By Gord Leathers

SOUPED UP

A new gene manipulation technology promises fast and furious results in plant development, without using foreign DNA

Time was if you wanted to hop up an old Chevy Beaumont, you parked it in your parents' garage, pulled out the engine, dismantled the drive train and beefed up the whole thing by dropping new parts in it.

Nothing made a stock streeter move like a 396 V8 with a Holley double-pumper carb pouring all that new power into a bigger train driving ET mags, while a Thrush muffler announced your departure with authority.

All that's changed and yesterday's gearheads are today's chipheads. They're more likely to plug a computer into the car's diagnostic port and rework the programming to adjust the fuelling, the drive-by-wire throttle response, the turbo control, engine load and torque limiters. It's not about changing the parts anymore. It's about changing the programming.

Time was when gene doctors hopped up a plant species by dropping new genes into the nucleus and hoped they would find their way into the twisted ladder we call a double helix.

Sometimes the plant would roar out of the ground, take a face-full of herbicide and blast on while weeds around it were decimated. More often then not, the splicing didn't work and the plant died.

"It's random and you don't know where it's going to insert the gene. It may insert 20 copies, it may insert one copy or it may interrupt gene function," says Cibus vice-president and research scientist Peter Beetham. "There's a number of unintended events that can occur."

We've been splicing genes for quite a while and, although our knowledge of genetics and splicing has improved a lot over the last couple of decades, it's still fairly crude. Plants can be very forgiving when it comes to incorporating foreign genetic material but the majority

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We actually got our first look at DNA when a German biochemist named Friedrich Miescher extracted it from cells in 1869. He could tell you that it contained phosphorus, it was white and it was slightly acidic. As for what it did, he had no idea and it generated no interest for a long time.

In 1929 a Russian-American biochemist named Pheobus Levene put the parts together. Levene was the head of the biochemical lab at the Rockefeller Institute of Medical Research in New York and he liked sugars. In fact, he made a professional hobby out of finding the structure of different types.

He discovered deoxyribose, that sugar in the ladder's frame, and then he isolated the four nitrogen bases. He named them adenine, guanine, thymine and cytosine. If you put one of those bases together with the sugar and the phosphate, the three made what he called a nucleotide.

Levene died in 1940 with no idea of the true significance of his discovery. In fact, biochemists were convinced that something as simple as DNA couldn't possibly have anything to do with something as complex as heredity. They were looking at proteins, large, mind bogglingly complex and surely the basis of inherited traits. DNA was just simple white goo that must do something, but what? Couldn't really say.

The breakthrough came in the 1950s when an American named James Watson met Francis Crick at Cambridge, England. Watson was there on a research fellowship to study the structure of molecules and it was here that he, and his new friend Crick, started to look at DNA.

It was when they saw a piece of X-ray crystallography produced by Rosalind Franklin of King's College in London that they imagined the now-iconic double helix. Everything fell into place and they could see how it worked. They published in 1953 and were awarded the Nobel Prize in 1962.

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of cases either don't survive or they don't present any improvement over the parent stock.

We only find out by growing generations of trials and errors before we develop something valuable. No matter how you slice or dice it, it takes time and money so it's a good ten to fifteen years before a new crop makes it to the field.

That may be set to change with RTDS (Rapid Trait Development System) technology from Cibus, a new way to get right inside a gene and change its basic coding. In essence, its the same thing those chip heads do with cars.

They haven't introduced any foreign parts. They've worked with the material that's already there and changed the inner programming. RTDS isn't genetic modification as we understand it, but gene conversion. Scientists using RTDS on a plant cell haven't introduced any foreign DNA. They've worked with the material that's already there and changed the inner programming.

"With gene conversion we're looking at a single gene and making a single nucleotide change and that's all that occurs," Beetham says. "It's really making small site specific changes in the gene to provide it with a new characteristic."

