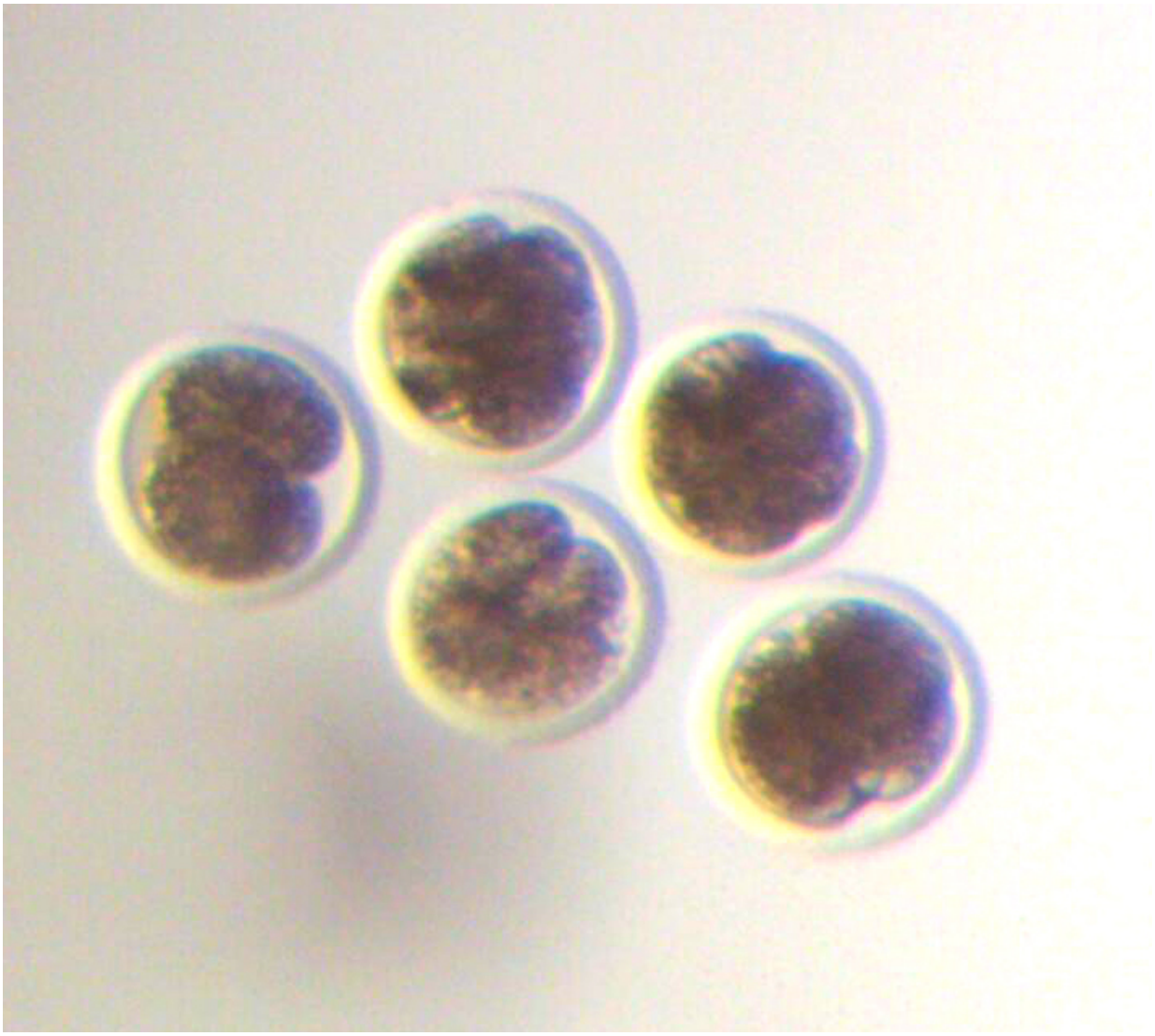
# Single-cell analysis of embryos reveals mis-segregation of parental genomes

April 12 2016



Bovine embryos were examined for abnormal chromosome segregation during development. Credit: Maaike Catteeuw, Ghent University

Single-cell embryos contain a set of maternal and paternal chromosomes, and as the embryo grows, daughter cells receive a copy of each. In a study published online today in *Genome Research*, researchers have discovered errors during the earliest stages of embryonic development can lead to entire sets of maternal and paternal chromosomes segregating into different cells, resulting in chimeric embryos.

"This is a novel fundamental insight into the origin of chimerism, a very rare condition in humans which can lead to birth defects," senior author Joris Vermeesh, from KU Leuven, said.

Previous studies involving in vitro fertilized (IVF) human embryos have demonstrated large fractions of embryos contain at least one cell with either whole or partial gains or losses of chromosomes. This chromosomal instability can lead to reduced fecundity and birth defects. To investigate in more detail, researchers from KU Leuven and elsewhere employed in vitro fertilization in cattle as a flexible system to study chromosomal changes in single embryonic cells.

Applying haplarithmisis, a method they previously developed, the researchers examined copy number and parental origin of chromosomes in single cells from 23 embryos. Nearly three-fourths of embryos examined contained at least one cell with either partial or whole chromosome aberrations, similar to findings in human in vitro fertilized embryos. Surprisingly, 39% of all embryos contained cells with abnormalities of entire sets of embryos, for example, cells with only one set of chromosomes, either maternal or paternal, or three sets (one maternal set plus two paternal sets, or vice versa). Many of these embryos resulted from fertilization errors, such as two sperm fertilizing a single egg. However, normally fertilized embryos also displayed this aberrant pattern. The researchers coined the cell division leading to the

segregation of parental chromosomes "heterogoneic," or of differential parental origin.

The finding that normal fertilization can result in embryos containing cells with different parental sets of chromosomes is a new mechanism for chimerism, which was previously thought to occur only as the result of fertilization errors, for example, the fusion of multiple sperm or eggs to form an embryo.

"The presence of chimerism in human IVF embryos was never conceived," Vermeesch said. "Knowing this might occur may improve approaches for embryo selection and ultimately the success of IVF/preimplantation genetic diagnosis."

**More information:** Destouni A, Zamani Esteki M, Catteeuw M, Tšuiko M, Dimitriadou E, Smits K, Kurg A, Van Soom A, Voet T, Vermeesch JR. 2016. Zygotes segregate entire parental genomes in distinct blastomere lineages causing cleavage stage chimerism and mixoploidy. *Genome Res* doi: 10.1101/gr.200527.115

Provided by Cold Spring Harbor Laboratory