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CRISPRed CANNABIS

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THE TECH ENTREPRENEUR SHARES HER GLOBAL VISION FOR THE FUTURE OF ONLINE CANNABIS



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READY OR NOT, MOLECULAR GENE-EDITING IS ALREADY CHANGING AGRICULTURE

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The most powerful genetic technology in history has arrived, and everyone is trying to figure out what they can do with it.

Humans have been messing with DNA since the dawn of civilization in the form of agriculture. Raising plants and livestock let humanity perpetuate desirable traits and screen out undesirable ones long before the discovery of DNA, reshaping our food and environments in a manmade spin on natural selection. In the 20th century, we learned to intervene more directly with the invention of restriction enzymes, which extract and insert foreign DNA strands from one species into another.

But CRISPR goes a step beyond. The acronym is the common shorthand for a new class of molecular tools that makes altering DNA in people and plants alike easier than ever before. Where restriction enzymes can only slash away or add in generalized sequences in an organism's genome, CRISPR is precise down to the specific gene one wishes to alter or insert. It's already being used to make pest-resistant crops, biodegradable plastic, climate change-reversing plants, antidotes to natural poisons, self-terminating mosquitoes and—in one illicit case—two HIV-resistant Chinese babies.

Since altering native DNA theoretically leaves no trace, regulators at the USDA have given CRISPR a free pass for agricultural use, considering it a faster method to achieve the same results as selective breeding. Though few CRISPR-enhanced products have made it to consumers, companies are experimenting with and

gobbling up patents for promising new applications like increasing rice crop yields, curing a genetic virus in tomatoes and creating allergen-free peanuts.

The cannabis industry is no exception. By letting scientists and businesspeople observe characteristics of seed-level genetics are a fast-track to realizing the plant's potential as a medicinal, recreational and industrial crop. After decades of prohibition, the long thaw of legalization has already jump-started knowledge on this front by bringing research out of the garage and into the lab with advents like marker-assisted breeding. Still, CRISPR could present another exponential leap in innovation, letting breeders create market-ready strains with predetermined characteristics faster than ever before.

According to CJ Schwartz, CEO of Sunrise Genetics—responsible for creating the first map of the cannabis genome last year—cannabis may already be approaching its upper threshold for THCA. However, production of other “cannabinoids of interest” still has room for “substantial improvement,” and CRISPR could breed plants that greatly overproduce specific ones like CBG to investigate their medical potential. Though his company doesn't employ CRISPR nor any other genetic modification technology, Schwartz also hopes CRISPR can expedite hemp's “agronomic” potential, boosting yields and outdoor resilience to reduce this and other industries' carbon footprint.

“CRISPR is a powerful technology,” says Schwartz, who holds a Ph.D. in Biochemistry, “but it relies heavily



on genomic knowledge of a particular species

—One first needs a specific gene target in order to effect changes in its behavior.”

On account of this, the research community will need to continue developing genomic resources and give CRISPR more precise targets, to catch up with non-marginalized crops like corn and soybeans. There usually isn't one gene corresponding directly with each observable trait — nature tends to be more holistic than that. Single DNA edits could have unintended consequences if the interacting genes' functions haven't been studied or characterized, especially since many of cannabis's most agronomically important traits are polygenic or determined by multiple genes.

As with the cannabis genome, we also need to understand more about CRISPR itself to ensure its safe and effective use.

“If these strains don't hold up to the standards ... of natural cannabis, they may present a problem for the overall gene pool if used for breeding,” explains Schwartz. “While a single gene edit via CRISPR is not technically considered to result in a GMO, it certainly bears close resemblance to technologies that make people very uncomfortable.”

Despite the USDA's go-ahead and some studies showing subsequent generations of CRISPR-ed plants free from genetic disruption, others have shown its use cause undesired gene deletions and complex rearrangements of foreign DNA, potentially even turning cells cancerous when gene-editing humans.

“We need to better understand this gene flow before we can be assured there are no off-target effects,” says Kevin McKernan, CEO and founder of Medicinal Genomics, another cannabis genomics company whose work may inform CRISPR's use, even if they don't use it themselves. “[But] people are not waiting for better references, and CRISPR Cannabis is here if you look in the US Patent and Trademark Office (USPTO).”

McKernan is more worried about the legal side-effects of CRISPR for cannabis than the biological, fearing it could lead to monopolization of modified strains by the well-funded negatively impacting small entrepreneurs — an age-old problem for new

agricultural technologies. Creating strains not found in nature gives them a better potential for patenting, but this ownership of living plant genetics could result in diversity-starved monocultures and costly legal battles if, say, some patented pollen was to land on a neighbor's crop, or another farm stumbled upon the same genetics naturally. Schwartz has similarly expressed concern over this “pharmaceuticalization of medical marijuana,” which could maximize profits but stifle sound research and transparency.

The rush to patent CRISPR-modified cannabis has already begun. On the books are promising space-age applications like plants that grow cannabinoid-producing trichomes in their vegetative state and water-soluble cannabis that metabolizes itself so your liver won't have to. Alarming, another patented strain shows improved resistance to the glyphosate — the active ingredient in Bayer (formerly Monsanto) 's artificial pesticide Roundup, ruled in several recent court cases to cause non-Hodgkins lymphoma.

This implies cannabis could be at risk of becoming just another bottom line-focused facet of big ag, rushing to monetize new technologies like CRISPR even at the expense of consumer safety. There are efforts to push back on this trend like the Open Cannabis Project, which is archiving thousands of strains to prevent them from being patented and the plant's biodiversity legally restricted.

Though stopping CRISPR's use now could be the equivalent of trying to put Pandora back in her box, McKernan emphasizes that products should differentiate between natural selection methods like marker-assisted breeding and polyploids, CRISPR edits that just delete genes, and CRISPR edits that introduce foreign DNA, at least until their varying effects can be better researched and regulated. That way, consumers will be equipped to decide with their own purchases what they value in cannabis genetics. For an industry long starved of credibility, it could be that we don't need more rushed commercial applications, but more scientific fact, even if it takes a little longer to realize our loftiest goals with the plant.

