic modifications, including TAG/TAA stop-codon replacements, deletion of subtelomeric regions, introns, tRNA genes, transposons and silent mating loci as well as strategically placed loxPsym sites to enable genome scrambling using an inducible evolution system termed SCRaMbLE. After writing, genome structure must be validated and most importantly validated for fitness biologically.

Strategies for other means of radically re-engineering genomes, including designer fusion of chromosomes to change the karyotype, will be described. We have also begun a discussion to develop technologies to write much larger genomes, like human. First steps in this direction will be described.

Dymond et al. Synthetic chromosome arms function in yeast and generate phenotypic diversity by design. Nature, 477:471-6. 011.
Annaluru et al. Total synthesis of a functional designer eukaryotic chromosome. Science. 2014 344:55-8. 2014.
Boeke et al. The Genome Project-Write. Science. 2016 353:126-7.

Genome scrambling and synthesis of neochromosomes

The synthetic yeast genome Sc2.0 features several systemic modifications, including a set of strategically placed loxPsym sites that enable genome scrambling, using an inducible evolution system termed SCRaMbLE (Synthetic Chromosome Rearrangement and Modification by LoxP-mediated Evolution). SCRaMbLE can be used as a novel method of mutagenesis, capable of generating complex genotypes and a variety of phenotypes. It can also be deployed in a wide variety of formats. The fully synthetic yeast genome will open the door to a new type of combinatorial genetics based on variations in gene content and copy number, rather than base changes. We also describe supernumerary designer "neochromosomes" that add new functionalities to yeast cells such as humanized pathways. Ideas for designer neo chromosomes with human applications will be introduced.

Mitchell et al. Versatile genetic assembly system (VEGAS) to assemble pathways for expression in S. cerevisiae Nucl. Acids Res. 2015 43:6620-30

About the Beach Lectures:

David W. Beach was born in 1925 in London, England. Following service in the Royal Navy, he married Doris Holmes and began his career as a Chartered Accountant. Feeling the urge to expand his horizons, he moved to Canada and began a series of jobs in the aluminum industry that included General Manager of Kawneer, Canada and Vice-President of Kawneer, Inc. As Vice-President of ALUMAX Aluminum Corporation he was instrumental in making it one of the largest and most profitable aluminum companies in the world, prior to his retirement. Inspired by his son's enthusiasm for science, he has chosen to share his good fortune by supporting this biochemistry graduate program. This long-term support is intended to promote intellectual curiosity, a commitment to excellence, and an appreciation of science in all those involved.