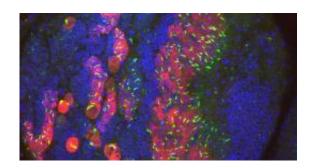


'Snakes' seen in human cells

October 3 2011, By Jonathan Wood



(PhysOrg.com) -- Curious snake-like forms have been spotted in cells from many different species across the evolutionary tree. Now Oxford scientists have shown they exist in human cells as well.

This apparent ubiquity across species from bacteria to <u>mammals</u> suggests the structures perform a crucial function in the cell. But how and why they form, and what role they play in the cell remain anyone's guess.

Three groups <u>reported</u> observations of the snakes in cells from a whole range of different species at around the same time in 2010, including Dr. Ji-Long Liu's group at the Department of Physiology, Anatomy and Genetics in Oxford.

Ji-Long and colleagues named the structures 'cytoophidia' because of how they looked under the microscope: cytoophidium is 'cell snake' in Greek.



"Cytoophidia have heads and tails and can move around. They really do look like snakes," explains Ji-Long Liu.

"I reported the finding in <u>fruit flies</u> early in the summer of 2010,' he says. "Two months later, two papers – <u>one from</u> Zemer Gitai's group in Princeton and <u>the other</u> from James Wilhelm's group at the University of California, San Diego – reported similar snake-like structures in <u>bacteria</u>, brewer's yeast, flies and rats."

Ji-Long's group has now reported the <u>first observation</u> of these cellular structures in <u>human cells</u> in the *Journal of Genetics and Genomics*.

"Amazingly, these snakes occur across the tree of life, from bugs to humans," he says. "Cytoophidia are found inside cells, and sometimes they stay near the surface of cells. It looks like the number of snakes in a cell is tightly controlled."

But what are they? Having initially observed the snakes in cells from fruit flies, Ji-Long got curious and decided to follow up the chance observation. He took advantage of a collection of fruit flies at the Carnegie Institution Department of Embryology [CIDE], where he worked before moving to Oxford.

In this collection, individual proteins in the fruit flies had been labelled with a fluorescent green marker, allowing Ji-Long to identify the cell snakes as containing the enzyme CTP synthase.

CTP synthase is a crucial but not necessarily glamorous enzyme, one of many such enzymes involved in necessary biological processes that keep our cells ticking over. In this case, the enzyme plays a role in making the molecule CTP, a building block that helps make up DNA and RNA. The CTP molecule also crops up in fat metabolism.



If the generation of CTP goes wrong, it could cause a lot of damage to the cell," Ji-Long says.

It is possible to speculate about why an enzyme would form these long filament structures in cells. For a start, cells are a long way from just being bags of biological molecules and enzymes that float around freely, magically carrying out their many functions, reactions and chains of metabolic processes.

The cell needs an organized structure to bring this industry of biochemical reactions under control, with many processes cordoned off in separate chambers, capsules and compartments. It allows related reactions to be better controlled and regulated, with the right concentrations of the different molecules brought together in the right environment. After all, you don't just bung all the ingredients into a chemical engineering plant, a brewery or a baking tin imagining that the recipe will be fine.

"The beauty of a well-organized cell has not been appreciated by everyone. Without the structure, a bag of the same amounts of all the molecules would not do the same thing as a living cell," explains Ji-Long. "Compartmentation could be a general feature for many enzymes in a cell," he believes.

He notes that six enzymes that produce a set of biomolecular building blocks called purines are known to cluster in a specific compartment, and studies have shown that many proteins are found localized in just one part of a cell. "It seems to us that the filaments are necessary for the CTP synthase enzyme activity," he says. "We are trying to understand the relationship between filament-forming and the overall function of the enzyme in a cell – but we have no clear answer yet."

His research group has found some drugs that affect the assembly of the



CTP synthase enzyme into snakes, making the filaments appear in human and fruit fly cells. This approach could give a new handle to study the snakes' function in the cell.

Another interesting question is why the enzyme forms a snake-like filament or rings rather than spheres or just irregular capsules. These shapes have different surface-to-volume ratios, which might give some clues as to the difference this makes to the activity of the enzyme.

"It would be fascinating to know more about what the role of the cytoophidium plays in regulating the production of CTP," says Ji-Long. He notes that the CTP synthase enzyme is found in larger amounts in many types of cancer cells, and that his group has shown that some potential anti-cancer drugs can promote the formation of cytoophidia. But that's still a long way from showing that this is important clinically or that there might be medical applications in understanding more about these cell snakes.

At the moment the existence of these snakes is an interesting observation that opens up intriguing new research questions, but what role the <u>snakes</u> play in our <u>cells</u> is unknown. Ji-Long also suggests that it's 'very likely' there are other enzymes packaged up in structures in the cell that we don't know about yet. "Time will tell," he says.

Provided by Oxford University

Citation: 'Snakes' seen in human cells (2011, October 3) retrieved 19 April 2024 from https://phys.org/news/2011-10-snakes-human-cells.html

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