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# New Models Predict Where E. coli Strains Will Thrive


Monk

Bioengineers at the University of California, San Diego have used the genomic sequences of 55 E. coli strains to reconstruct the metabolic repertoire for each strain. Surprisingly, these reconstructions do an excellent job of predicting the kind of environment where each strain will thrive, the researchers found.

Their analysis, published in the Nov. 18, 2013 early edition of the Proceedings of the National Academy of Sciences, could prove useful in developing ways to control deadly E. coli infections and to learn more about how certain strains of the bacteria become virulent.

And when “nasty new versions” of E. coli appear, the metabolic models may someday help researchers quickly identify and characterize these new strains, said Bernhard Palsson, professor of bioengineering at UC San Diego Jacobs School of Engineering and a corresponding author on the paper.

The reconstructions map out all the genes, reactions and products of metabolism for each strain and allow the researchers to probe their coordinated functionality. Each strain’s metabolic capabilities, the researchers discovered, correspond to specific environmental niches. Commensal or “friendly” E. coli strains also can be distinguished from pathogenic strains using this technique.

“This paper shows that you can predict the microenvironmental niche where human pathogenic strains of E. coli grow, whether it’s in your bladder or your stomach, or your blood or elsewhere, based on these sequences,” Palsson said.

Jonathan Monk, a chemical engineering graduate student in the Jacobs School of Engineering Department of NanoEngineering and lead author of the paper, said that the metabolic reconstructions might also help researchers figure out ways to deprive pathogenic E. coli of the nutrients they need, “so that you can prevent them from getting an advantage in that niche, and maybe better control an infection that way.”

The first E. coli strain was sequenced 15 years ago, but the plummeting cost of gene sequencing has made a plethora of other E. coli genomes available to compare with this first “model” strain. The wealth of genome data, Palsson said, has led some researchers to wonder whether the model organism fully represents the E. coli species.

In the PNAS study, Palsson and colleagues identified a core metabolic network shared by all the strains, as well as all the differences in metabolic content among the strains. Most of these differences appear to be in the ability to break down various nutrients, said Adam Feist, a project scientist in the UC San Diego Jacobs School of Engineering, alumnus of the Palsson lab in the bioengineering department, and the other corresponding author on the paper.

In retrospect, this variety isn’t too surprising, he said, given the number of “diverse environments—on the skin, inside the body, outside in the dirt— that E. coli are found in.”

In future studies, Feist said, the researchers hope to “drill deeper” into this variation and explore whether strains that contain the same metabolic content “use that similar content differently.”

The researchers found that their models could also identify E. coli strains that lack the genes to help them manufacture certain essential compounds, such as niacin. This phenomenon, called auxotrophy, often goes hand in hand with virulence. Many experiments have shown that when these missing genes are restored, the bacteria become less virulent. “So finding out why these strains have become auxotrophs could shed a lot of light on how an organism becomes a pathogen,” Monk said.

The predictive success of the metabolic models has the team thinking about applying the method to other bacteria such as Staphylococcus aureus, said Palsson. “We intend to move aggressively forward with categorizing many human pathogens in this way.”

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