DISEASE

Salmonella suspected in Aztec decline

Ancient DNA links bacterium to catastrophic epidemics.

BY EWEN CALLAWAY

One of the worst epidemics in human history, a sixteenth-century pestilence that devastated Mexico's native population, may have been caused by salmonella from Europe, a pair of studies suggest.

In one study, researchers say they have recovered DNA of the gut bacterium from burials in Mexico linked to an epidemic that killed up to 80% of the country's native inhabitants in the 1540s (Å. J. Vågene *et al.* Preprint on bioRxiv at http://doi.org/bz26; 2017).

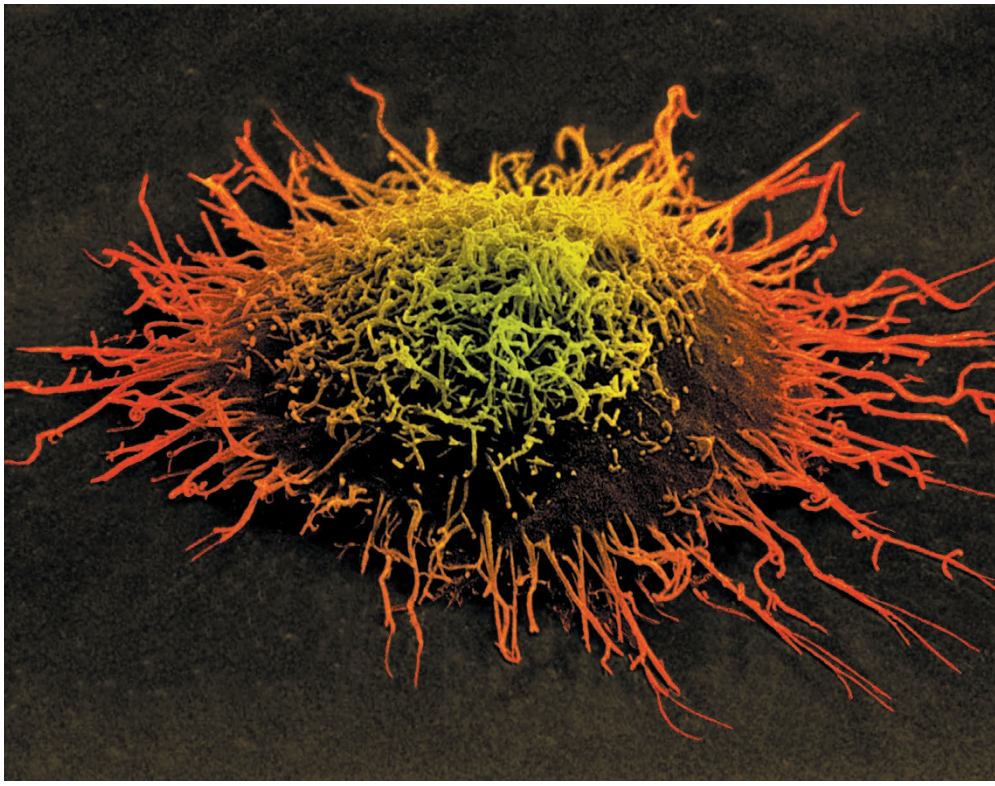
Spanish conquistadors arrived in Mexico in 1519, when the native population was an estimated 25 million. A century later, after a series of epidemics, numbers had plunged to around 1 million. The largest of these outbreaks were known as *cocoliztli*, but there has been little consensus on their cause.

In an attempt to settle the question, a team led by evolutionary geneticist Johannes Krause at the Max Planck Institute for the Science of Human History in Jena, Germany, extracted and sequenced DNA from the teeth of 29 people buried in southern Mexico. All but five were linked to a *cocoliztli* that researchers think ran from 1545 to 1550. Bacterial DNA recovered from several of the people matched that of a *Salmonella enterica* strain called Paratyphi C.

This is potentially the first genetic evidence of the pathogen that caused the massive decline in native populations after European colonization, says Hannes Schroeder, an ancient-DNA researcher at the Natural History Museum of Denmark in Copenhagen. Yet María Ávila-Arcos, an evolutionary geneticist at the National Autonomous University of Mexico in Mexico City, isn't convinced. She notes that if a virus caused the *cocoliztli*, it wouldn't have been picked up by the team's method.

Another study also raises the possibility that Paratyphi C arrived in Mexico from Europe (Z. Zhou *et al.* Preprint on bioRxiv at http://doi.org/bz27; 2017). A UK-led team collected and sequenced the now-rare strain from the remains of a woman buried around 1200 in Norway. It is the earliest evidence of the strain, and shows that it was circulating in Europe 300 years before it appeared in Mexico. ■

See go.nature.com/2lbwns0 for a longer version of this story.



