Abstractions

FIRST AUTHOR

Some consequences of climate change are already unfolding. Glaciers and ice sheets are melting, and sea levels are rising as a result. However, scientists aren't certain by how much the rate of sea-level rise might accelerate; current predictions for increases until 2100 range from 0.3 centimetres to 1.4 centimetres per year. But Paul Blanchon, a geoscientist at the National Autonomous University of Mexico in Cancún, and his colleagues have learned that a sudden, catastrophic increase of more than 5 centimetres per year over a 50-year stretch is possible. On page 881, they describe their discovery that a sea-level jump of 2–3 metres already happened about 121,000 years ago. Blanchon tells *Nature* how and why it could recur.

How did you find out that sea levels had risen so quickly in the past?

We were studying fossil reefs along the Yucatán peninsula in eastern Mexico, looking for interruptions in the reefs' development, when we found two reef crests. One crest was about three metres above the current sea level, the other six. Some event had clearly disrupted their growth, killing the lower reef first and, within 50 years, allowing the higher one to develop into territory that is now farther inland. One possible cause of such disruption is an earthquake, but we know the peninsula was stable in the reefs' lifetimes. The only other possibility is a rapid sea-level jump of two to three metres, which would essentially have drowned the lower reef.

Did you have to dive to the ocean floor to study the fossil reefs?

No, a theme park has been excavated in the middle of these reefs, which are on land south of Playa del Carmen. There's no other place in the world where reefs of this age are so exposed. From the excavations, we were able to reconstruct the reef's internal structure in three dimensions.

Were there any challenges involved with working in a theme park?

One key site was in the middle of a jaguar and puma exhibit. We had to get up at five in the morning, lower our ladders into the pit, do our studies and get out of there before the jaguars and pumas were let out.

What do your results mean for sea-level rises in the future?

This earlier ice-sheet collapse happened during an interglacial, when it was warm and there wasn't a lot of ice around — just as it is on Earth today. We're assuming rapid ice loss from an ice sheet produced the jump in sea level, because it's the only known process that could generate such a rapid increase. This could happen again. ■

MAKING THE PAPER

Susan Lea

Structure of meningitis protein with human 'coat' yields vaccine clues.

Although relatively uncommon, meningitis — inflammation of the membranes covering the brain and spinal cord — can kill within hours. Immediately after infection, one major bacterial culprit — *Neisseria meningitidis* — coats itself with a human protein so that immune cells no longer recognize it as an intruder. Using X-ray crystallography, Susan Lea of the University of Oxford, UK, and her colleagues now describe the interaction between the microbe and the human protein.

Christoph Tang at Imperial College London had previously discovered that *N. meningitidis* uses a protein on its surface, dubbed factor-H-binding protein, to grasp hold of the human protein factor H. "Chris contacted us hoping that we could help to characterize these interactions further," recalls Lea.

Factor H is part of the complement system, an arm of the immune system that attacks foreign bodies in the bloodstream. To prevent the system from targeting the body's own cells, factor H circulates in the bloodstream and binds to sugar molecules on human cells, flagging them as 'self'. *N. meningitidis* is one of several bacteria that have highjacked this mechanism by producing proteins that can also bind factor H.

Human factor H is a long molecule, made up of 20 domains strung together like beads on a string. Tang and Lea's groups determined that only two such 'beads' — numbers six and seven — are key to binding the bacterial protein. "This was good news because it meant we could look at the structure of just two domains," says Lea.

But although the researchers had no trouble purifying and crystallizing the two factor-H domains in complex with the bacterial binding protein, solving the complex's structure proved tricky. "Some crystals are well behaved and some aren't. This one wasn't," laughs Lea. Because the X-ray diffraction data were not of sufficient quality to deploy one of the two classical phasing methods, which use X-ray and computational information to resolve molecular structures, Lea and her colleagues had to find new ways to combine the information from both methods.

On page 890, the hard-earned structure reveals that the bacterial protein folds in the middle. Each half comprises a sheet of amino acids twisted into a barrel shape, with the human factor H portion stacked on top. "The structure essentially looks like two mugs side by side with a croissant on top," says Lea.

Lea and her co-workers singled out two amino acids that seemed to be crucial to the two proteins' tight association. When they mutated the two amino acids, the bacterial protein no longer bound factor H. "Without the structural information we would have had to mutate every single amino acid in the protein to identify these two," says Lea.

Meningitis is usually caused by viral or bacterial infection. For bacterial meningitis, the more severe form of the disease, there are vaccines for all but one type: meningitis B. Two candidate meningitis-B vaccines that are currently in clinical trials both use factor-H-binding protein as part of the vaccine formulation. However, this latest work suggests that the bacterial protein will immediately become bound by factor H and so will not generate an optimal immune response. "The mutated bacterial protein we have produced could make a better vaccine candidate," Lea says, "because it doesn't bind factor H." ■

FROM THE BLOGOSPHERE

Glimpsing how a chemist views the world — both inside and outside of science — enlightens and inspires on The Sceptical Chymist, NPG's chemical-community blog. In the 'Reactions' series, *Nature Chemistry* associate editor Neil Withers probes the personalities behind the pipettes.

In the latest instalment, Jonathan Clayden, an organic chemist at the University of Manchester, UK, shares why he switched from molecular biology during his first year at university (http://tinyurl.com/cpp4rc). "The way that mechanistic explanations apply equally in flasks and in cells intrigued me. I found the ... way you can write a structure on paper and then plan how to make the molecule in the lab very appealing too. I spend a lot of my time now trying to bend those same mechanistic rules to see when they break."

And if he weren't a chemist? Clayden says he'd like to be a gentleman farmer, circa 1910, with a well-stocked vegetable garden for cooking. It seems he cannot completely escape his teenage fascination "with the way that complicated things grow when simple rules collide." ■

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