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Abnormalities in centrosome behavior are frequent in the first mitotic division of non-rodent mammalian zygotes

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Post-zygotic or “mosaic” aneuploidy, i.e. the presence of a subset of cells with an aberrant number of chromosomes, is a frequent feature of human preimplantation embryos. A high incidence of aneuploidy within an embryo is recognized as the major cause of developmental arrest and miscarriage. Post-zygotic aneuploidy often arises during the first cell divisions in the embryo and it is not only exclusive of human embryos, but has a similar occurrence in nonhuman primate, bovine, and equine embryos. Despite the wide incidence and often severe developmental consequences of postzygotic aneuploidy, it is still unclear why the early cleavages are so prone to errors.

In somatic cells the centrosomes, formed by two centrioles surrounded by the pericentriolar material, are the two major microtubule-organizing centres (MTOCs) and play an essential role in spindle assembly and chromosomes segregation. Mammalian oocytes lack of centrosomes and, although two centrioles are re-introduced by the spermatozoon at fertilization, we recently showed that centrosomes make only a minor contribution to zygotic spindle assembly. Although not essential for spindle assembly, the role of centrosomes in ensuring fidelity during the zygotic division is still unclear. Here, we evaluated the incidence and consequences of centrosomes abnormalities in the zygotic division of bovine embryos, a species which, similarly to human embryos, inherit centrioles paternally at fertilization. To this end we imaged the first mitotic division in real-time live bovine zygotes (n=55) injected with mRNA encoding for H2B-mCherry and MAP4-eGFP to allow visualization of chromatin an microtubules respectively.

Abnormalities in centrosome behaviour were observed in 40% of the zygotes imaged. The most observed abnormality was failure (15%) or delay (10%; range: 10-30min after nuclear envelope break down) of one of the centrosome to engage to the metaphase spindle. Premature fragmentation of one of both of the centrosomes (10%; range 6-21 min before anaphase) and abnormal positioning of one of the centrosomes (5%) within the mitotic spindle were also observed. Centrosome failure to engage to the mitotic spindle resulted in 60% of the cases in the inability of one or more chromosomes to be captured by spindle microtubules. In contrast, chromosomes lagging after anaphase onset (50%) was observed with the same frequency also in zygotes displaying normal centrosomes behaviour. Non injected zygotes (n=350) fixed at different stages of the first mitotic division showed similar type and frequency of centrosome abnormalities as the ones observed in mRNA injected zygotes. Taken together our observations suggest that centrosomes partially contribute to chromosomes segregation fidelity during early embryonic development, however other players are probably responsible for the high incidence of lagging chromosomes. Further studies are needed to elucidate the reason why in mammalian zygotes centrosomes are less active as MTOCs than in somatic cells.

Keywords: zygote, centrosomes, aneuploidy