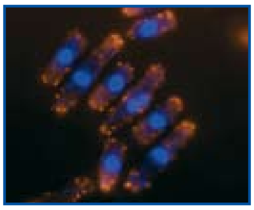

divide and conquer

What can an obscure species of yeast tell us about cell division, cancer and rare genetic diseases? Anna Meyer talks to Professor Jeremy Hyams to find out.

Yeast. The word conjures up images of crusty bread, frothy beer, vegemite sandwiches and, although we may rather not think about it, some less-than-pleasant infections. But that's not all these single celled creatures are good for – yeast is also a powerful tool for genetic research, an excellent 'model organism' for how our own genes behave. Using yeast, Professor Jeremy Hyams, Head of the Institute of Molecular BioSciences, is combining genetic techniques and modern microscopy to study cell division; unravel how cells take up extracellular materials; and shed light on a devastating genetic disease.

Professor Hyams's species of choice is *Schizosaccharomyces pombe*, otherwise known as fission yeast. Unlike the more familiar brewer's or baker's yeast, *Saccharomyces cerevisiae*, which reproduces by budding, fission yeast replicates by dividing in half, making it a very useful model of how human cell division behaves. "Those of us who work with it say that fission yeast is a much nicer organism, because it shares more properties with mammalian cells than budding yeast does," says Professor Hyams. "Budding yeast is the best organism on the face of the planet to do genetics with, but then again it's a weird, weird organism, because it divides by budding, which is a very unusual mechanism."

Though not as widely used as *S. cerevisiae,* fission yeast is also excellent for genetic research. It contains many genes that perform a similar function to those in humans, meaning that information gained from studying yeast genetics can often be translated into learning more about how our own genes operate. It is also very easy to produce mutant fission yeast strains which have specific genes missing, and the organism proves surprisingly viable despite this manipulation. "We can knock out genes very easily, and look at the effect on the cell," says Professor Hyams. "Surprisingly, you can delete most of the genes in the genome. It's bizarre – a mystery as to what is going on in evolutionary terms."

Professor Hyams, who moved to New Zealand from London just under two years ago, is currently the only fission yeast researcher in the country, and one of only a relatively small number worldwide. "That's quite good, because I know I'm the best fission yeast person in New Zealand!" he jokes. "It's nice, actually, being part of a smaller community, because you know everyone."

Professor Hyams's main, longstanding interest is in unravelling how the cell division cycle is regulated. This is not only interesting for its own sake, but is relevant to understanding the causes of cancer, and how it could be treated. "Cancer is exclusively a problem of cell division," he explains. "Yeasts don't actually get cancer, but everything we learn about cell division is relevant." Any new gene that is identified as having a role in regulating how cells divide is potentially of interest to cancer researchers. Not only could such genes be involved in causing the disease, they are also potential new targets for chemotherapy.

Professor Hyams and his colleagues use genetic techniques to visualise the dynamic processes that occur in cells as they divide. Commonly, this involves 'tagging' specific proteins inside living cells with markers such as green fluorescent protein, and watching how the proteins move around and change in cells throughout the cell cycle with a powerful microscope and imaging equipment. "We do lots of cloning and a lot of biochemistry, but the ultimate aim is to go back to the cell and see where things are, who talks to what, and how that changes through the cell cycle," he says.

Recently, Professor Hyams has taken up a new scientific interest, prompted in part by his move halfway around the world. "I came to New Zealand and I thought – it's a new life, I'll start something completely different," he says. His new research programme involves studying endocytosis – the process by which cells take up materials from outside by engulfing them into a fold in their cell membrane, which then buds off to form a 'vesicle' that stores and processes the material inside the cell. "Fission yeast has a cell wall, so you might think it would have trouble getting things inside," he says, "but it just sucks stuff up. We don't know why, because we have mutants that don't endocytose, and they grow fine anyway - so it's not necessary for survival."

The process of endocytosis, and the mysterious reason why it exists is interesting in itself, but the path that led Professor Hyams and his colleagues to study the process was the role it was thought to have in a serious human neurodegenerative disease, known as Batten disease. The condition is an inherited disorder of the nervous system that usually manifests in childhood. Although rare, it is very serious, causing progressive vision problems, seizures, and loss of motor skills. Usually, it eventually proves fatal. The condition is known to be caused by a single gene defect, though what the gene does, or how mutations to it lead to the condition, has been a mystery.

When the fission yeast genome was sequenced recently, it became apparent that the organism contains a gene that is equivalent to the one that causes Batten disease in humans. Professor Hyams decided to begin a research programme to discover what this gene does in yeast, to see if this could shed any light on the cause of the disease in humans. After cloning and examining the yeast gene, it seemed that mutations to the gene might cause defects to endocytosis – a process about which relatively little was known. This prompted the major new research programme for his group – the study of endocytosis itself.

As they learned more about endocytosis, it eventually became apparent that the Batten disease gene mutants did not have an endocytosis defect, and for now, the function of the gene still remains a mystery. "We know more about the Batten disease gene than anyone in the world," says Professor Hyams, "but the only thing we don't know about it is what it does. There's a saying in science that if you want to get your paper in a really good journal, you need three things: mechanism, mechanism, mechanism, so that gene has been a real bugger!"

The endocytosis research programme is, however, a classic example of how one question in science can lead to something else entirely, something that Professor Hyams believes is vitally important. "I think you need to just follow your nose. You write a grant, and say we're going to do A,B,C,D and E, and then you do A, and you find, crikey, A is much more interesting than I thought, we'll carry on with that, and then you find F, which you didn't know existed. I think you have to trust your instincts. You've just got to support basic science. You've no idea where it will go and what will come out of it."

Professor Jeremy Hyams

British born and bred, two years ago Professor Jeremy Hyams decided it was time for a change. "I spent 25 years in London, at University College, and it was important to me to do that, although you don't get a gold watch or anything!" he says. "Then I thought, I've got 10 more years left to work, if I'm going to do something different, I've got to do it now. I had a nice job with good colleagues, but decided to have an adventure." Soon after, he applied for his job at Massey, and moved to New Zealand.

"I'm a microbiologist by training, and a geneticist by inclination," he says. "There's nothing like looking at living cells. It's just amazing what you can see. Now, with good cameras, you can see things in a microscope that you can't see with your eyes. You hardly look down a microscope now. In one way, the days of being a great microscopist are gone, where they just sat and looked – that was just remarkable. Now, you have all this imaging equipment, but it means you just do things so much quicker." Microscopy, he believes, has had something of a comeback in recent years. "There was a time when people dismissed microscopy as just 'looking at cells', and not analytical or experimental, but now there are even various biochemical assays that you do by looking at cells. Microscopy is now no longer limited by the laws of physics, because it's all done through computers and you can enhance things."

Professor Hyams strongly believes in linking New Zealand scientists with those working overseas – something that he sees as particularly important for the intellectual development of postgraduate students. "One of the things that I think I can contribute is to bring people from outside," he says. Professor Hyams is convenor of this year's Queenstown Molecular Biology Meeting, which brings a variety of well-respected researchers to New Zealand from countries including the US, Australia, the UK, Japan and Mexico. "Because it's me, it's called Molecular Biology of the Living Cell," he laughs.