A gene is a collection of several different pieces of information coded onto a molecule we know as DNA. It's almost like a coiled ladder, where the rungs are made up of compounds called nucleotides. Each rung has two.

The people at Cibus have found a way to get into that molecule and rework the rungs by changing the nucleotides. We all know that when cells divide, genes have to copy themselves so each new cell has an exact copy of the original genetic plan. We also know that this can go wrong so DNA comes with a way to correct mistakes made during replication.

"RTDS is like a spell checker for genes," Beetham says. "We call it gene conversion because we're only changing a single letter of the DNA code in that gene. You're converting it from one nucleotide to another."

That spell checker is a small unit called a Gene Repair Oligo Nucleotide or GRON. In a normal cell it's dispatched to find a broken spot on the DNA where the nucleotide rungs don't connect properly. The GRON slides into position, fixes the mistake and then disappears. Code repaired, genome restored.

What the Cibus people have found is a way to dispatch a GRON to a specific site, change the code and then disappear. Code rewritten. Genome changed. Now it's a different gene that will program the cell to make a different protein and a plant to produce a different product or behave in a different way.

This brings a level of precision to genetic manipulation that we've never known before. It means that we can make meaningful changes to an embryonic plant in a fraction of the time it takes through traditional breeding or conventional gene modification. It also means that the final result is not a transgenic. No foreign genes have been introduced so it hasn't been genetically modified in the same sense.

It puts our knowledge of genetics to work in ways that are useful and relevant to the market. We know what genomes are and the more we find out about what individual genes do within genomes, the more useful gene conversion becomes. In short, it's a smart new tool for the plant breeder.

"We're like kids in a candy store," Beetham laughs. "Now we have all these opportunities to provide farmers, processors and consumers with products that Nature could provide if you do enough selection. But it could take 30 to 100 years by doing it the traditional or conventional way." ⊕

DECEPTIVELY SIMPLE

The Eiffel Tower on one hand is very simple — it's nothing more than puddled iron girders held together with rivets.

On the other hand it's very complicated because there are over 18 thousand of those girders held together by close to two and a half million rivets. It's a truly elegant piece of construction and the only one of its kind in the world.

The DNA molecule is also very simple since it's nothing more than a twisted ladder-like structure made of five building blocks carbon, hydrogen, oxygen, nitrogen, and phosphorus. It's simpler than a loaf of raisin bread. On the other hand, it's very complicated because several thousand of those rungs put together in the right sequence makes a gene. It's a truly elegant piece of construction and as common as dirt since the vast majority of living, breathing organisms are stuffed to the gunnels with it.

If you could climb DNA, as you would a ladder, you would find yourself moving upwards in right-hand spirals because the molecule twists that way. The frame of the ladder is made up of two rails composed of a phosphate bolted to a special sugar molecule called De Oxy Ribose. It's jagged, almost like it's been cut with pinking shears, and it's built like that all the way up.

If you paused for a rest and placed both your hands on one of the rungs you'd be grabbing what chemists call a base pair. Your left hand would be resting on one while your right hand would be on something else, with both bases joined in the middle. It's all nitrogen, hydrogen and maybe oxygen but there are four distinct bases. This is the very core of DNA coding and it's these four bases that give rise to the variations of all living organisms that contain it.

We've given those bases names: adenine, guanine, thymine and cytosine. If you have adenine on one side of the ladder it's going to pair with thymine on the other. Same with guanine and cytosine. It really is simple. Three rungs in a sequence are called a codon and each of those tell the cell to make a specific amino acid.

When you start building sequences of one thousand to upwards of three thousand of those base pairs, you have a gene. Once you have several million genes you get tremendous complexity coming out of something fundamentally simple. It's the numbers game that makes something as complicated as heredity rise from something as simple as DNA.

It just goes to show that you can take five different types of Lego blocks and, if you have enough of them, you can build a cathedral. If you like you can step back and marvel at the creation but remember, it's only Lego.