P-205 Epothilone D as an actin cytoskeleton stabilizer improved mitochondria bioenergenesis and blastocyst formation of mouse preimplantation embryo

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Study question: What is primary factor of bioenergetics product activity between microtubule instability and the functional activity of mitochondria in embryo?

Summary answer: The actin cytoskeleton instability is presumably the primary cause for the bioenergenesis of mitochondrial function to the preimplantation embryo development.

What is known already: Mitochondria are cellular organelles dynamically moving and morphological changes. It provides for homeostatic energy to the cell. The dynamic property of the mitochondria is associated with the microtubule network in the cell. However, the stability of the microtubule was clearly identified for preimplantation embryo development.

Study design, size, duration: This study is designed to assess the ATP productivity of the mitochondria, and specifically to observe what its primary factor is in terms of providing microtubule stability in mammalian cells. Additionally, we investigated the relationship between blastocyst formation and actin cytoskeleton stabilization by EpD with 2-cell mice.

Participants/materials, setting, methods: We prepared the microtubule stability regulation model with the HEK293 cell line by using the microtubule stabilizer as an Epothilone D (EpD). Then we analyzed the metabolic activity of the cells through oxidative phosphorylation (OXP) ratios analysis. Also, we performed confocal live imaging to observe mitochondria morphology depending on the cells' microtubule. Next, we treated EpD to 2-cell culture media for the analysis of blastocyst development ratios.

Main results and the role of chance: EpD significantly increased fusion form. Also, EpD enhance bioenergy ratios like OXP in the mitochondria and functional activity related marker, like mTOR compared with the control. These results suggest that microtubule stabilization enhances mitochondrial metabolism by increasing oxygen consumption. Also, EpD in 2-cell culture media led to a significant increase in the speed of development and 50% higher hatched out blastocyst formation ratios compared to the control group.

Limitations, reasons for caution: This study had limited animal experiments. For the next study, we are planning with an aim to improve the quality and development ratios of human embryos by EpD.

Wider implications of the findings: Microtubule stabilizer has a possibility to recover the mitochondria's functional activity in the preimplantation embryo development. Mitochondrial functional activity along the actin cytoskeleton may play a pivotal role in determining the embryo quality and development ratios for archive pregnancy.

Trial registration number: non-clinical trials