From the Editor

Variant explosion

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Recently, a very interesting, and thought-provoking paper by Alon Keinan and Andrew Clark, titled “Recent explosive population growth has resulted in an excess of rare genetic variants,” appeared in the pages of *Science* (1). Keinan and Clark explored the consequences of rapid population growth on the pool of human genetic variants. The upshot was fairly simple—the human population has expanded more than three orders of magnitude (now at 7 billion) in past 400 generations resulting in an accelerating rate of rare genetic variants entering the population. And this expansion is actually leading to a distortion of the basic principles of population genetics, when it comes to the human population, that we all learned in freshman biology.

But what does this all really mean? Well, it might be most interesting to examine Keinan and Clark’s finding from both a technological as well as a biological perspective. Technology-wise, this discovery means that sequencing platforms are going to have to get cleaner. Finding and cataloguing these rare genetic variants that have occurred within the past thousand years or so will require the sequencing of an even greater number of individuals than we might have previously thought. Common variants (those that are often hunted using microarray approaches) occur at a frequency of 5% or higher. This means that sequencing a few hundred individuals should result in their discovery. But what about more recent variants, those occurring at a frequency of 1% or less? In these cases, hundreds of genome sequences will not be enough, thousands of individuals will be required to be sequenced. Here, the challenge becomes determining the variant from the sequencing error. At the moment, sequencing still has a certain error rate (1 in 10,000 bases by most accounts), so finding that one very rare variant as opposed to that sequencing artifact is crucial. This means that sequencing companies need to do more than just produce machines with enormous outputs—they need to strive to make those outputs even more accurate as we enter this new era of exploring rare genetic variants, a point that I would argue has been lost in recent years.

So, that brings us to the biological question of why it is so important to locate and catalogue rare variants. Well, it turns out that rare, de novo mutations could be the genetic lynchpin behind many complex human diseases, including autism. In this issue, contributing writer Sarah

Webb goes into this point in some detail in a Tech News feature article, noting that de novo mutations may account for as many as 20% of all cases of autism spectrum disorder. In the long run, exploring these rare variants could provide key insights into a multitude of human ailments.

Moving forward, researchers are going to have to take rare variants and our altered population growth dynamics into consideration when examining the genetics of human traits and complex diseases. Simply put—we need the technology available to easily and robustly identify these variants, and a more complete understanding of our population structure and biology to make use of that data. As always, please share your thoughts with us by posting at our Molecular Biology Forums under “To the Editor” (<http://molecularbiologyforums.biotechniques.com>) or sending an email directly to the editors (bioeditor@biotechniques.com).

And a final note on the 2012 Virtual Symposium...

As I’m sure many of you are aware, the 2012 *BioTechniques* Virtual Symposium is nearly here. On October 3, 2012, 11 speakers from around the globe will take part in a one-day conference focusing on single-cell biology and related methods and techniques. From isolating and sorting cell populations to deciphering the human microbiome, these talks are designed to provide attendees with new insights into the roles various biomolecules and cells play in human biology and disease. This year’s speaker list includes microfluidics pioneer, Stephen Quake; director of the Human Variome Project, Richard Cotton; gene expression analysis leader, Daniel Larson; and metabolomics guru, Gary Siuzdak. Take this chance to hear leading researchers talk about the latest methods and technology developments being applied in single-cell research. Best of all, this one-day educational event is free to all. For more information, visit biotechniques.com/symposium.

1. Keinan, A., A.G. Clark. 2012. Recent explosive human population growth has resulted in an excess of rare genetic variants. *Science*. 336(6082):740-743.

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