New type of kill switch to prevent genetically modified microbes from wreaking havoc

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(Phys.org)—A combined team of researchers from MIT and Harvard has come up with two new ways to hardwire a kill switch into a genetically modified microorganism to prevent it from going rogue. In their paper published in the journal *Nature Chemical Biology*, the team describes their technique, why they think it is better than other approaches and the ways it could be used.

Science Fiction writers dreamed up the idea of mad scientists creating microorganisms that somehow get out into the world and kill everyone long before modern scientists had the skill to actually do it—but now that technology does exist and along with it fear that in trying to do something good, such as creating a cure for a bacterial disease, researchers could create a monster virus that not only harms patients, but jumps to others and causes serious harm or death. That fear is not ungrounded, as most biological researchers will attest, and that is why some of them are working on making genetically modified organisms safe.

The idea is to modify genes to cause the organism to note when some chemical is present, and if so, to self-destruct—a modified virus or bacteria, for example, would die if exposed to a chemical present in the atmosphere. While such an approach is deemed practical by many, others would like to have access to a means for using the same technique on different organisms—those who hold patents on GMOs, for example, would like to be able to kill off their product if it gets into the hands of another entity. To meet that need, the researchers with this new effort came up with two new types of kill switches, which they have named 'Deadman' and 'Passcode.'

The Deadman solution is a new take on the kill switch idea from old time trains, a certain chemical must always be present or the modified microbe will die. Passcode, on the other hand is more complex, it combines the idea of a needed chemical and the absence of another. Microbes could be modified to be able to live only in the presence of two different molecules, for example, and the absence of another, or the reverse could be true. The designer could choose whichever "passcode" they desire.

The main hurdle facing these new ideas and any others that may come along, of course, is in being able to prove that the microbes they modify will not evolve in ways that overcome the kill switches, either alone or by interacting with native microbes, making such efforts moot and possibly putting everyone at risk.

More information: Clement T Y Chan et al. 'Deadman' and 'Passcode' microbial kill switches for bacterial containment, *Nature Chemical Biology* (2015). DOI: 10.1038/nchembio.1979

Abstract
Biocontainment systems that couple environmental sensing with circuit-based control of cell viability could be used to prevent escape of genetically modified microbes into the environment. Here we present two engineered safeguard systems known as the 'Deadman' and 'Passcode' kill switches. The Deadman kill switch uses unbalanced reciprocal transcriptional repression to couple a specific input signal with cell survival. The Passcode kill switch uses a similar two-layered transcription design and incorporates hybrid LacI-GalR family transcription factors to provide diverse and complex environmental inputs to control circuit function. These synthetic gene circuits

efficiently kill Escherichia coli and can be readily reprogrammed to change their environmental inputs, regulatory architecture and killing mechanism.

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