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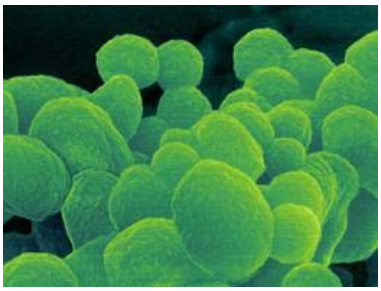
News

Single-celled life does a lot with very little

Bacterial biochemistry mapped in detail.

Lucas Laursen

The blueprint of a small organism's cellular machinery has been unveiled, offering the most comprehensive view yet of the molecular essentials of life. But the research also shows just how far biologists have to go before they understand the complete biochemical basis of even the simplest of creatures.



Mycoplasma pneumoniae: a bug's life laid bare. *D Kunkel/Photolibrary*

"Our whole attempt was to establish a model organism for systems biology," says Peer Bork, a bioinformaticist at the European Molecular Biology Laboratory in Heidelberg, Germany, and one of the coordinators of the project which surveyed *Mycoplasma pneumoniae*, a bacterium that causes respiratory infections.

The scientists catalogued the proteins produced in the cell, the RNA molecules transcribed from the DNA genetic code, and the chemical reactions which make up the cell's metabolism — also known as the proteome, the transcriptome and the metabolome.

"Our technology makes things possible that were unimaginable before."

Eva Yus
Centre for Genomic Regulation in Barcelona, Spain

The researchers found that with its relatively short genome — it has just 689 protein-coding genes, compared with 20,000 or so in humans — *M. pneumoniae* presses some of its molecular machinery into multiple jobs. And the transcriptional activity of the organism seems to replicate that of larger, more sophisticated organisms.

The blueprint could help researchers to control or manipulate the bacteria that are already used to create desirable molecules, such as pharmaceutical compounds or enzymes that digest industrial waste. "The large amount of data focused on one organism is really valuable," says Erik van Nimwegen, a bioinformaticist at the University of Basel in Switzerland. The bacterium's metabolome, for example, should help biologists to model molecular activity in other cells.

"The results are a significant advance towards treating cells as the systems that they are," says molecular biologist Norman Pace of the University of Colorado in Boulder. The three studies are published today in *Science*[1,2,3].

Old bug, new eyes

Although *M. pneumonia* is not the smallest organism on Earth, the researchers selected it because they had access to the lab protocols and notes that the retired German biologist Richard Herrmann had accumulated over the course of his career spent studying the bacterium.

The latest genetic sequencing technology meant that Bork and his collaborators could create a near-comprehensive description of the minimum molecular activity required to sustain *M. pneumoniae*. "Our technology makes things possible that were unimaginable before," says Eva Yus of the Centre for Genomic Regulation in Barcelona, Spain, the lead author on the metabolism paper[3]. "We can sequence a genome in a morning; a transcriptome in a few hours."

Their choice of a simple model organism sped up the genetic analysis and made the metabolic network analysis manageable. *M. pneumoniae* "has fewer than 200 enzymes", Yus notes, "so we could practically work out the reactions by hand".

Back to basics

Once Yus and her team had a metabolic map, they predicted the minimum nutrients necessary to grow the cells *in vitro* and tested 1,300 combinations of nutrients to learn how the organism responded to different environments. They eventually settled on a stripped-down medium with just 19 nutrients[3], suggesting that the organism can use some enzymes for multiple tasks.

"One thing is clear," says Bork, "a single protein has several different jobs in a cell." This may help it to survive in many environments.

"This sounds plausible," says van Nimwegen. He adds that the result reinforces the idea that simplistic metabolic models, which assign just one function to each enzyme, "might be off by a lot".

Because the bacterium's genetic code did not seem to correlate with the complex protein activity observed using a mass spectrometer, the researchers are now looking for an intermediate regulatory pathway that adjusts protein behaviour.

van Nimwegen notes that the real fruits of such large, technology- and data-driven projects often take time to materialize. For now, the researchers "have set the example of how far you really have to go to more completely capture what is going on in an organism". But, he adds, there is still a long way to go before scientists can produce a complete molecular description of even the simplest cells.

References

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2. Güell, M. *et al. Science* **326**, 1268-1271 (2009).
3. Yus, E. *et al. Science* **326**, 1263-1268 (2009).

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