THE AUSTRALIAN

Scientists crack code for new drugs to fight disease

ANDREW TROUNSON THE AUSTRALIAN SEPTEMBER 25, 2015 12:00AM

Australian scientists have mapped the nano-sized “gateways” in cell membranes in an extraordinary world first that could lead to the development of a host of new drugs to battle disease and infection.

The team has solved the mystery over how molecules such as proteins pass into cell structures, providing a scientific “road map” for designing new drugs.

The revolutionary technique refined by Monash University microbiologist Trevor Lithgow and his colleagues here and in Japan was achieved over 15 years and is published today in the prestigious journal Science.

It will be jumped on by global medical researchers as a guide to showing how they could design drug molecules to get through different cell membranes.

Using techniques reminiscent of science fiction, Professor Lithgow and fellow lead researcher Takuya Shiota used genetically modified “probes” from yeast, and sub-atomic imaging to fully map and recreate in three dimensions the membrane gateway in mitochondria, the energy generators within our cells.

It means researchers now know exactly how to design molecules to enter the mitochondria and potentially tackle disorders such as diabetes and mitochondrial disease. The same technique can be used to map the different gateways across all membranes within a cell.

“By having this detailed architecture for this gateway it really does open a road map for whatever good ideas people have now,” Professor Lithgow said.

Mapping the mitochondrial gateway, dubbed Tom-40, has been a painstaking process over more than 15 years, working at a nanometre scale of one-billionth of a metre, where the only way to “see” anything is to record microscopic data and recreate it on a computer.

Professor Lithgow said it had been like trying to solve a massive Rubik’s cube. It had involved using a genetically modified amino acid from yeast, which is an almost perfect match for human proteins.

The trick with the new amino acid is that, if flashed with a burst of UV light, it will reflect onto nearby structures, making it possible to “see” them in computer data recovered by electron microscopes. By inserting hundreds of these amino acids, or probes, into the structure of Tom-40 in yeast, the researchers have been able to painstakingly piece together what it looks like.

It took years for the researchers to reconstruct Tom-40 in a way that fits the data they were getting back from the “probes’’.

But by last Christmas they had cracked it, the computer printing out an image where, metaphorically speaking, all the cube’s colours were aligned.

Professor Lithgow said that having spent years “banging his head” against Tom-40 he was almost sad to

finally know all its nooks and crannies.

But he was already applying the technique to map the membrane of the E. coli bacteria in a bid to map how it is able to latch on and infect human cells

“If you can understand how that works you are in a great position to have a drug that would stop it from working and cause the bacteria to be flushed out of human tissue before they can get a toehold,” he said.