Gastrulation research reveals novel details about embryonic development

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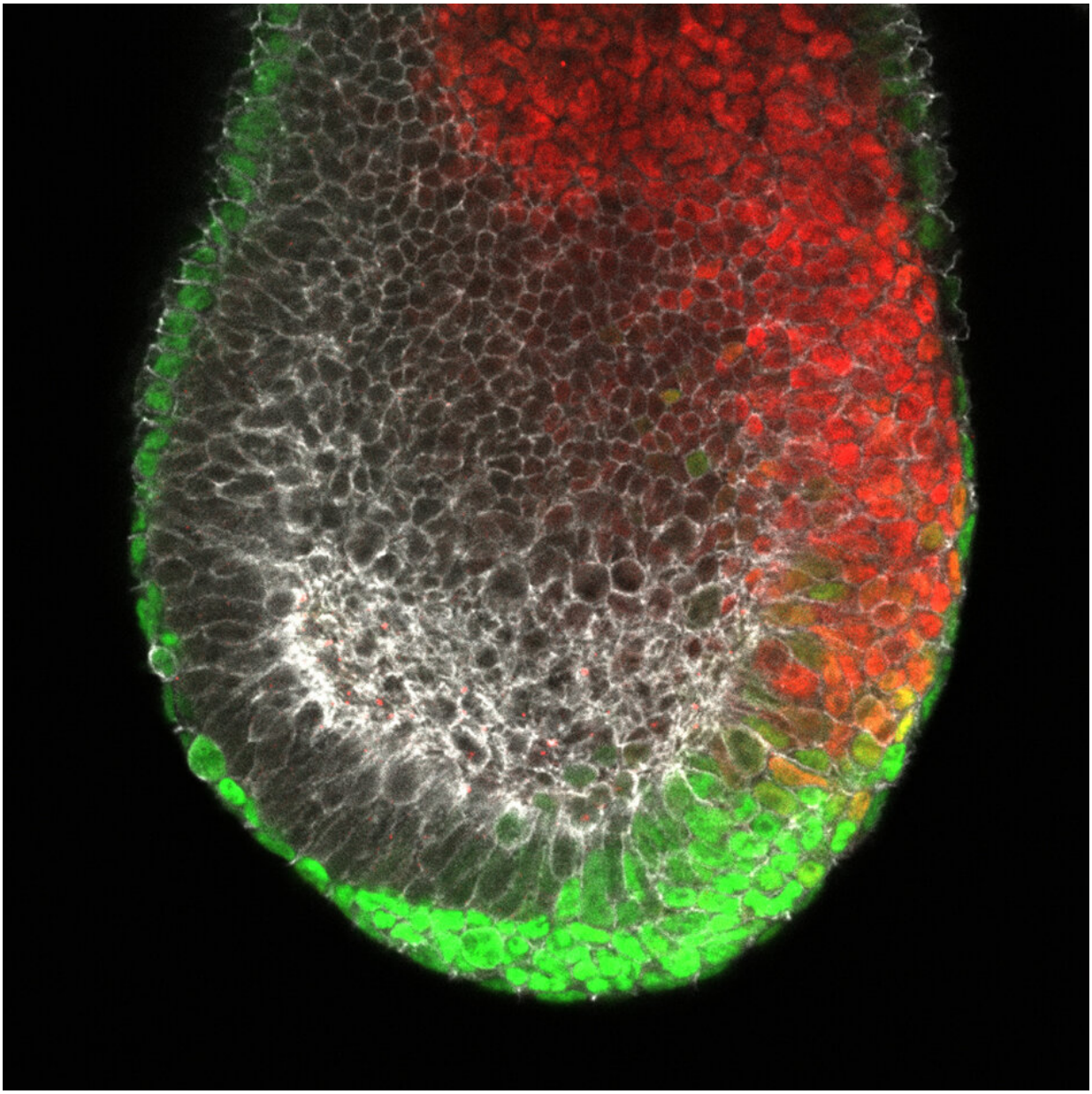

Stained image of an early mouse embryo (gastrula) showing the forming endoderm in green and the forming mesoderm in red. Credit: © Helmholtz Zentrum München / Silvia Schirge

Scientists from Helmholtz Zentrum München are revising the current textbook knowledge about gastrulation, the formation of the basic body plan, during embryonic development. Their study in mice has implications for cell replacement strategies and cancer research.

Gastrulation is the formation of the three principal germ layers—endoderm, mesoderm and ectoderm. Understanding the formation of the basic body plan is not only important to reveal how the fertilized egg gives rise to an adult organism, but also how congenital diseases arise. In addition, gastrulation serves as the basis to understand an embryonic development process called epithelial-to-mesenchymal transition, which is known to lead to cancer metastasis in adulthood when dysregulated.

"The famous biologist Lewis Wolpert once said that it is not birth, marriage or death, but gastrulation which is truly the most important time of our life. However, there are many things we still don't know about this phenomenon," says study leader Heiko Lickert.

In a new study, researchers could show that the formation of the endoderm germ layer is driven by a different mechanism than has long been assumed. In contrast to the mesoderm, which undergoes an epithelial-to-mesenchymal transition, the endoderm forms independent of this process. The researchers revealed that its formation is regulated by mechanisms of epithelial cell plasticity, which allow cells to leave an epithelium and migrate away. During this process, a gene regulatory protein shields the endoderm from undergoing a mesenchymal transition.

A better understanding of endoderm formation has the potential to advance cell replacement therapy (by improving stem cell differentiation into endoderm in vitro). Moreover, epithelial cell plasticity might be an alternative mechanism of cancer cell metastasis and further studies could identify novel targets for therapeutic intervention.

"Our study has not only revealed further details of germ layer formation, but also has broader implications for stem cell differentiation and cancer metastasis of the most common and deadliest cancers worldwide," explains first author Katharina Scheibner.

More information: Katharina Scheibner et al, Epithelial cell plasticity drives endoderm formation during gastrulation, *Nature Cell Biology* (2021). DOI: 10.1038/s41556-021-00694-x

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