Scientists now able to view critical aspects of mammalian embryonic development using new technique

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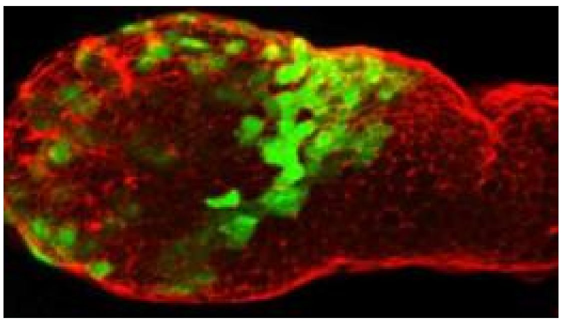

A mouse embryo in which the outer membranes of all cells are glowing red. A subset of cells are expressing a green glowing protein that identifies them as cells that will signal head development. Credit: Lab of Professor Magdalena Zernicka-Goetz , Gurdon Institute

A novel approach in the study of the development of mammalian embryos was today reported in the journal *Nature Communications*. The research, from the laboratory of Professor Magdalena Zernicka-Goetz of the University of Cambridge, enables scientists to view critical aspects of embryonic development which was previously unobservable.

For several decades it has been possible to culture embryos from a single cell, the fertilised egg, to the blastocyst, a ball of some 64 cells all derived from the first by repeated rounds of cell division. In practical terms this has allowed the development of the in vitro fertilisation techniques that are used world-wide to assist fertility.

It has also enabled scientists to learn much about these early stages of development during which cells take the very first decisions about their future. This is because in the first 4 days it is possible to observe developmental events as they happen and, in model systems such as the mouse, manipulate the expression of the genes involved in the process in order to better understand their roles.

The 64 cells of the blastocyst comprise three cell types, a small number of stem cells that will develop into the future body, cradled by two extra-embryonic cell types that will contribute to the placenta but will also signal developmental events as the stem cell population expands. Currently, there is quite a good understanding of the molecular and cellular events resulting in the formation of these three cell types.

By contrast, scientists' knowledge of subsequent events has been extremely restricted. This is the stage (around the fourth day) at which the developing embryo implants into the mother's womb and its development becomes hidden from view as this is taking place. Yet this is a very important phase of development that will see the extra-embryonic tissues signal to the stem cells where to start making the head and the rear of the body.

It has been possible for researchers to recover embryos from model systems, such as the mouse, as this is taking place and so from snap-shots build up a picture of what is happening. Until now, however, it has been impossible to record this process as it is happening, let alone carry out experimentation in order to understand the processes involved.

Using the mouse embryo as a model, Professor Zernicka-Goetz and her colleagues, with funding from the Wellcome Trust, have developed a method that has allowed them to overcome the barrier of implantation into the womb by culturing and imaging embryos outside the body of the mother for the first 8 days of their development.

Most importantly, the movies that Professor Zernicka-Goetz' team can now make of this critical developmental stage are revealing secrets about the origins of clusters of extra-embryonic cells that signal where to make the head of the embryo. They have used a gene expressed only in this "head" signalling region marked by a protein that glows to track these cells in mouse embryos living in culture.

In this way they have been able to determine that these cells originate from one or two cells at the blastocyst stage and their progeny ultimately cluster together in a specific part of the embryo before collectively migrating to the position at which they signal head development. The cells that lead this migration appear to have a particularly important role in leading the rest and act as pioneers.

Professor Zernicka-Goetz, lead author of the research, said: "Not only is this approach uncovering events previously hidden from view, but it has other important potential applications. This is the period of development during which the natural population of stem cells undergoes expansion to form the foundation upon which the body can be built.

"In the mouse it is fairly easy to establish stem cell lines from embryos at the blastocyst stage that have the capability of contributing to all body tissues and indeed from which an entire new organism can be built. In humans, however, such lines are more difficult to establish. The new technique offers hope that by permitting the expansion of the natural stem cell population in a manner that resembles normal development, it should make establishing stem cell lines much easier. What is certain is that it will allow direct experimental access to this stage of development and should therefore provide the means of gaining greater understanding of embryonic stem cells in their natural development."

More information: The paper 'Dynamics of anterior–posterior axis formation in the developing mouse embryo' will be published in the 14 February 2012 edition of Nature Communications.

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