SUMMARY

The ability to control spatial organization in cells is highly valuable. Clustering into micro-compartments or onto scaffolds helps direct substrate flow in-between interacting proteins, limits cross-talk between signaling pathways, and generally increases specificity and yields of sequential metabolic reactions. De novo spatial organization could be achieved using engineered nanoscale polynucleotide architectures expressed by the cells and designed to template specific metabolic pathways.

Here, we report the design and assembly of multi-dimensional polynucleotide structures, and their use as scaffolds for the spatial organization of bacterial metabolism. We systematically characterized these assemblies, and used them to control the spatial organization of a biofuel-producing biochemical pathway, which resulted in a significant increase in yields as a function of scaffold architecture. Taken together, these results indicate that self-assembling polynucleotide structures can be used to rationally construct functional architectures in vivo.

INTRODUCTION

Over the past few years, hydrogen has emerged as a promising renewable energy source as pressure mounts to replace fossil fuels (White House 2003 Energy Report).
Among its primary advantages, hydrogen is energetically denser than all other combustible fuels, it combusts into pure water, and its utilization in fuel cells is more efficient than current combustion engines. Moreover, the downstream technology to store, supply and use hydrogen is already available (e.g. hythane technology). Currently, hydrogen is produced commercially primarily by coal gasification, steam reforming of natural gas, and water electrolysis. (Dum et al, Int. J of Hydrogen Energy, 2002). These methods are not only too costly for hydrogen to compete with gasoline as a fuel, but they are also energy intensive and therefore not environmentally friendly. Given the factors described above, biological hydrogen production may present a useful alternative due to its use of renewable biomass or sunlight as its primary energy source (Waks et al, Appl Environ Microbiol, 2009).

However producing biologically hydrogen is far from trivial. Hydrogenases, the enzymes catalyzing electron exchange in between common electron carriers and molecular hydrogen, have the issue of being both extremely oxygen-sensitive and bad electron acceptors (Vignais et al, Cur. Issues Mol. Biol., 2007).

In cells multienzymatic pathways are often physically and spatially organized onto scaffolds or clusters or into microcompartments. Spatial organization helps substrates flow between interacting proteins, limits cross-talk between signaling pathways, and increases yields of sequential metabolic reactions. We report here the creation of micro-environments within bacterial cells, “synthetic organelles” made out of assembling RNA strands and specialized in producing hydrogen more efficiently.

OTHER SUBTITLES


RESULTS

1) We provided with a new level of control in Synthetic Biology – the ability to control spatial organization of synthetic metabolic pathways;
2) We used the toolbox from a previously unrelated science, RNA Nanotechnology, and translated it in vivo;
3) We improved biological hydrogen production by 48 fold and showed a relationship in between scaffold architecture and yields.

CONCLUSIONS

Papers :

Organization of intracellular reactions with rationally designed RNA assemblies
   Cover of the Science
   Issue Selected for pre-press publication under “Science Express”
   Featured as a “Research Highlight” in Nature
   Commented in Science with a 2 pages “Perspective” article
   Featured in Nature Methods Featured in ACS Chemical biology
Assembling proteins in vivo on designed RNA scaffolds

International Awards:

Grand Price Winner 5th International Meeting in Synthetic Biology 2011
Premiere international conference on Synthetic Biology
Grand Price Winner of the French-American Innovation Day 2011
Selected amongst a panel of the best French and American scientists
Best Student Presentation International FNANO Conference 2011
Premiere international conference on DNA Nanotechnology

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