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Press Release: Where to put head and tail?

Teaser: beta-Catenin discovered as a new key player in the formation of the main body axis during mammalian embryogenesis

Formation of the body axes is a critical part of embryonic development. They guarantee that all body parts end up where they belong and that no ears grow on our backs. The head-tail axis, for example, determines the orientation of the two ends of the body. It was previously assumed that this axis is largely determined by the interplay between the Nodal and BMP signals. However, there appears to be another player in this system, as the research groups led by Christian Schröter at the Max Planck Institute of Molecular Physiology in Dortmund and Ivan Bedzhov at the Max Planck Institute of Molecular Biomedicine in Münster have now discovered by using an embryo-like model system they developed. In the absence of BMP, the signalling molecule beta-catenin takes on the role of the Nodal antagonist. This new mechanism could be a flexible solution for axis formation in embryos with different shapes.

Our basic body plan is determined early during embryonic development by the formation of three body axes. Put simply, they determine where up and down, front and back and right and left are. The head-tail axis determines the position of the two body openings, the mouth and anus. The activation of various regulatory genes along the head-tail axis and two further body axes leads to the development of certain cell types and tissues. In this way, the axes determine the blueprint for the later body shape. However, despite this important role, many questions about axis formation remain unanswered.

Mice look like cups ...

In evolutionary terms, the head-tail axis is the oldest body axis and is determined early on in embryonic development. In mice, it develops just a few days after fertilisation. At this stage, the embryo looks like a cup consisting of two layers of cells and a thick lid. At the bottom of the cup, a new cell population develops in the outer cell layer, the visceral endoderm. The cells of this so-called anterior visceral endoderm (AVE) then move towards the edge of the cup and stop approximately halfway. At this point, the head develops from the inner cell layer of the cup, the epiblast, and the tail develops on the opposite side. It was previously assumed that this process is triggered and controlled by the antagonism of two molecular signals. The epiblast emits Nodal, while the lid, the extraembryonic endoderm, releases the counterpart BMP. The bottom of the cup, which is furthest away from the lid, receives the least amount of the BMP signal. As a result, the Nodal signal predominates there and the AVE population differentiates.

... Humans like discs

In their current study, the Max Planck researchers were able to identify another key player in axis formation. To this end, they developed a novel embryo-like model system consisting of a layer of epiblast and a layer of VE cells - a cup without a lid. They achieved this with the targeted and controlled treatment of embryonic mouse stem cells with growth factors. And despite the lack of BMP signalling from the extra-embryonic tissue, an AVE cell population was able to form from the VE cells - the starting point for the development of

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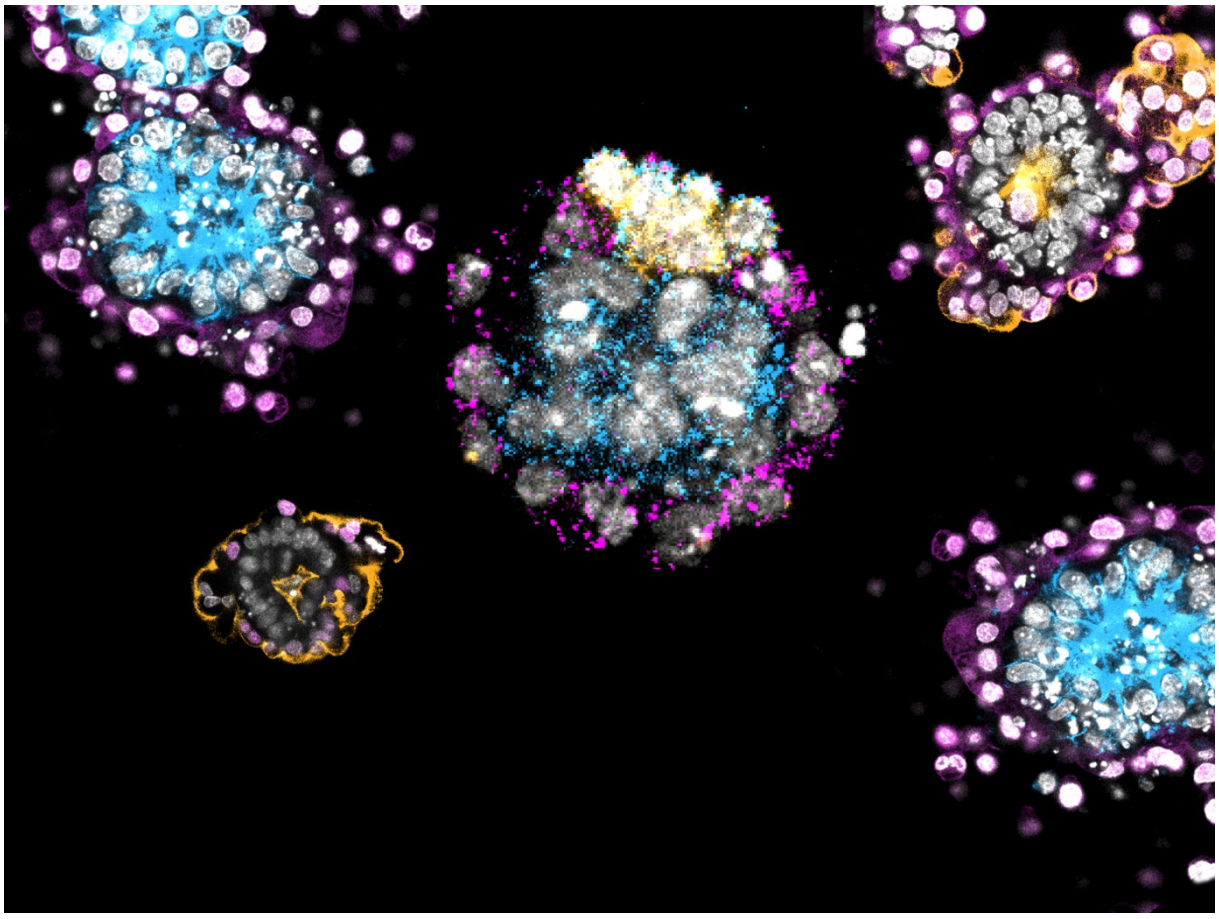
the first body axis. The researchers were able to show that beta-catenin, a signalling molecule that was previously only known as a regulator of another body axis in embryonic development, is required for this. "It is quite possible that beta-catenin also plays an important role in the development of the head-tail axis in human embryos. The human embryo is more reminiscent of a disc than a cup. It is therefore quite likely that the distribution of BMP is quite different from that in the mouse embryo and that other mechanisms play a role in the formation of the first body axis," says Christian Schröter.

