THE AUTHOR FILE

Yannick Doyon

Teamwork on and off the ice, and tipping the odds to find CRISPR hits sans markers.

Yannick Doyon joined the research team at the genome-editing company Sangamo Biosciences, now called Sangamo Therapeutics, near Berkeley, California, after completing his PhD in molecular and cell biology at Université Laval in his hometown of Quebec City. Doyon had caught the eye of Sangamo scientist and strategist Fyodor Urnov, who is now at Altius Institute for Biomedical Sciences. Doyon's idea to stay for a year and plan a postdoctoral fellowship turned into a seven-year stint at Sangamo, where he eventually ran a lab with a dozen scientists.

Yannick Doyon and his son.

Doyon arrived at Sangamo as genome editing was taking off and, he says, "I thought it was amazing." He focused on zinc-finger nucleases, then TALENs and CRISPR. In 2013 he switched from industry to academia and joined the faculty at Université Laval.

In his latest work, Doyon and his team present a way to isolate cells with edited genomes—CRISPR hits—without the need for markers. Finding a CRISPR hit is labor-intensive, especially when there is no phenotype to screen for. The new method, he says, "allows you to reduce this burden significantly."

To repair an induced double-stranded break, most cells will favor nonhomologous end joining. But genome-editing labs often prefer the more precise homology-directed repair, or HDR, which promises to make gene editing for many cell types and loci more precise and efficient.

The scientists created 'selectable' alleles at one genomic location to increase the likelihood of finding an edit at a second, unlinked location. They made gain-of-function mutations in the locus governing a sodium–potassium pump, which enriched the population for cells with precise edits at both loci. The mutations make the cells resistant to the heart drug ouabain, which normally shuts down this pump, leading to a way to isolate the CRISPR hits. The big advantage, says Doyon, is that these CRISPR hits do not need exogenous markers, which are incompatible with therapeutic applications.

Development of the method involved finding an optimal protein–drug combination so the coselection would work well, says Doyon. The sodium–potassium pump was chosen as a crucial protein that is expressed in all cells. Speaking about the experiment, he says, "I have been thinking about it for a long time and I finally got the chance to test it in my lab, which is great." He has filed a patent for the process, which might be "an acquired trait from having worked in the biotech sector." But it is, he says, a potential way to generate money for a public university in return for the governmental support of science.

When Doyon joined Sangamo, the first thing he did, says Urnov, was to try something that nobody thought would work; he kept at it, and soon after, the skeptics fell silent. "He's just not afraid to take on, and take down, a big challenge." Doyon is also a perfectionist about his data, and "his gels are fit for a textbook," a habit he passes on to others. "Because his data are always so crisp, he has a really neat ability to chase down surprising results," says Urnov. Doyon's work has had a major impact in the genome-editing field, he says.

Although Doyon's lab is small—he has three PhD students—he has good resources, and he is happy that his students' hard work led to this new paper, an important confidence-builder for them. Young researchers need to find a niche in order to survive. Doyon had originally promised himself that he would not try to compete in the gene-editing field, but he had to admit that this was "a fail, obviously," he says. "Passion won."

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When Doyon originally arrived at Sangamo, he felt his English skills were lacking, and he was a bit intimidated. But he liked the company's collaborative approach to science and the steady interaction with academics, all of which made for "the kind of environment I thrive in," he says.

In his lab, Doyon encourages collaboration and looks for students who want to be team players. It's an approach fueled by his love for the team sports hockey and soccer. When he moved to California, he played hockey twice a week. "Amazing to go to the rink in flip-flops," he says. He is a goalie and feels he is still reliable in the net.

Now back in Quebec, Doyon continues to play both sports. He plays hockey in a "beer league" with members in their late 30s and early 40s for the fun of the game and to enjoy the other players' company—and also for a post-game beer.

Vivien Marx

Agudelo, D. *et al.* Marker-free coselection for CRISPR-driven genome editing in human cells. *Nat. Methods* **14**, 615–620 (2017).