Editorial Overview

The Era of Synthetic Biology and Genome Engineering: Where No Man Has Gone Before

Synthetic biology seeks to integrate our knowledge of engineering principles with living systems for novel biological design and fabrication. The central focus of synthetic biology has been to increase the ease, efficiency, and scale of how biological devices and systems can be designed, constructed and manipulated for diverse biological, environmental, and therapeutic applications. We owe to this discipline some of the most remarkable recent scientific advances including successful recoding of a bacterial genome [1], *de novo* chromosome synthesis [2–4], engineering of a biosynthetic pathway for industrial-level production of the precursor of the antimalarial drug artemisinin [5], and so on. However, the design of novel biological systems remains constrained in scale, speed, precision, and predictability due to the challenge of establishing effective engineering approaches in the face of incomplete understanding of complex regulatory and signaling circuits in living organisms. With this special issue, we wanted to engage a discussion on current challenges for the field and update the reader on some of the most promising aspects it has to offer.

Zomorrodi and Segrè introduce the issue by providing an overview of mathematical models used for bottom-up engineering of complex synthetic microbial consortia and the important applications these have in connection to human health, biofuel production, and bioremediation [6]. Bradley *et al*. also focus on microbial engineering, more specifically on the design principles and existing tools for gene circuit design [7]. As an example of the field's efforts to develop new tools, Rodrigo *et al*. deploy *de novo* sequence design strategy to engineer a bifunctional riboregulator that could be interfaced with other circuits, conceptually expanding the spectrum of regulatory circuits used in synthetic biology [8]. Ma *et al*. further expand the discussion by introducing key principles for engineering artificial biological circuits [15].

Intracellular compartmentalization in bacteria and viruses has proven to be an effective strategy to efficiently perform biochemical processes in locally controlled environments. Giessen *et al*. specifically discuss how such compartments can be engineered to control metabolic pathway fluxes and produce compounds of interest [9]. Venturelli *et al*. stress that, while significant advances have been made in reprogramming information in cells under laboratory settings, it is yet to be shown that these devices function reliably in real-world environments [10]. This is particularly relevant for ongoing efforts seeking to employ synthetic biology approaches to improve human health or impact environmental processes. Haellman *et al*., for instance, discuss current use of synthetic biology to create therapeutic delivery tools, namely cell and gene therapies such as theranostic cells capable of targeting and killing tumor cells or cell implants allowing treatment of diet-induced obesity [11]. Chandrasegaran and Carroll offer their perspectives on the origins of programmable nucleases for genome engineering and their applications in biology and medicine [12]. In addition, Voziyanova *et al*. illustrate how the current repertoire of yeast site-specific tyrosine recombinase systems, namely Flp/Flp recombination target, can be expanded by engineering-enhanced TD and R recombinase variants that can mediate efficient genome engineering in both mammalian cells and *Escherichia coli* [13]. Lajoie *et al*. conclude this issue by carefully analyzing the biochemical, genetic, and technological challenges that must be overcome to reengineer the genetic code [14].

We hope that the various topics at the forefront of synthetic biology in this special issue of *Journal of Molecular Biology* will be very informative and serve as a valuable resource for the at-large scientific community, especially to young scientists and new entrants to the field.

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