A scanning electron microscope image of a cervical cancer cell.

STEVE GSCHMEISSNER/SPL

CELL BIOLOGY

Cell atlases race to map the body

State-of-the-art imaging and molecular biology are combining to map cancers and human tissues cell by cell.

BY HEIDI LEDFORD

The first time molecular biologist Greg Hannon flew through a tumour, he was astonished — and inspired. Using a virtual-reality model, Hannon and his colleagues at the University of Cambridge, UK, flew in and out of blood vessels, took stock of infiltrating immune cells and hatched an idea for an unprecedented tumour atlas.

"Holy crap!" he recalls thinking. "This is going to be just amazing."

On 10 February, the London-based charity Cancer Research UK announced that Hannon's team of molecular biologists, astronomers and game designers would receive up to £20 million (US$25 million) over the next five years to develop its interactive virtual-reality map of breast cancers.

The tumour that Hannon flew through was a mock-up, but the real models will include data on the expression of thousands of genes and dozens of proteins in each cell of a tumour. The hope is that this spatial and functional detail could reveal more about the factors that influence a tumour's response to treatment.

The project is just one of a string that aims to build a new generation of cell atlases — maps of organs or tumours that describe the location and make-up of each cell in painstaking detail.

Cancer Research UK awarded another team up to £16 million to make a similar tumour map that will focus on metabolites and proteins. Later this year, the US National Institute of Mental Health will announce the winners of grants to map mouse brains in extraordinary molecular detail.

And on 23–24 February, researchers will gather at Stanford University in California to continue planning the Human Cell Atlas,

an as-yet-unfunded effort to map every cell in the human body.

"This is a very hot topic," says Ido Amit, who studies the genomics of the immune system at the Weizmann Institute of Science in Rehovot, Israel. "It's all location, location, location. The community knows this has to be the next step."

Over the past few years, researchers have flocked to techniques that allow them to sequence the full complement of RNAs — tens of thousands of them — in individual cells. These RNAs can reveal which genes are expressed, and provide clues as to a cell's unique function within an organ or tumour.

But sequencing methods typically require that the cells first be plucked from the tissue in which they live. That destroys valuable information about where the cells were and what neighbours they interacted with — information that could hold new clues to a cell's function and how it can go awry in diseased tissue.

"There is a lot of excitement and promise with single-cell sequencing technologies," says Nicola Crosetto, a molecular biologist at the Karolinska Institute in Stockholm. "But when we think of cancer and complex physiological tissues, we need to be able to put that information into spatial context."

Techniques are emerging to do so. On 6 February, Amit and Shalev Itzkovitz, also at the Weizmann Institute, and their colleagues reported that they had created a cell-by-cell map of mouse liver lobules, complete with RNA sequences from each cell (K. B. Halpern *et al. Nature* **542,** 352–356; 2017). The lobules of the liver are conventionally divided into concentric layers; the team found unique gene-expression patterns in cells lying at the interface between two layers. "This region of the tissue is not just a transition zone," says Itzkovitz. "It's a new zone with a specified function."

"When we think of cancer and complex physiological tissues, we need to put information into spatial context."

Meanwhile, Hannon has teamed up with biophysicist Xiaowei Zhuang at Harvard University in Cambridge, Massachusetts, who has developed a method that encodes RNAs with binary barcodes that can be read within cells using imaging techniques. The technique detects thousands of RNAs in a single cell simultaneously, without dissociating it from its neighbours. "Every time I look at the images with the barcodes sticking out, it reminds me of the movie *The Matrix*," Zhuang says.

The molecular cartography of RNA is simple in comparison to working with proteins and other molecules. Josephine Bunch of the National Physical Laboratory in Teddington, UK, and her colleagues are developing tumour atlases with detailed information about small molecules, such as lipids, drugs and metabolites, as well as large molecules such as proteins. The methods will allow her team to assess about 50 proteins per sample.

That may sound less impressive than the thousands of RNAs measured by other techniques, but information about 50 proteins — which can be selected to suit specific tissues — present in different combinations is enough to identify major cell types and gauge key molecular pathways operating in them, says Garry Nolan, a molecular biologist at Stanford University.

Proteins offer a more direct view into the function of a cell than does RNA, he notes, and can better allow researchers to link their data to previously published cell atlases dating back decades.

Whatever the methods that make it to the top, researchers will also need to develop new ways of displaying the data, says Hannon. "Virtual reality is very powerful," he says. "But the amount of information is going to be so vast, we're going to need new ways of interacting with information." ■