Abstractions


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The ocean will no doubt have an important role in global warming. Yet predicting its role remains a challenge without a better understanding of how marine microorganisms interact to drive carbon and nutrient cycles. On page 387, Frede Thingstad, a marine microbiologist at the University of Bergen in Norway, and his diverse team describe counterintuitive findings from an experimental Arctic ecosystem — that adding carbon to a marine food web reduces the system's total carbon. Thingstad says solving this conundrum sheds light on the seas.

Why were these findings counterintuitive?

Finding less total carbon after adding it to the system was a surprise. The individual data, from bacterial abundance to total organic carbon levels, did not tell a consistent story until we worked through the mechanisms involved. Microbial growth rates can be limited by either organic carbon or nutrients. When carbon is limiting, bacteria compete for — and immobilize — mineral nutrients, which reduces their ability to produce new organic matter, lowering the total organic carbon.

Why are marine food webs hard to study?

Marine food webs are less accessible than land-based webs. Like all microbes, marine microorganisms are difficult to see, and scientists can grow only a tiny fraction of them in the lab. We are dependent on developing techniques to determine which organisms are present and what properties they have. Although these techniques are improving, there are still many unknowns in the system that surprise us.

What research is needed to untangle marine food webs?

Rather than taking ocean measurements, we need to experiment with the system's dynamics. We used mesocosms — experimental systems holding a cubic metre of seawater — to study microbial interactions under controlled conditions. Ideally, we'd like to place them offshore to conduct replicated, real-world tests in diverse, open waters.

Has the field developed as you imagined?

Early on, I thought that mathematically modelling the entire microbial food web sounded ridiculous. Not any more. The main lesson of this work is that we can better understand basic mechanisms with models.

What do you hope to learn before you retire?

I hope to understand how microbial biodiversity is controlled in the ocean. It must be partly driven by how organisms with different life strategies optimize nutrient competition and defend against viruses or predators. ■

MAKING THE PAPER

Charles Cobbs

Human virus requires common receptor to infect cancer cells.

Most days, Charles Cobbs is a neurosurgeon at the California Pacific Medical Center in San Francisco. But once a week, he is a virus hunter. For the past ten years, Cobbs has focused on whether viruses have an association with brain tumours. Now, he and his co-authors have discovered that human cytomegalovirus (HCMV) needs a particular cellular receptor, normally involved in growth-factor signalling, to infect a type of cancer cell in the brain.

HCMV is a widespread herpesvirus that causes defects at birth and fatal diseases in immunocompromised people, such as patients with AIDS. Infection with HCMV is also associated with the occurrence of glioma, an extremely aggressive form of brain cancer that is difficult to treat and has a poor survival rate.

"If HCMV turns out to be a causal pathogen [for cancer], it would be a very important finding as we're desperate to find novel approaches to treat brain tumours," says Cobbs.

While investigating how HCMV affects growth-factor signals in cells, Cobbs's team found that the virus phosphorylates and activates an unknown protein. To identify the protein, Cobbs's co-worker Liliana Soroceanu infected human fibroblast cells with HCMV, broke the cells apart and spread their contents over an antibody array that captures and identifies all the major growth-factor receptors in their active, phosphorylated states. The only receptor found in this active state was PDGFRα, a receptor for platelet-derived growth factor. Furthermore, the receptor could bind to a regulatory subunit of PI3K, an important signalling protein for brain tumours and other malignancies.

"Based on that first experiment, I suggested that we look at it backwards, forwards, upside down and sideways to make sure," says Cobbs.

Cobbs's team next knocked out PDGFRα in fibroblasts and glioma cells, and found that the absence of the receptor meant that the virus could not infect the cells. Reintroducing the receptor into the knockout cells restored their susceptibility to infection.

The team then used two drugs to block the receptor in normal, non-cancer cells. They found that both the PDGFRα-blocking antibody IMC-3G3 and Gleevec (imatinib), an anticancer drug that targets this family of receptors, stopped the virus entering cells — suggesting that these drugs might be useful for preventing HCMV infection (see page 391).

"This result strongly suggests that the virus uses this growth-factor signalling pathway and that the receptor is critical for it to enter the cell," says Cobbs. He adds that although it is not yet certain whether the virus triggers cancer, brain tumours do create an immunosuppressive environment that allows HCMV to settle within them. "Even if the virus is not causal in the tumour, it could be used as a homing target for vaccine-based therapy."

With this finding, the cancer field may now have come full circle, explains Cobbs. It was accepted in the 1960s that viruses might be involved in cancer, but as the genetics of the disease were unravelled, interest in the role of infectious agents was overshadowed, he says.

"We've nailed down many of the signalling pathways and mutations in cancer, but that doesn't really tell us why people get it," Cobbs says. "Now, the idea that it might be caused by chronic inflammation from infections is coming back." ■

FROM THE BLOGOSPHERE

Can you persuade an eminent scientist to start blogging? As reported at the Science Blogging 2008 conference in London on 30 August (http://tinyurl.com/5tsga9), not many senior scientists have a blog, despite the usefulness of this communication tool for education and outreach. To help scientific blogging gain momentum, Nature Network is coordinating a challenge to increase the number of senior scientists who write online. Points will be awarded for the seniority and reputation of the blogger, their previous lack of experience with blogging, the quality and quantity of posts, the blog's relevance to science and its demonstrable positive impact.

Nominations can include self-nominations, and must be submitted by 5 January 2009. (See http://tinyurl.com/6fcdjw for more details.)

The winning blog will earn the chance to be included in *The Open Laboratory: The Best Science Writing on Blogs 2008*. The blogger and instigator will also earn an expenses-paid trip to Science Foo Camp 2009 — an invitation-only 'unconference' on emerging technology held at Google headquarters in California. ■

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