Bovine embryos as a model for early human development

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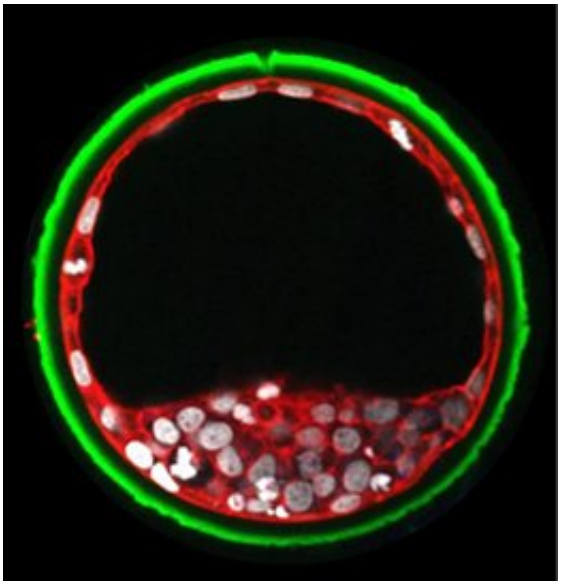

Bovine embryo at blastocyst stage. Credit: Felix A. Habermann

The mechanisms that underlie early embryonic development in humans and cattle are very similar. Therefore, LMU researchers argue that bovine embryos might well be a better model for early human development than the mouse system.

Many fundamental aspects of the early stages of embryonic development in humans are found to be conserved in other mammals. This is why studies carried out on animal models can help us to understand the development of the human embryo. Most of these studies have been

done on mouse embryos. Researchers led by Professor Eckhard Wolf, Chair of Molecular Animal Breeding and Biotechnology at the Gene Center and the Department of Veterinary Sciences at LMU, now report in the journal PNAS, that early phases of the development of bovine embryos, might offer a better system for the understanding of the earliest differentiation steps.

Embryonic development in mammals begins with the division of the fertilized egg, which is then followed by several further rounds of division to form the blastocyst, a sphere of cells made up of two layers of cells surrounding a fluid-filled cavity. The cells of the outer layer will later give rise to the extraembryonic membranes and the placenta after the blastocyst implants in the wall of the uterus, while the embryo itself develops from the inner cell mass. The differentiation of the outer layer of blastocyst cells from the inner cell mass is already underway by the 8-cell stage. However, some of the early cells in the inner cell mass remain pluripotent, i.e., they retain the ability to differentiate into most of the diverse cell types found in the adult. "The genetic regulation of these early differentiation processes has been extensively investigated in the mouse. The mechanisms involved, however, are not always evolutionarily conserved," says Wolf. "New methods such the CRISPR-Cas9 system for gene editing now make it possible to carry out functional studies in other species, and this will in turn lead to decisive advances in our understanding of early embryonic development in mammals."

Wolf and his colleagues have used the CRISPR-Cas9 system in bovine embryos to delete OCT4, a gene that is known to play a key role in the regulation of pluripotency in mammalian embryos. In the mouse, loss of this gene results in the inability to generate cells that express a transcription factor called GATA6, while cells that express a marker of pluripotency named NANOG are not affected. "In the bovine embryo, we found precisely the opposite effect," says Kilian Simmet, first author

of the new study. "In this case, deletion of OCT4 inhibited the emergence of NANOG-expressing cells, while GATA6-expressing precursor cells developed normally." A recently published paper had previously reported that human cells react to deletion of the same gene at the same stage in exactly the same way. In addition, this is not the only case in which the regulatory circuits that control early embryonic development in humans show greater similarity to those employed in bovine embryos than to those that operate in the mouse system.

More information: Kilian Simmet et al. OCT4/POU5F1 is required for NANOG expression in bovine blastocysts, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1718833115

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