Podcast Interview: George Church

PNAS: I'm your host Prashant Nair and welcome again to Science Sessions. Ever since the dawn of recombinant DNA technology in the early 1970s, biologists have been trying to genetically engineer desirable traits into organisms and harmful traits out of them. Those efforts spawned the field of biotechnology, giving rise to improved crops, vaccines and drugs against diseases, and an ever-expanding toolbox for basic medical research. But over the course of the last decade, recombinant DNA technology has received something of a facelift, going from relatively simple cut-and-paste operations to sophisticated maneuvers such as editing entire genomes and creating life from scratch. Harvard Medical School geneticist George Church, perhaps best known as a pioneer of DNA sequencing technology, is at the vanguard of this now-familiar form of genetic engineering called synthetic biology. Church says synthetic biology combines the principles of biology, physics, chemistry, engineering, and architecture to build sophisticated living modules for specific goals. I asked Church what’s really new about this rarefied form of recombinant DNA technology.

Church: The major difference is the intentional embracing of standard engineering practices. Genetic engineering was really an extension of biology and molecular biology; it was very much one gene at a time, tinkering about, kind of handcrafted, while engineering is more a matter of models, computer-aided design, hierarchical abstractions, and testing of multiple components simultaneously and so on.

PNAS: Through synthetic biology, researchers have been trying to decode life’s basic design principles, rewire cellular genetic circuits, and tinker with entire signaling cascades – all in the hope of endowing cells with novel capabilities. The field took off when biologists demonstrated that simple bacterial cells could be rewired into sophisticated timers, counters, logic processors, and pattern detectors. Someday such wholesale tinkering might lead to an array of benefits, like fighting antibiotic resistance and developing molecularly targeted drugs and vaccines for intractable diseases. But to reach those targets, Church says, researchers must take baby steps.

Church: The major bottleneck in these is knowing what will be helpful and what will be harmful in advance or discovering it, actually getting them integrated into the genome untested. If you try to make too large a construct at once that’s too radical, then you have a chance that you’ll make the cell inviable or disable a part of the cell that you need for production, and so your best bet is to make smaller pieces and test them out individually, and then in pairs, and triples, and sort of exponentially grow into something that’s fully viable and useful.

PNAS: And professional researchers are not the only ones riding this new wave in genetic engineering. Amateur biologists, supported by academic scientists, have struck out on their own in a handful of garage labs across the US, harnessing technology to read and write DNA sequences.
**Church:** There is a possibility that this is the kind of revolution that could start in garages the way that Apple computer did, and we want to carefully monitor that and nurture it if that is the case. I think the do-it-yourself reading is even more likely to take off in the sense that people want to understand about themselves, and the cost of figuring out whether you have a particular genetic predisposition towards a well-characterized medical genetics is something that’s getting well in the hands of young students and adults that are interested.

**PNAS:** Church says there’s something about being in a non-traditional research environment, well beyond the realms of academia and industry, that fosters outside-the-box thinking.

**Church:** Industrial settings and academic institutions have bottom lines; they either have grant submissions or industrial profit. There is a bit more creativity – not necessarily productivity but creativity – that can occur in a garage environment. And as the costs plummet, which they have been doing, by a million-fold or more in reading and writing DNA, that’s a terrific opportunity where the playing field is a little more level, and there’s opportunity there.

**PNAS:** For an in-depth look into Church’s work in synthetic biology, read his recent PNAS Profile at our Web site. You can find more podcasts at pnas.org