

## A Natural Case Like Diabetes Rat as A New Approach on Understanding Alert of Glucose Methabolism

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### INTRODUCTION

Currently, diabetic case as a degenerative disease has widely known that it can be cure by insulin. A remain puzzle is proliferation do not found in rest Beta cells, so insulin injection has to be applied entire life of diabetic patient. So far, there is no diagnostic approach that expresses such of thing which may indicate an early anomaly on glucose metabolism process. The aim of this research to get case model of hyperglycemic rat that has long period in process.

### MATERIAL AND METHOD

In order to understand more about the early indicator of diabetes cases a series of research were done to get a model of chronic diabetes rat. Epigenetic approach is one of option method that may worth to be done other than genetic manipulation using advent technology. In this approach microenvironment manipulation on uterus was done by using valproic acid (VP). Pregnant rats were intra-peritoneal road injected using VP in 250 mg/kg BW of dose at 3 various day of application groups. The born litters were raise up in a natural way, they have been nursery by their mother up to 1 month and later on they were separated in the different cages with standard rat food and water access *ad libitum*. The litters as an object were evaluated for pancreatic endocrine cell development and other parameter such as blood glucose, insulin cell and body weight at interval of 4 week up to 32 week evaluation. Blood glucose was evaluated using enzymatic colorimeter (Glucose kits base/GOD-PAP). Insulin cell was observed by immunostaining method using antibody anti-human insulin that crosses react to rat tissue.

### RESULT AND DISCUSSION

The result showed that the number of litter size decrease significantly ( $3.7 \pm 0.8$ ) compare to those in control ( $10.5 \pm 1.4$ ), while the newborn body weight is increase significantly ( $8.5 \pm 1.1$ ) compare to control ( $5.4 \pm 0.9$ ). This data implies a fact that VA in the dose seem harmful to any-fetuses. Decreasing litter number give an opportunity to the struggles fetus, which have better growth with new born body weight found

much bigger compare to it in control. In the end of study all treated group showed not les then 150 mg/dL blood glucose level and one group reach to  $214.8 \pm 13.8$  mg/dL. Here easily to be understood that all litter became suffering hyperglycemic in adulthood although they look normal in a childhood. In these litter the hyperglycemic process is gradually by the time, as it found in human cases. Furthermore, we also done immunostaing for insulin cell and the result indicated that morphological changes are found in endocrine pancreatic cells immunoreactivity especially for group II, it is found very peal compare to the other group. The immunostaining confirm that the hyperglycemic in these litter is caused by dysfunction of pancreatic beta cells rather than triggered by others.

### CONCLUSION

This study could be conclude that epigenetic approached by influencing microenvironment of uterus will affect pancreatic beta cell, which cause hyperglycemic in adulthood of delivered litter. These litters express a similar sign as it found in human diabetic case, which currently found common in comunity.

### REFERENCES

- [1] Jensen J. 2004. Gene regulatory factors in pancreatic development. *Dev Dyn.* 229:176–200.
- [2] Kurihara Y, Suzuki T, Sakaue M, Murayama O, Miyazaki Y, Onuki A, *et al.* 2014. Valproic acid, a histone deacetylase inhibitor, decreases proliferation of and induces
- [3] Shkreta L, Chabot B. 2015. The RNA splicing response to DNA damage. *Biomolecules* 5:2935-2977.
- [4] Seki Y, Williams L, Vuguin PM, Charron Mj, 2012. Minireview; Epigenetic Programming of Diabetes and Obesity; Animal Models. *Endocrinology.* 153(3):1031-1038. Doi: 10.1210/en.2011-1805