TOMORROW'S PIs

Fifth Annual Young Investigators

From the most basic to the more translational sides of the spectrum, 'omics-related research is moving fast. At the forefront of these changes are young investigators who are poised to make an impact on the field.

BY CIARA CURTIN, MATTHEW DUBLIN, CHRISTIE RIZK, AND TRACY VENCE

There are many researchers doing great work in systems biology. For our search to uncover the brightest minds — profiled here — *Genome Technology* turned to the established pros of the field to recommend those young researchers who are rising stars. This series wouldn't be possible without that insight. *GT* would like to thank all those who responded to our requests for recommendations.

The following pages include snapshots of the work of two dozen investigators — which ranges from studying diversity in dogs to deciphering cancer pathways to making better wine — with a lot of promise. To learn more about each of these scientists, please head to our Web site for their complete, in-depth profiles. Without further ado, here are the fifth annual *GT* Young Investigators.

Julie Dunning Hotopp: The Impact of Inter-Domain Lateral Gene Transfer

Recommended by: Claire Fraser-Liggett

When she began working on *Wolbachia* genomics with the University of Maryland School of Medicine's Steven Salzberg, Julie Dunning Hotopp had no idea she would eventually dedicate her career to investigating the effects of inter-domain lateral gene transfer on human health. It wasn't until she and Salzberg stumbled upon a particularly unusual fruit fly genome that her career hit a turning point. "It turned out the reason it was truly bizarre was that there was an entire bacterial genome [within] the insect chromosome," she says.

In 2005, she and Salzberg co-authored a *Genome Biology* paper in which they reported the complete sequence of the bacterial genome they'd found in *Wolbachia*. The team later confirmed that the bacterial genes had in fact been incorporated into the fruit fly chromosome. Soon after, Dunning Hotopp began to investigate gene transfers from *Wolbachia* to filarial nematodes as well as whether they contribute to human lymphatic filariasis. Equipped with funding from the Bill and Melinda Gates Foundation, she's currently investigating potential drugs to target the bacterial component of the filarial nematode genome.

In addition, she'd like to determine how certain bacterial infections appear to affect cancer development as many as 20 years later. "The idea there is that if you get [a gene] transfer from your microbiome, it could disrupt genes," Dunning Hotopp says. "If you disrupt an oncogene, you could get the development of cancer." — *TV*

Adam Boyko: Genetic Architecture of Dogs

Recommended by: Carlos Bustamante

Some dogs are not quite feral, yet not quite pets either. They hang around human settlements and rely on people for food, but aren't actively bred. These village dogs are a "natural or randomly breeding population of dogs that pretty much live how dogs have lived throughout the ages," says Adam Boyko. Studying the diversity of village dogs, he adds, may help researchers understand canine morphological diversity as well as when and where dogs were domesticated.

Boyko is using dense SNP genotyping arrays and next-gen sequencing to dive into the genetic architecture of these village dogs. "My background is in evolutionary biology, and I thought it was astounding that we were mapping all of these terrific traits and we really don't know where they arose, when they arose, [and] how selection acts on them in natural populations," he says.

Recently, Boyko and his colleagues reported loci that affect dog body size in *PLoS Biology*. In purebred lines, he says, the variation in body size can be accounted for by just a few loci, including IGF1. In village dogs, however, it's a different story. "The same loci that control body size in purebred dogs control body size in the village dog, but they explain a much smaller proportion," Boyko says.

And the Nobel goes to …

"I would definitely want to win the Nobel Prize for medicine for curing some sort of disease that has been a scourge of humanity," Boyko says. — *CC*

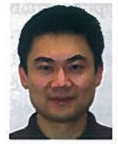
Dalila Pinto: From CNVs to Pathways

Recommended by: Stephen Scherer

As the search for the missing heritability goes on, Dalila Pinto says that the role of rare variants in common diseases is being increasingly recognized. Pinto was part of a team that developed a high-resolution map of CNVs in a healthy population, which was reported in *Nature* in April. Then, she applied that map to the study of CNVs in autism, looking at children with autism and their parents. That study, Pinto says, had two components: first, she and her colleagues searched for SNPs that were more common in cases than in controls. From their 1,500 samples, Pinto and her team didn't find a single one. "We were not able to find common variants — common SNPs — that would pass the threshold of significance," Pinto says. But in looking at rare variants in the second part of the study, her team had better luck. The genomes of the children with autism were enriched for rare copy number variants. "This was really important," she says.

While there may be different rare variants associated with disease, Pinto says that they may affect the same pathway or interacting pathways. "One or two individuals might have a specific type of deletion and another two individuals might have a totally different variation in a different gene, but it could be that these two genes, they interact … in the same pathway, or related pathway," she says. — *CC*

Ting Wang: Transposable Elements, Regulatory Networks, and the Epigenome



Recommended by: Francis Collins

While working toward his doctorate degree in computational biology at Washington University in St. Louis, Ting Wang disregarded repetitive elements while writing algorithms to screen for transcription factor binding sites. Then, as a postdoc in David Haussler's lab at the University of California, Santa Cruz, he made a surprising discovery: more than 30 percent of human p53 binding sites were the result of transposable elements. "Then, all of the sudden, my scientific career was about repeats," Wang says.

In his own lab at Washington University in St. Louis, Wang now seeks to understand how transposable elements have shaped regulatory networks and the human epigenomic landscape over time. Transposons, he says, have really come into their own as more and more labs have transitioned from microarray-based studies to next-gen sequencing projects. Still, many investigators "throw away most of the reads that cannot be uniquely aligned to the [reference] genome," Wang says.

Wang and his team have also taken a keen interest in understanding the role of transposable elements in epigenetic regulation, and in particular, DNA methylation. Using zebrafish models, the Wang lab is monitoring DNA methylation changes throughout embryogenesis to establish baseline reads. From there, "we want to know the [phenotypic] impact of manipulating transposon methylation," he says. — *TV*

Nicholas Buchler: The Dynamics of Regulatory Networks in Yeast

Recommended by: Hunt Willard

Nicholas Buchler has made a career out of forging a marriage between his strengths as a theory-oriented biophysicist and his propensity for wet lab, curiosity-driven biology. While he says he'd always been interested in chemistry and physics, it was an introductory biochemis-

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