

## CHAPTER 7

### CONCLUSION AND SUGGESTION

#### 7.1. Conclusions

From this study, we conclude that:

1. Expression 99CGG in the form of RNA is toxic.
2. Tet-on-99CGG-eGFP system could work properly *in vivo*, while Tet-on-11CGG-eGFP lost the expression.
3. Inducible transgenic mouse model Tet-on-99CGG-eGFP/GFA2-rtTA did not work *in vivo*.
4. Inducible transgenic mouse model Tet-on-99CGG-eGFP/PrP-rtTA worked *in vivo*, the expression of transgene in the brain was mainly found in hippocampus, cerebellum and striatum.
5. Bigenic mice Tet-on-99CGG-eGFP/PrP-rtTA gave expression outside the brain, in the kidney.
6. The best founders of each transgenic line were founder 31 for the Tet-on-99CGG-eGFP transgenic mouse, and founder 3 for PrP-rtTA transgenic mouse.
7. Tet-on-99CGG-eGFP/PrP-rtTA mice could mimic neuropathological hallmark of human FXTAS, the formation of ubiquitin-positive intranuclear inclusions. Twelve weeks of dox induction was enough to form the inclusions.

8. Inducible transgenic mouse is a powerful tool to find the possible FXTAS therapies

## 7.2. Suggestions

The suggestions for further studies are:

1. New microinjections have to be established to make new founders for failed founders: the Tet-on-11CGG-eGFP and GFA2-rtTA.
2. FISH (fluorescent in situ hybridization) is necessary to be conducted to observe the presence of CGG aggregates and the disappearance after dox cessation.
3. The presences of other proteins in inclusions such as alpha-beta crystalline, sam68, and lamin A/C by immunohistochemistry need to be checked.
4. The percentages of inclusions need to be counted.
5. Double staining can be done to distinguish between neurons and glial cells by using specific antibody such as GFAP which is specific to glial cells and neuron-specific enolase which is specific for neurons.
6. The real reversibility study can be performed by observing the disappearance of ubiquitin inclusions after cessation of toxic CGG RNA expression (cessation of dox).
7. This research can find possible therapeutic for FXTAS, and this will be useful for genetic counseling for the patient in the future treatment.