LMU GRK2062

WHAT'S GOING ON

In the Research Training Group Molecular Principles of Synthetic Biology

NEWSLETTER #3 2016

FOCUS ON RESEARCH

Figure 1. *A comparison of the structures surrounding the metal for hydrated Fe^{3+}, heme and catalase.*

Prof. Dr. *Sherif Mansy*

Metal catalysts at the origins of life

Darwinian evolution began on Earth approximately 3.5 billion years ago through a process that transformed much of geochemistry into biochemistry. What exactly transpired may never be known, because fossil records of primitive cellular life have yet to be found. Nevertheless, we do know that physics and chemistry are unchanged between geological and biological settings. In other words, as Stanley Miller's work in the 1950s helped popularize, the components of life can be synthesized by laboratory simulations of early Earth conditions. However, extant life does not consist solely of organic material. Even autotrophic organisms depend on metal ions acquired from the environment. In fact, estimates put the number of metalloproteins somewhere between ¼ to ½ of all proteins. RNA and protein folding is largely dependent on metal ion coordination and much of central metabolism is driven by metal ions, either by directly mediating catalysis within enzyme active sites or by forming energy yielding concentration gradients.

In 1959, Melvin Calvin noted that the ability of free Fe^{2+} to catalyze the decomposition of hydrogen peroxide in water and oxygen was increased 10^3-fold by coordination to porphyrin (Figure 1). An additional 10^2-fold improvement resulted from coordination of the iron-porphyrin, i.e. heme, to the large protein enzyme catalase (Figure 1). Although several intermediate steps would have had to transpire for a reaction catalyzed by free ferric ions to be transformed into a protein enzyme mediated process, this example illustrates how the intrinsic activity of a metal center can be augmented by genetically encoded material. However, it may not just be a case of evolution improving upon the innate activity of metal ions. The prevalence of metalloenzymes may reflect a difficulty in evolving metal independent sequences, at least with the nucleotides and amino acids exploited by life as we know it. For example, *in vitro* evolution methods used to identify catalytic sequences invariably select for RNAs and proteins with metal dependent activity suggesting that sequence space is more sparsely populated with metal independent folds. In other words, although enzyme active sites devoid of metal centers can be envisaged, evolution is more likely to hit upon a metal-dependent solution.

We have begun probing the space between free metal ions and modern day proteins to gain insight into what could have transpired on prebiotic Earth. For example, we identified model prebiotic dipeptide sequences from bioinformatics and DFT and molecular dynamics calculations. The peptides were then synthesized and evaluated for metal affinity and specificity. We found that cysteine containing dipeptides were not associated with metal affinities that followed the Irving-Williams series, as would have been expected, but rather followed the concentration trends found in seawater. We have also shown that short dipeptides can coordinate an iron-sulfur cluster and that these iron-sulfur peptides can mediate the exchange of electrons. We are now bringing the different parts together to build protocellular structures supported by an internal, metal dependent metabolism.

GRK2062 PUBLICATION

Angew. Chem. Int. Ed. 2015, 54, 13508 - 13514

CRISPR-Cas: From the Bacterial Adaptive Immune System to a Versatile Tool for Genome Engineering

Marion Kirchner and Sabine Schneider

Abstract

The field of biology has been revolutionized by the recent advancement of an adaptive bacterial immune system as a universal genome engineering tool. Bacteria and archaea use repetitive genomic elements termed clustered regularly interspaced short palindromic repeats (CRISPR) in combination with an RNA-guided nuclease (CRISPR-associated nuclease: Cas) to target and destroy invading DNA. By choosing the appropriate sequence of the guide RNA, this two-component system can be used to efficiently modify, target, and edit genomic loci of interest in plants, insects, fungi, mammalian cells, and whole organisms. This has opened up new frontiers in genome engineering, including the potential to treat or cure human genetic disorders. Now the potential risks as well as the ethical, social, and legal implications of this powerful new technique move into the limelight.

http://dx.doi.org/10.1002/anie.201504741

We are looking forward to highlight future GRK2062 publications in this section. Therefore we kindly ask you to inform the GRK2062 office in a timely manner about your accepted papers.

NEW MEMBERS

PhD-students

Karsten Miermans, M.Sc. Applied Physics, is supervised by Chase Broedersz since February 2016. Working title of his PhD thesis: "Physical aspects of chromosome condensation and segregation".

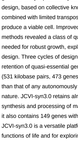
EVENTS

Retreat 2016

Report

All GRK2062 doctoral students, postdocs and several PIs enjoyed our first Retreat in the Benediktbeuern abbey of Frauenwörth on the Fraueninsel. Additionally, several team members of the iGEM Team 2016 accepted our invitation and took advantage of these days for networking, discussions and refining their iGEM project. Talks and posters from all junior researchers, as well as plenary talks of Chase Broedersz, Nina Köhler, *Sherif Mansy* (see also Focus on Research) and Kai Papenfort gave interesting insights into different aspects of Synthetic Biology. Despite the rain, participants had fun during the excursion to the great Royal Palace of Herrenchiemsee. The artist Finan Yoldos gave a very impressive presentation demonstrating new ways to bring about confrontations to the public with topics such as the influence of plastic on our ecosystem. Her surprising designs of possibly evolving plastic incorporating organisms are more current than ever: a recently published article in Science demonstrates that "some bacteria think plastic is fantastic".

Group Photo: *Retreat 2016 April 7-9, 2016*



Upcoming Transferable Skills Courses

Scientific Writing, Science Craft

This course will run on the 26th and 27th of July 2016 in room 000.013 at LMU Biocenter. For a full description please click here. Please register by **May 31, 2016** via e-mail to grk2062@bio.lmu.de.

Adobe Illustrator

Date of the course (presumably in autumn 2016) will soon be announced.

JOURNAL CLUB

Science 25 March 2016: Vol. 351, Issue 6280

Research article

Design and synthesis of a minimal bacterial genome

Clyde A. Hutchison et al.

Abstract

We used whole-genome design and complete chemical synthesis to minimize the 1079-kilobase pair synthetic genome of *Mycoplasma mycoides JCVI-syn1.0*. An initial design, based on collective knowledge of molecular biology combined with limited transposon mutagenesis data, failed to produce a viable cell. Improved transposon mutagenesis methods revealed a class of quasi-essential genes that are needed for robust growth, explaining the failure of our initial design. Three cycles of design, synthesis, and testing, with retention of quasi-essential genes, produced *JCVI-syn3.0* (531 kilobase pairs, 473 genes), which is genetically smaller than that of any autonomously replicating cell found in nature. *JCVI-syn3.0* retains almost all genes involved in the synthesis and processing of macromolecules. Unexpectedly, it also contains 149 genes with unknown biological functions. *JCVI-syn3.0* is a versatile platform for investigating the core functions of life and for exploring whole-genome design.

Full text: http://dx.doi.org/10.1126/science.aad6253

MISCELLANEOUS

Laborjournal 4/2016:

Special focus on Synthetic Biology (p. 32-45)

Süddeutsche Zeitung March 25, 2016:

Popular science article about "Design and synthesis of a *minimal* bacterial genome" (see also Journal Club).

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