The first tree in the United States with symptoms was reported in Miami in 2005. "We had the 'uh-oh' moment," says Fred Gmitter, who breeds new citrus varieties at the University of Florida in Lake Alfred.

Some researchers have had accidental success against the disease. Gmitter's team released a mandarin variety called Sugarbell just as the outbreak was getting under way. Although those trees have since become infected with *C.* Liberibacter, farmers are able to reap a reasonable crop of sweet oranges if the plants receive proper pruning and nutrition. But it is difficult to build on that success: why the trees are relatively tolerant of the disease remains a mystery.

For years, Southern Gardens Citrus has been genetically engineering plants to express genes taken from spinach that defend against the disease. The company says that the results of field trials suggest some degree of protection. But this approach will take many years to meet regulatory requirements for marketing a genetically modified crop. And consumers may not take kindly to a fruit or juice that comes from a genetically modified tree.

"Growers needed answers ten years ago."

So Southern Gardens Citrus added a different approach, and began the USDA approval process for engineered CTV in February. Instead of modifying the trees, the company wants to alter the genome of a harmless strain of CTV so that it produces the spinach defence gene. The company intends to graft tree limbs infected with the virus onto trees. In April, the USDA announced it would start work on an environmental impact statement, a process that typically takes about two years and will be needed before the department allows the modified virus to be used commercially.

Because the virus does not alter the fruit, this approach may allow farmers to argue that the oranges are not genetically modified, and so avoid regulation and reduce public doubt.

That is also the goal of separate projects looking for genes that confer disease resistance when switched off. If researchers can find such genes, they could use CRISPR to inactivate them. Nian Wang, a plant pathologist also at the University of Florida, is using this approach to edit orange trees, and hopes to know by 2019 whether they are disease-resistant. Others are using RNA interference in psyllids to switch off genes that allow the insects to transmit the bacteria.

For now, one question dominates: whether the citrus industry will still be alive by the time these solutions make it to the groves. "It's an incredibly devastating disease," says Gmitter. "Growers needed answers ten years ago." ■

GENOMICS

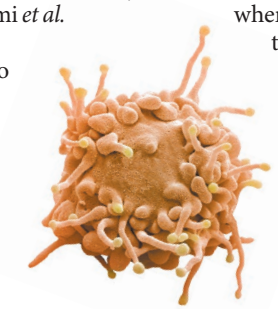
Old tumours offer rare cancer clues

DNA sequences from 100-year-old tumour samples could bolster childhood-cancer research.

BY HEIDI LEDFORD

Deep in the basement archives of London's Great Ormond Street Hospital for Children, cancer researcher Sam Behjati is finding clues that might help him to treat his patients today. This month, he and his colleagues published DNA sequences from the genomes of three childhood-tumour samples collected at the facility almost a century ago (A. Virasami *et al. Lancet Oncol.* **18,** e237; 2017).

Those historical cells help to address a modern problem: the small number of tumour samples from rare cancers that are available for researchers to sequence. Behjati knows this problem well. At the Wellcome Trust Sanger Institute in Hinxton, UK, he tracks the genomic miswiring that can lead to rare childhood cancers. And as someone who also treats patients, he has been frustrated by the paucity of evidence to back up much of his practice.



STEVE GSCHMEISSNER/SPL

A lymphoma cancer cell.

"The treatment regimens for children with rare cancers are essentially made up," Behjati says. "If you've got three or four patients nationally, how are you ever going to conduct a reasonable clinical trial?"

To expand the pool of samples that he could sequence, he decided in 2014 to harness advances in genome sequencing that had already made it possible to sequence DNA from pathology samples a few decades old. The hospital's 165-year archive of samples and patient records provided the opportunity to see how far back in time he could go.

The work highlights the wealth of material that is available in such archives, says Danielle Carrick, a programme director at the US National Cancer Institute in Rockville, Maryland. Mining old samples can expand the options for learning about rare conditions and understudied ethnic populations, she notes, and make population-scale studies possible.

Researchers have analysed DNA from much older specimens: fragments of genome sequence have been used to study ancient-human populations from hundreds of thousands of years ago. But DNA tends to degrade over time, and cancer researchers need high-quality sequences to pinpoint the many individual mutations that can contribute to tumour growth.

Behjati and pathologist Neil Sebire of the Great Ormond Street Hospital Institute of Child Health at University College London directed their team to begin searching the hospital's archive for samples from the 1920s, when the terminology used to classify tumours was comparable to modern diagnoses.

The samples arrived as small paraffin-wax cubes with sides roughly the size of fingernails, which each contained tissue that had been soaked in a solution containing formaldehyde to preserve it and make it rigid. Sebire and his colleagues then took a thin slice of each block and dyed the tissue red and pink with stains.

The team analysed three samples: a muscle cancer called rhabdomyosarcoma, a blood-vessel tumour known as cellular capillary haemangioma, and a lymphoma. After the researchers confirmed the original diagnoses using the stained slices, Behjati's team extracted DNA from much of the remaining sample and sequenced 366 genes in each one. They found cancer-associated mutations in all three samples.

Behjati plans to keep searching through the Great Ormond Street Hospital collection, and then perhaps to mine the archives of other hospitals for relics of childhood cancers. As his collection grows, he will look for commonalities and potential drug targets.

But as these century-old samples find a modern use, the pathology techniques that were used to create them are on the wane, he adds. Not long from now, Sebire predicts, pathology labs will give up their microscopes altogether in favour of instruments that rapidly sequence DNA and proteins, and identify metabolites.

"The process hadn't really changed for over 100 years," he says. "But by the time I retire, I fully expect that you won't need to do what I do now." ■ SEE WORLD VIEW P.267