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SYNTHETIC BIOLOGY

Just add water — programmable *in vitro* diagnostics

Concerns about biosafety, practicality and costs have traditionally confined engineered synthetic gene circuits hosted in living cells to research environments, despite the great potential that these molecular tools hold for biotechnology and medical applications. Now, US researchers have circumvented these difficulties by using porous materials such as paper as host substrates for cell-free synthetic gene networks that can be activated by adding water.

The researchers combined transcription and translation enzymes with engineered gene circuits and freeze-dried these onto paper to create various portable synthetic gene networks, comprising genetically encoded tools with trigger, regulatory transducer and output elements, that are stable outside of the cell. The purpose-built gene networks were responsive to synthetic RNA, mRNA and small molecules. Moreover, to make their system widely usable without extensive technical infrastructure, the investigators incorporated several enabling features, including an enzyme-mediated colorimetric reporter system visible to the naked eye, and quantification and automation through a low-cost electronic optical reader with high sensitivity for the colorimetric signal.

To demonstrate the potential of their tool as an *in vitro* diagnostics platform, the team developed sensors that react with LacZ induction in the presence of mRNAs of microbial antibiotic resistance genes, for example, ampicillin and kanamycin. Further benefits of the paper-based platform for diagnostics include low manufacturing costs and short design-to-production cycles, as evidenced by the development of 24 mRNA sensors that could distinguish between the Sudan and Zaire strains of the Ebola virus in less than 12 hours.

"Sensitivity is a remaining challenge," comments senior investigator James J. Collins (Wyss Institute for Biological Inspired Engineering, Harvard University). "We currently have detection into the picomolar range, but a number of technologies under development promise to provide the boost to sensitivity that we need, a goal that we anticipate reaching within the next 12 months." Of note, the study reports sensitivities in the low nanomolar range, which hints at the fast pace of advances in this field.

The study described here opens the door for molecular tools that are normally limited to the laboratory to be embedded into daily life, and highlights the potential of bringing the rational design of synthetic biology to the clinic.

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ORIGINAL RESEARCH PAPER Pardee, K. *et al.* Paper-based synthetic gene networks. *Cell* http://dx.doi.org/10.1016/j.cell.2014.10.004 (2014)