Samak Sutjarit 2014: Development of Apoptosis and Changes in Apoptosis-related Genes Expression in Developing Mouse Brain from Fusarenon-X-treated Pregnant Mice. Doctor of Philosophy (Genetic Engineering), Major Field: Genetic Engineering, Interdisciplinary Graduate Program. Thesis Advisor: Associate Professor Amnart Poapolathep, Ph.D. 97 pages.

Fusarenon-X (FX), a type B trichothecene mycotoxin, is mainly produced by *Fusarium crookwellense*, which occurs naturally in agricultural commodities, such as wheat and barley. FX has been shown to exert a variety of toxic effects on multiple targets *in vitro*. However, the embryonic toxicity of FX *in vivo* remains unclear. In the present study, we investigated FX-induced apoptosis and the relationship between the genetic regulatory mechanisms and FX-induced apoptosis in the developing mouse brain of FX-treated pregnant mice. Pregnant mice were orally administered FX (3.5 mg/kg b.w.) and were assessed at 0, 12, 24 and 48 hours after treatment (HAT). Apoptosis in the fetal brain was determined using hematoxylin and eosin staining, the TUNEL method, immunohistochemistry for PCNA and electron microscopy. Gene expressions were evaluated using microarray and real time-reverse transcription polymerase chain reaction (qRT-PCR). Histopathological changes showed that, the number of apoptotic cells in the telencephalon of the mouse fetus peaked at 12 HAT and decreased at 24 and 48 HAT, respectively. FX induced the up-regulation of Bax, Trp53 and Casp9 and down-regulated Bcl2 but the expression levels of Fas and Casp8 mRNA remained unchanged. These data suggested that FX induces apoptosis in the developing mouse brain in FX-treated dams. Moreover, the genetic regulatory mechanisms of FX-induced apoptosis are regulated by Bax, Bcl2, Trp53 and Casp9 or can be defined via an intrinsic apoptotic pathway.

_____ _____ ___ / ___ / ___

Student's signature Thesis Advisor's signature