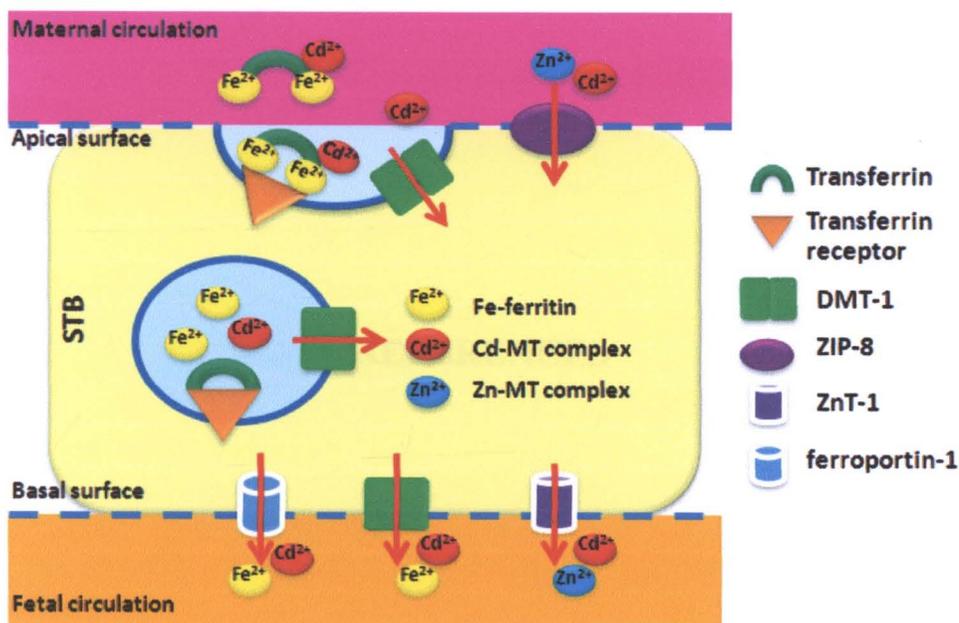


## CHAPTER VI

### CONCLUSION

These findings demonstrated a markedly increased Cd concentration in maternal blood and in placenta of pregnancies living in Cd contaminated area. Therefore, we suggested that pregnant women who exposure of environmental Cd cause of increased of Cd in maternal blood and Cd can be accumulated in placenta which probably mainly mediated by DMT-1 transporter because Cd in maternal blood can be transported to the placenta by competition with Fe for DMT-1 transporter. And, infant has an early life dosage of Cd contamination. In fetal portion of placenta showed that DMT-1 localized in the apical surface of cytoplasm and the basal surface of syncytiotrophoblastic cell, endothelium of fetal capillary which are a component of placental barrier. According to this result supports that DMT-1 acts as endosomal Fe transport and also transports Cd in placental membrane. In addition, we also found DMT-1 localized in Hofbauer cell in fetal portion and decidual cells in maternal portion of placenta. That may be implied that DMT-1 may also transport Fe and Cd in these cells. Under accumulation of Cd, we found DMT-1 protein and mRNA showed upregulated in placental tissue. Hence, Cd can induce DMT-1 expression by facilitate MTF-1 functions within intracellular matrix and resulting in transcription of DMT-1 gene and protein translation. According to these results, we suggest the novel mechanism of placental Cd transport mediated by DMT-1 transporter in STB. Cd, Zn and Fe are competitive transportation with DMT-1. Both Cd and Fe can bind to transferrin in maternal blood and other proteins such as albumin, after that both complexes may influx to placental tissue through transferrin receptor (TfR) or DMT-1 on apical surface of STB that was invaded to endosome by endocytosis. Moreover, Zrt-, Irt-like protein-8 (ZIP-8) can transport Zn and also Cd from maternal blood into STB. Following this pathway, Cd and Fe were exported from endosome by DMT-1 at endosomal membrane. In part of Zn and Cd that accumulated in cytoplasm of STB, these metal ions induced MT synthesis and bounded to MT resulting in Cd-MT and Zn-MT complexes. Whereas Fe bounded to ferritin and it was stored in cytoplasm.

metal ions can induce MT synthesis and bind to MT forming Cd-MT and Zn-MT complexes. Whereas Fe binds to ferritin and it is stored in cytoplasm of STB. Under the condition of highly Cd level in intracellular of STB, these expressed Cd can be transported to fetal circulation by three transporters which present on basal surface of STB. These transporters are ferroportin-1, DMT-1 and Zn transporter-1 (Znt-1). We conclude that DMT-1 expressed in STB may play a role in import and export Cd as shown in figure 46.



**Figure 46 Novel mechanism of placental Cd transport mediated by DMT-1 transporter in STB: DMT-1 was found on apical surface of cytoplasm of STB that can import Cd from maternal blood to cytoplasm of STB by endocytosis became to endosome. DMT-1 was found in endosomal membrane was responsible for export Cd from endosome to intracellular resulting in Cd placental accumulation. After increasing of Cd level in STB, Cd was exported by DMT-1 that was found in basal surface of STB.**

