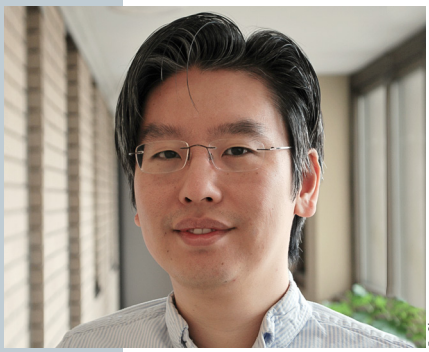
THE AUTHOR FILE

Harris Wang

A regulatory vocabulary for synthetic biology and why baby diapers matter.

At age two and a half, Theodore Wang is the youngest member in his dad's lab. His dad is Harris Wang, a synthetic biologist at Columbia University. Theodore lights up with joy when he learns or recognizes something, says Wang. It's the kind of joy all researchers should feel when they find something new. Theodore's spot on the lab's web page recognizes his other contributions. "We've been collecting poop samples from him," says Wang, who studies the microbiome of the human gut, among other things.



J. Chu

Harris Wang

Wang and his lab have developed a resource of characterized microbial regulatory sequences that he hopes will empower the synthetic biology community. When engineering complex circuits, labs can draw on these 'parts' and predict how these components will react when placed in different genetic backgrounds.

To build the resource, the team mined 184 microbial genomes, selecting them for their diversity, the way they reflect the microbial tree of life, as well as for their potential importance for bio-industrial, health or agriculture applications, says Wang. Using genetic reporters, the team measured and validated regulatory sequence activity and studied the sequences under a range of conditions, such as when cells are stressed or grown in a nutrient-rich environment. The team characterized the natural regulatory components in different genetic backgrounds. They can be used in a high-throughput, parallelized pipeline such that "instead of doing a single measurement you do ten thousand or a million measurements at the same time," says Wang.

Although labs know plenty about bacteria such as *Escherichia coli* or *Bacillus*, "they don't often study how *E. coli* parts behave in *Bacillus*," says Wang. To him, it's the essence of synthetic biology to introduce a foreign element into an organism of interest and to be able to predict and understand how that element will function in that different context. Wang hopes the resource will enable labs to build complex genetic circuits and help them explore more fundamental questions, too. DNA moves around a community via horizontal gene transfer by plasmid or phage, but "we don't understand, for example, what makes certain promiscuous mobile genetic systems very successful," he says.

Some genetic elements are especially good at propagating across a microbial community, possibly representing a kind of universal microbial language, says Wang. Some bacteria have specialized sequences that are expressed by just a subset of community members. That might allow them to communicate with one another on a kind of "secret channel." Once these sequences are better understood and characterized, it becomes possible to turn on some engineered function in just a subset of members of a microbial community. For example, says Wang, in the gut one might want to turn on the expression of a cytokine to tailor anti-inflammatory properties of a subset of the resident microbial community.

As an undergraduate at MIT, Wang was passionate about physics and math and he always enjoyed building things. He combined these interests as he completed his PhD in biophysics in George Church's lab at Harvard Medical School, where he co-developed MAGE, a method for editing multiple sites across an organism's genome. Wang received a joint PhD degree in medical engineering and medical physics in the Harvard–MIT Health Sciences and Technology program. After a research stint at Wyss Institute, in 2013 he joined the Columbia faculty. He has received numerous young investigator awards and was on the Forbes list of '30 under 30' in science.

"It's important for everyone to find their own path."

Wang was recruited to Columbia because he stood out for the cutting-edge, interdisciplinary MAGE technology he co-developed, says Virginia Cornish, Wang's colleague, collaborator and mentor at Columbia who works at the interface between chemistry and biology. She is also touched to see Wang's devotion to undergraduates.

Wang enjoys mentoring young scientists. Science is a marathon that takes endurance, stamina and passion. "You want to be excited because you're excited, not because everyone around you is excited," he says. "It's important for everyone to find their own path."

When he is not spending time with his family, Wang enjoys reading, for example, about the history of science. Being a productive scientist means understanding the context of a given discovery. Biology textbooks are filled with experimental evidence and theories. What is not known is sometimes filled in with "our best guess," he says. Especially in synthetic biology, it's important to study evidence because "if you don't understand something, you can't make it."

Vivien Marx

Johns, N.I. *et al*. Metagenomic mining of regulatory elements enables programmable species-selective gene expression. *Nat. Methods* **15**, 323–329 (2018).