Unfortunately, the same end points were not examined in ovarian fragments and cultured follicles, no rotational control group was included, and the number of repli cates per group and other experimental details were not provided. By contrast, exposure to either sim ulated microgravity or simulated hypergravity lengthened oestrous cycles due to lengthened dioestrous, whereas space flight resulted in cessation of cycling, suggesting that other exposures (such as stress or circadian rhythm disruption) during space flight besides microgravity affect the hypothalamic–pituitary–ovarian axis. By contrast, nearly 40% of morula or early blastocyst stage embryos cultured in simulated microgravity progressed to the expanded blastocyst stage by 48 h. Both simulated microgravity and rotational control morula or early blastocyst stage embryos had upregulation of SAPK (a stress–activated protein kinase) phosphorylation at Thr183 or Thr185, a marker for activation of SAPK signalling, after 24h of culture compared with static controls; all of these effects were similar but less severe in rotation controls than in animals in simulated microgravity. As a result of the similarity of lengthened vaginal dioestrous during microgravity with lengthened vaginal dioestrous dur ing pseudopregnancy in rodents (which is elicited by cervical stimulation that causes a surge of prolactin secretion), suppression of prolactin secretion was tested and found to block the induction of lengthened dioes trous by hypergravity52. Exposure of pregnant rats to hypergravity during the second half of gestation did not alter gesta tion length, duration of parturition (time from birth of first pup to birth of last pup), litter size or birth weights; however, the frequency of lordosis contractions during labour decreased by half45 and neonatal pup mortality was increased in rats exposed to hypergravity46,59. Oocytes were harvested at the germinal vesicle stage (which is the metaphase of the first meiotic division) from immature Kunming mice 48h after injec tion of 7.5IU equine chorionic gonadotropin to stimu late development of a cohort of preovulatory follicles. This find ing under microgravity was related to abnormal meiotic spindle formation during both the first and second meio tic divisions, with abnormal localization of ?–tubulin (which is essential for spindle formation) around the chromosomes of oocytes cultured in simulated micro gravity. Exposure of female and male mice to hypergravity before mating and through gestation decreased pregnancy rates up to 2.9g (with no pregnancies at 3.5 g), decreased fetal size and altered skeletal development (the longest dimension of most bones measured was increased at 2.3 g, the longest dimension and perimeter of most bones were decreased at 2.6g and these parameters were decreased for all bones at 2.9 g) compared with 1 g controls48. Rather, decreased neonatal survival of pups born to dams exposed to hypergravity was associated with decreased glucose oxi dation and lipogenesis in mammary glands, decreased size of adipocytes with decreased rate of lipolysis and an increased rate of glucose incorporation into lipids in the liver53. Fertilization of mouse oocytes occurred normally under microgravity simulated using a 3D clinostat; how ever, continued culture under microgravity resulted in delayed development to the blastocyst stage and fewer trophectoderm cells in those embryos that reached the blastocyst stage compared with embryos at normal grav ity57. No differences in mating ability or gestation length were observed in rats adapted to hypergravity (2.2g or 3.1g), but the number of fetuses and maternal care of pups were dose–dependently decreased compared with those of 1g controls50. In other work, luteal cells from the corpora lutea of pregnant rats were cultured in microgravity simulated using a high aspect ratio vessel and compared with cells from spinner flask controls or in microgravity

simulated using a clinostat with static controls. Luteal cells cultured in the clinostat model for 2 days had increased DNA damage as measured by the Comet assay, increased apoptosis and decreased numbers of active mitochondria compared with static controls[42]. In contrast to the abnormal organization of microtubules, microfilament organization and function, which are necessary for migration of the chromosomes and spindles to the periphery of the oocyte, were not disrupted under simulated microgravity[55]. Preimplantation development of mouse embryos has also been investigated using a rotary cell culture system with high aspect ratio culture vessels to simulate microgravity compared with static culture controls and rotation controls[58]. Luteal cells cul tured in both microgravity models exhibited decreased progesterone secretion compared with their respec tive control cultures during up to 8 days of culture[42,43]. Moreover, exposure to hyper gravity for >=8 h during the dioestrous phase of the oestrous cycle, but not during other cycle stages, induced a surge of prolactin secretion[49].

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