Stem cells on the same wavelength

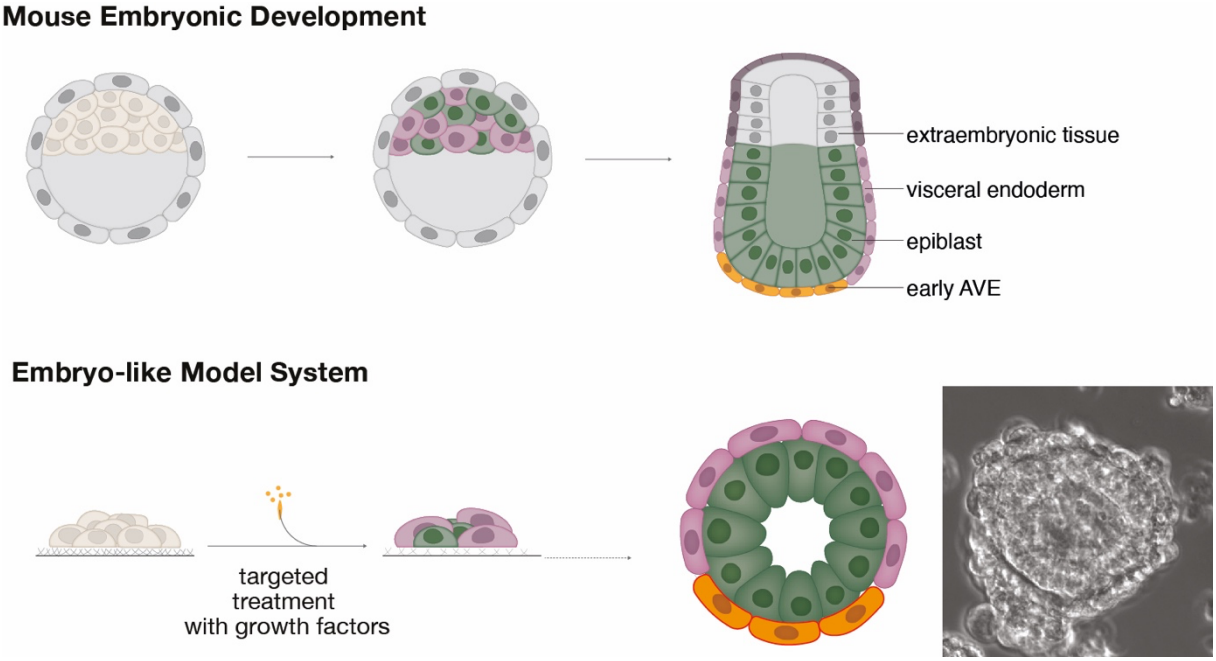
"Our two-layer embryo-like aggregates were the key to our success. Other studies usually use a mixture of different stem cell lines. However, the cell populations we used come from just one stem cell line. This means that they not only have an identical genetic background, but also utilise the same communication systems. You could also say that they are on the same wavelength," says Schröter. "Aggregates of human embryonic stem cells modelled on our system could be a promising experimental tool for investigating events during embryonic development in the future."

Teaser Image



Embryo-like model system under the microscope.

Image 1



Schematic of mouse embryonic development (top) and the embryo-like model system (bottom) for modelling the interactions between epiblast (green), visceral endoderm (violet) and extraembryonic tissue (grey).

Original Publication:

Schumacher S, Fernkorn M, Marten M, Chen R, Kim YS, Bedzhov I, Schröter C. Tissue-intrinsic beta-catenin signals antagonize Nodal-driven anterior visceral endoderm differentiation. ***Nat Commun.*** 10.1038/s41467-024-49380-0.

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