Outsmarting the superbugs

September 27 2012, by Liz Porter

Defeating the deadly Clostridium difficile is no easy task but, step-by-step, microbiologist Associate Professor Dena Lyras is helping piece together the puzzle.

Monash University microbiologist Associate Professor Dena Lyras has many significant relationships in her life: with her husband, her son and daughter, and her parents. She also has an important ongoing relationship with 'Dif', as she and her colleagues call Clostridium difficile – a hospital superbug.

This bug has been the focus of her work as a medical researcher for

more than a decade. It causes severe diarrhoea in elderly patients and has become increasingly more deadly over the past decade. It is responsible for epidemics in Canada, the UK and Australia as well as in the US, where its cost to healthcare is estimated to be as high as US$3.2 billion a year.

The bug flourishes in hospitals, where prescribed antibiotics attack the bacteria that cause particular ailments. However, these antibiotics also wipe out the 'good' and protective natural bacteria in a patient's intestine, allowing 'bad' bugs such as Clostridium difficile to invade and thrive.

For the past 14 years, Melbourne-based Associate Professor Lyras has been on a quest to understand exactly how this bacterium works and to learn how – and why – newer versions of it have become so potent. In Australia, she is pushing for hospitals and nursing homes to start tracking the current extent of Clostridium difficile infection in their patients.

Associate Professor Lyras says Dif is not much to look at: a simple rod-shaped organism, and only visible if magnified many thousands of times through a powerful microscope. But she still regularly wakes up thinking about it and is often still pondering its workings late at night, when she emails colleagues in the 'Dif community', as she calls it. These fellow scientists in Perth, the UK and the US are also working on the bug.

Her husband understands, she says. "He is a microbiologist as well, so he listens. Every research scientist becomes a bit obsessed," she adds with a laugh.

And Clostridium difficile is a tough opponent: it is intriguingly hardy.

"It won't grow in the presence of oxygen, so you'd think it would be easy to kill," Associate Professor Lyras says. But the bug makes two versions of itself: the vegetative cell that makes people sick and the 'spore', which

is the key to its transmission. It is this tough seed-like spore that survives in oxygen and resists many antibacterial chemicals.

"When people are infected, the bacteria make lots of spores, which spread very efficiently. Once Dif is in the hospital environment it is almost impossible to get rid of it."

Scary? "And clever," Associate Professor Lyras says. "I am driven by curiosity. These tiny little entities can do so much damage and we can't even see them without very powerful imaging equipment … and they constantly change. As soon as you find a way to fight them they find a way to get around it, and really quickly."

While Associate Professor Lyras finds this capacity for change "fascinating", she recognises that it must be infuriatingly difficult for clinicians and affected patients.

Associate Professor Lyras began studying the way that antibiotic-resistant genes move from one bacterium to another when she was a PhD student at La Trobe University in Melbourne. By 1992 she was a postdoctoral fellow at Monash, working with Professor Julian Rood on the movement of DNA in a related bug and common cause of food poisoning, Clostridium perfringens. By 1995 the scientists were studying the same kind of gene movements in Clostridium difficile, which is present in every hospital in the world where antibiotics are used.

By 2005, epidemics in hospitals in Canada and the UK had lent urgency to the research: an international community of scientists were working long hours to unlock the genetic secrets of Clostridium difficile. Soon the Monash researchers began making significant discoveries, each shedding successive light on the bug's increasing virulence.

Clostridium difficile makes two main toxins, toxin A and toxin B, and

these are responsible for disease. Thirty years of research suggested that toxin A was more important in causing disease. Then, in 2009, the international journal *Nature* published groundbreaking research by Professor Rood and Associate Professor Lyras, which overturned previous beliefs about toxin A and implicated toxin B as the main cause of intestinal disease in Dif infections.

"All the work done previously was on purified toxins," Associate Professor Lyras says. "But when you take one factor and study it in isolation from everything else it can misrepresent what happens during infection."

Professor Rood and Associate Professor Lyras worked on the bacteria directly, adding several years to the project because they first had to genetically engineer the bacteria: to make one form missing the gene that made toxin A, and one form missing the gene that made toxin B.

Late last year, Associate Professor Lyras accomplished the next step in cracking Clostridium difficile's DNA code. Her research team showed exactly how a particular mutation in one gene of the bug allowed toxin production to go out of control, creating hypervirulent strains.

"There is a particular 'repressor' gene, which under normal circumstances controls how much toxin is made – and keeps it at a certain level," she explains. "In the epidemic or hypervirulent strains, that gene is not intact. It has a mutation in it that stops it from being functional."

In that experiment, reported in the international microbiology journal PLoS Pathogens, Associate Professor Lyras and her colleague Dr Glen Carter were able to put the intact gene back into the bacteria and see how the gene reduced the bug's virulence.

Along with pharmaceutical company Immuron, Associate Professor Lyras is now working on methods – including a vaccine – to treat or prevent the diseases caused by Clostridium difficile. Meanwhile, other research projects involve trying to plot the exact path of the damage the bug causes in human and animal intestines.

"I think you have to be creative to be a research scientist," Associate Professor Lyras says. "[Research science] is like a big jigsaw puzzle. You add pieces to the puzzle and can see a clearer picture. And as soon as you add one piece, it brings into question another 10 pieces."

Provided by Monash University

Citation: Outsmarting the superbugs (2012, September 27) retrieved 11 July 2024 from https://medicalxpress.com/news/2012-09-outsmarting-superbugs.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.