（学位第３号様式）

学 位 論 文 要 旨

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題　目	Disturbance to metabolic profiles and malformation in Japanese medaka embryos exposed to oxygenated polycyclic aromatic hydrocarbons. （含酸素多環芳香族炭化水素類のヒメダカ胚中代謝攪乱と奇形誘発に関する研究）

Oxygenated polycyclic aromatic hydrocarbons (oxyPAHs) are directly discharged into the atmosphere with exhaust gas from the diesel engine automobiles and industries, and are also generated through the photo-oxidation and/or microbial metabolism of parent polycyclic aromatic hydrocarbons. Because oxyPAHs have diversity of forming the process, they distribute widely in environment and are not exception in aquatic environment. They are already known to cause the gene toxicities in fish embryos. However, the studies for their toxicities to aquatic organisms have been limited, although several effects of them to mammals were already well-known. Therefore, in the present study, we examined the effects in Japanese medaka (*Oryzias latipes*) embryos exposed to 4 individuals of oxyPAHs by the observations with microscope, metabolomics approach, and biochemical method. At last, the affected mechanisms in the embryos exposed to oxyPAHs and larvae were also explored.

The embryos exposed to individual oxyPAH showed the characteristic effects with each substance dependence; for example, caving in yolk sac, blackened oil droplet, and underdevelopment in the embryos. The exposures of any oxyPAHs also caused the poor development of cephalic part, unabsorbed and hypertrophied yolk-sac, tubular heart as blue-sac syndrome and other symptoms. These effects for the hatching larvae were too serous to swim well.

Metabolomics approach with GC/MS predicted that ascorbic acid and hydroxyproline, which are essential components for the collagen synthesis, decreased in the embryos exposed to oxyPAHs. In fact, poor formations of the cartilage were confirmed especially in the cephalic and caudal part of hatching larvae. Hydroxyproline composing also decreased, and could form the deficient collagen in the embryos. Metabolomics also suggested that the excess ammonia existed in embryos exposed to oxyPAHs. This phenomenon was also confirmed by the measurement of ammonia in the embryos. Excess ammonia can cause the serious toxicities in organisms. The embryos exposed to oxyPAHs could affect to the ammonia, and cause the severe effects including deformations in the hatching larvae.

The present study could show that the embryos exposed to oxyPAHs were induced the oxidative stresses in the lipids and proteins. These oxidative stresses could also cause the serious effects in embryos exposed to oxyPAHs. In addition, we could confirm that oxyPAHs could be metabolized by CYP1A. Until now, although the possibilities of xenobiotics metabolism in embryos were not well-known, their oxidative metabolism possibly causes the gene toxicities even in fish embryos.