Study shows frogs can play key role in stem cell research

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It sounds like one of those curiosities which pops up in wildlife documentaries, but the African clawed frog could prove a powerful ally for scientists working in the key area of stem cell research.

Researchers at the University of Edinburgh have discovered that the distinctive species – which has become popular in recent years as a domestic pet – shares with humans the same genetic mechanism that enables embryonic stem cells to divide without limit. This process, which gives embryonic stem cells the capacity to become any of the 200 cell types in the body, is fundamental to all research in the discipline.

Until now, stem cells have been obtained from mice, primates and humans, but never from amphibians. But, because the African clawed frog is easier to study than mice and humans, the Edinburgh team anticipate that it will become an important research tool in their quest to understand and, ultimately, treat disease using stem cells. The results of their study are published in the current edition of the journal *Development.*

The key protein in humans, called Oct4, which governs the process of unlimited division of stem cells, has an equivalent in the African clawed frog, called PouV. This new research shows that the two proteins are not only similar, but perform the same function - both bind to DNA and activate certain genes that keep stem cells dividing. Indeed, embryonic stem cells lacking the Oct4 protein stop dividing and become specialised.

In the study, Dr Gillian Morrison introduced frog PouV proteins into mouse embryonic stem cells lacking Oct4 and found that the frog proteins “rescued” the stem cells – in other words, the cells recovered their ability to divide without limit. Dr Morrison obtained similar effects when she introduced PouV proteins from another amphibian, the axolotl (a type of salamander).

To find out exactly what function PouV proteins perform in frog embryos, Dr Morrison injected special compounds into very young embryos, to inactivate the native PouV proteins. These embryos continued to grow, but had defective heads and tails.

When the scientists looked closely at these embryos, they found that cells had become specialised before they were supposed to – before the embryo was ready for them. Consequently, the structures they make are severely affected.

This suggests that the PouV proteins are holding the cells in an uncommitted state, waiting for the time to come when they will decide what type of cell they are going to be. This is probably what Oct4 is doing in mouse and human embryonic stem cells.

The findings are also interesting because they highlight that the remarkable capacity of embryonic stem cells to divide without limit is at least 300 million years old. “It was very exciting, and humbling, to find that the proteins from such an ancient animal such as the frog can rescue the behaviour of ‘modern’ mouse embryonic stem cells. It told us so much about where this behaviour comes from, and how long ago,” said Dr Morrison.

Dr Josh Brickman, group leader at the Institute for Stem Cell research says, “Our results show that mammals have adopted the function of the amphibian PouV proteins to maintain their embryonic stem cells. These

features of dividing without limit and giving rise to many types of cell are thus ancient features of early embryonic cells, crucial for the correct development of both frogs and humans."

Source: Institute for Stem Cell Research

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