Podcast Interview: James Collins

PNAS: I’m your host, Ann Griswold, and welcome back to Science Sessions. Synthetic biology is a relatively new field of research bringing together engineers, computer scientists, molecular biologists, and others to design different biomolecular components, in particular synthetic gene networks that can be used to reprogram cells and endow them with new functions, for example, the ability to convert biomass to fuel. In a PNAS paper, James Collins devised a way to rewire bacterial cells by regulating multiple genes in parallel. He calls this a “genetic switchboard” and he spoke with PNAS to explain the concept.

Collins: Our system is based on a set of RNA switches that we designed a few years ago. These operate in bacteria, so we exploit different aspects of prokaryotic gene expression. We coined the term “genetic switchboard” in the same sense as, kind of, the old telephone systems where you might be able to flip a number of different switches and/or connect a number of different people at any given time, and in our case, the genetic switchboard allows us, for example, to rewire a cell and, for example, shift flux from one metabolic pathway towards another metabolic pathway, and/or have different pathways talking to each other in ways that typically don’t occur naturally but ones that we can actually now tweak and modify on demand.

PNAS: I asked Collins what a genetic switchboard looks like.

Collins: In the lab, it’s basically a set of genetic components that we put inside a bacterial cell. So the system itself consists of a series of plasmids. We can design it so that there are multiple switches on any given plasmid. And we then insert the plasmid into the bacterial cell and we can design the switches so that they respond to either chemical inducers or different environmental inducers or in some cases even internal biological, physiological inducers or stimuli. So it could be classical inducers like IPTG or arabinose, it could be heavy metals like iron or copper, it could be environmental stimuli or external stimuli like UV radiation or pH or salinity.

PNAS: Collins constructed a switchboard in E. coli that controlled four different genes to direct the movement of carbon through three pathways of glucose metabolism.

Collins: We developed a large number of RNA switches, or riboregulators, that could act simultaneously and independently inside the same cell. And so we were able to design them so they wouldn’t interact with each other. And we could then use these to independently control the expression of multiple genes in a dynamic way and in a simultaneous way inside the same cell. Most of the switches to date are transcriptional, in that the teams are engineering protein-DNA interactions to either activate or repress transcription. What we developed in this study with our RNA switch was a post-transcriptional switch, wherein you primarily already have transcription having taken place but now you’re interrupting the translation process and exploiting those engineered properties then to get what turns out to be a very fast and highly versatile
switch, primarily because it’s based in the sequence space. These switches are basically a two-component system that we developed in the context of synthetic biology.

**PNAS:** Collins described how the biotech industry could use the switchboard to engineer bacteria capable of converting biomass into fuel and other useful products.

**Collins:** One would typically engineer, for example, bacteria or yeast to convert, for example, a biomass into a fuel or biomass into some product of interest. But commonly one would like to be able to dynamically modulate that at different times of day or at different times of the growth cycle in your organism. Our genetic switch allows one to do that, such that you could have the flux through a set of pathways during a certain growth phase or during certain times of day switch on the genetic switchboard and redirect that flux to another part of the cell, during another part of the growth cycle or during another part of the day.

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