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Tiny fish like zebrafish and medaka have been helping Singapore researchers to understand more about human diseases for years. **The Sunday Times** looks at some of the research projects which have made great strides, thanks to the fish.

Zebrafish may be key to beating osteoporosis

Feng Zengkun

Cut away a third of a zebrafish's heart and it can regrow the organ fully within two months.

Chop off its fin and it can regenerate that too, within two weeks.

The ability of the fish to rebuild itself is partly why scientists at the National University of Singapore (NUS) are studying it. They want to find out how to beat osteoporosis, a disease that causes bones to waste away faster than usual and become prone to fracture.

The genes of the fish are almost 90 per cent identical to those in people, so if the researchers can discover which of the fish's genes are activated when it regrows its bones, pharmaceutical companies could use that information to hopefully develop drugs to make people's bones stronger.

Associate Professor Christoph Winkler from the NUS Department of Biological Sciences explained that people's bodies have cells that destroy bones, and other cells that form them.

When these are balanced, they help people to replace their bones over time so their skeletons remain healthy and strong.

Everyone starts to lose bone density eventually, especially after the age of 35, but osteoporosis occurs when a person's bone-destroying cells become unusually active, more so than the bone-growing ones.

This could be due to hormonal changes, lack of calcium and vitamin D or hereditary genetic causes.

The treatment of the disease comes in two forms: drugs that block the destructive cells and drugs that boost the bone-growing ones to increase the rate of bone formation.

While the United States Federal Drug Administration has given the green light to several drugs to prevent and slow bone loss, it has approved just one drug to accelerate bone growth.

Prof Winkler said the NUS team's research could lead to more compounds that increase the number of bone-forming cells and stimulate their activity.

The scientists have already cracked part of the creature's regeneration process. While some scientists believe that the fish turns its muscle, blood or other cells into bone cells when it needs to regrow the bones of its fins, this is not the case, said Prof Winkler.

"In fact, they turn their mature bone cells back into immature bone precursor cells. These then migrate to the regrowing fin and turn into mature bone cells to help the rebuilding process," he said.

The discovery has helped the scientists to narrow the field of genes at work that could eventually help people.

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Fishing for clues to cancer link

What can the humble zebrafish and medaka fish species tell us about human cancers? Plenty, as it turns out.

Researchers at the National University of Singapore (NUS) have been using the fish for years, to learn how liver and skin cancers may grow and spread in humans.

So far, they have discovered that a gene linked to skin cancer can also cause liver cancer, and that a type of skin cancer called melanoma may be lethal because it disables immune systems.

The scientists said that the fish are genetically similar to people, which makes them an ideal substitute when studying human diseases.

Professor Manfred Schartl is a visiting professor at NUS who is using the fish to study skin cancer. He is also head of physiological chemistry at the University of Wurzburg in Germany. He said the fish are small and easy to breed, so thousands can be kept in the laboratory for extensive tests.

Their embryos and larvae are also transparent, allowing researchers to easily observe what happens inside the fish when they grow and when they have to fight diseases like cancer.

"We know that the genes that cause cancer are only an ignition spark for a lot of things that happen in the cells," said Prof Schartl.

He found that when melanoma developed in the fish, the cancer immediately disabled its immune system. "We know that melanoma is a very malignant cancer in people, and that may be why," he said.

Professor Gong Zhiyuan, a professor at the NUS Department of Biological Sciences, has used zebrafish to study liver cancer since 2002. It is the fourth most common cancer in men in Singapore.

His team has published papers showing that liver cancer in zebrafish and people have the same molecular signatures, a crucial first step to showing that studying the disease in the fish is likely to yield dividends for people.

The scientists are focusing their attention on 12 genes that are known to cause liver cancer, to unlock how each one works. They have published papers on three of the genes, and developed some chemicals that stopped the cancer progressing in fish.

HOW SMALL FISH ARE A BIG HELP

Cancer is one of the world's most devastating diseases, and scientists are increasingly turning to small fish such as zebrafish and medaka to help understand and fight it.

On Tuesday, the National University of Singapore (NUS) will host a talk by Professor Manfred Schartl, one of its visiting professors, on how the small fish are used.

The free talk, The Basis Of Cancer: How Small Fish Can Help To Understand Human Disease, will be held from 7pm to 9pm at the Kent Ridge Guild House at 9 Kent Ridge Drive.

Prof Schartl is the NUS Society Professor this year. The post was created in 1996 to invite leading academics from universities around the world to share their expertise.

He is a professor and head of the physiological chemistry department at Germany's University of Wurzburg, and oversees 17 institutes from three faculties at the school.

He is also the vice-president of the German Genetics Society and is on the editorial board of several international journals.