S41-5 Phenotype analysis of GPx4 knockout mice

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Selenium is an essential trace element for human and many other forms of life, and a deficiency of this element induces some pathological conditions, such as cancer, coronary heart disease, liver necrosis and infertile. It is also well known that selenium is essential for cell culture. Selenium is an essential component of 25 selenoproteins such as glutathione peroxidase (GPx), which contain selenium as selenocysteine. Phospholipid hydroperoxide glutathione peroxidase (GPx4) is one of the family of glutathione peroxidase and an intracellular antioxidant enzyme that can directly reduce phospholipid hydroperoxide generated in membrane by oxidative stress. In this symposium, we will present our recent results using tissue specific and organelle specific GPx4 knockout mice. GPx4 is transcribed from one gene into three types of GPx4, mitochondrial, non-mitochondrial and nucleolar GPx4. Targeted disruption of all exons of the GPx4 gene in mice caused embryonic lethality at 7.5 days post coitum. Depletion of GPx4 in MEF and embryos could not grow normally and induce cell death. Transgenic rescue analysis demonstrated that non-mitochondrial GPx4 is essential for embryogenesis and mitochondrial GPx4 is required for the structure of tail and mitochondrial function of sperm. We established testis-specific GPx4 KO mice, that are male infertile showing significant reduction of the number of spermatozoa and abnormal structure of flagella. These results demonstrate GPx4 is essential for embryogenesis and spermatogenesis.