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JURNAL LASALLIAN

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PRECURSOR ADIPOCYTE DEVELOPMENT AS MEDIA OF LIPID METABOLISM

Laurentius J.M. Rumokoy[1.2.)]

[1)]*Department of Nutrition and Feed Science, Faculty of Animal Sciences, University of Sam Ratulangi.* [2)]*Agriculture Laboratory, Faculty of Agriculture, University of De La Salle - Manado*

Abstrak

Penelitian mengenai fungsi jaringan adipose dewasa telah banyak dilakukan dibanding dengan penelitian mengenai perkembangan tahap precursor adiposa. Perkembangan jaringan ini pada tahap neonatus sangat penting dipelajari dengan harapan dapat memberikan kontribusi mengenai diferensiasi dan proliferasinya sehingga dapat dikaitkan dengan upaya mengantisipasi dan menanggulangi permasalahan obesitas dan penyakit degeneratif lain sebagai efek dari pola konsumsi dan fungsi jaringan adiposa.

Manusia dan berbagai jenis ternak mamalia monogastrik memiliki jaringan adiposa yang bertanggung-jawab dalam menyimpan kelebihan energi yang masuk ke dalam tubuh. Jaringan ini telah berkembang sejak masa prenatus. Pada penelitian yang dikerjakan pada hewan Sus crova menunjukkan bahwa jaringan ini masih dapat mengalami proliferasi dan diferensiasi pada masa awal setelah lahir.

Kelebihan energi yang dimaksud adalah keadaan dimana jumlah energi yang masuk kedalam tubuh melalui konsumsi makanan melebihi dari jumlah yang dibutuhkan tubuh. Kelebihan energi yang bersumber dari makanan akan di simpan dalam bentuk lemak dalam sel-sel adiposity. Semakin banyak energi yang tersimpan dalam sel-sel ini, maka akan menampilkan tubuh semakin gemuk pula. Pada mamalia monogastrik jaringan adipose, secara khusus jaringan adipose putih (WAT) terdapat di bawah kulit dan di daerah rongga perut. Namun selain bertugas mengakumulasi lemak sel-sel adipocyte dapat juga mensintesis dan memobilisasi lemak untuk keperluan energi tubuh.

Understanding of Precursor of Adipose tissue

The precursors of adipose tissue are cells, originate from mesenchymateuse pluripotent cells, are able to differentiate and after that will be as mature adipose cells. These cells can be observed under the culture cells. Mesenchymal Stem Cells (MSCs) can be successfully differentiated into adipose cells. Alexander et al. (2009) reported that there are several limitations to using MSCs to obtain adipose cells such as their limited *in vitro* proliferation and differentiation ability. According to Sonoda et al (2008) adipose tissue is suggested to

be an endocrine organ that affects the biological behavior of various cell types through its production of adipokines. In general, adipose tissue consists of mature and immature adipocytes and endothelial cells, but it also has been shown to contain mesenchymal stem cells (MSCs) that produce various mesenchymal cell types, *e.g.* adipocytes, osteoblasts, myocytes, and chondrocytes.

Lipid Metabolism in Adipocyte

Adipocyte is a specific cell that stores excess energy in the form of lipid droplet especially the energy comes from food intake. This function it is connected to the food consummation manner. In the certain circumstance, generally in underdevelopment country, there are people who have low ability to get good quality of food which means they may consume unbalance nutrient.

The lipid metabolism in adipocyte is described briefly in the following scheme.

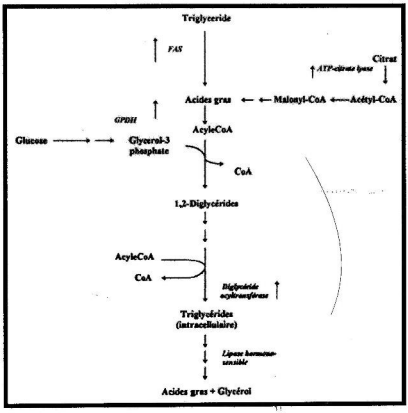

Figure 1. Lipid Metabolism Pathway in Adipocyte Cell

The restriction of ingredients sources in their area minimize their possibility to accomplish their balance nutrients needs. In other hand people may eat cheap food to avoid hunger without care the importance of nutrient proportion. Unfortunately cheap food has generally high content of carbohydrate or lipids only compared to the others of high protein sources of food. However, people who come from wealthy family often forget the balance nutrients in their food. Consequently they consume energy from food in excess.

What is the consequence of energy intake in excess? For example the habit to take food that contains high level of carbohydrate, lipids and protein will be transformed in lipids and accumulated in WAT. When the adipocyte store the over energy intake, then the adipocyte will be over loaded and become "balloon" which lead to the obesity and increasing of body weight (Rumokoy, 2010).

Gregoire (2001) underlined that obesity is a disorder that results from excess white adipose tissue (WAT) and is a major risk factor for type 2 diabetes (NIDDM) and cardiovascular disease. A dramatic increase in the incidence of both obesity and NIDDM is currently observed in Western countries, but so far strategies to combat excess body weight and/or WAT mass have not been effective in most individuals. If body has insufficient energy from food, the adipocyte will hydrolyze the triglyceride and deliver fatty acid (acid grass) to be used as combustible in body cells. If this situation is occurred in a period, then the body become meagre because the lipids in. Therefore white adipose tissue (WAT) has an important role in energy balance of body.

Based on the adipocyte role in lipid metabolism for maintain the energy supply from food, it is certain to discuss some techniques to experiences the investigation of preadipocyte development. Other than lipid metabolism function, Alexander et al. (2009) reported that adipose tissue can be used as filler material for reconstructive and cosmetic surgeries such as breast reconstruction for mastectomy patients. However, transplantation of autologous adipose tissue is unfavorable for numerous reasons such as "poor revascularization, graft shrinkage, and volume loss, often resulting in a poor cosmetic outcome" (Hillel et al. 2009).

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Development of Precursor of White Adipose Tissue (WAT)

There is several factors influence the precursor's development. Breed, age, and media substances are included in these factors. In other hand hormone of insulin like growth factors (IGFs) is used as the early stage marker because for its sensitivity in the preadipocyte development process. This type of hormone inhibit the multiplication which can permit the capture of the tardif marker of mature adipose function to accumulate, synthesize or hydrolyze the lipids according to body needs.

The adipocyte differentiation and proliferation derives largely from studies with preadipose cell lines in culture, notably the C3H10T1/2 and NIH 3T3 fibroblastic cell lines and the 3T3-L1 and 3T3-F442A preadipocyte lines. This study can be conducted in defined media (Rumokoy, 2010) which is generally based on the DME/F12 as basal medium supplemented with some antibiotics like penicillin and streptomycine. The others supplements are FBS (fetal bovine serum), vitamins insulin, nystatin, cortisol and L-glutamine. Treatment of multipotent C3H10T1/2 cells with 5-azacytidine gives rise to cells committed to the myogenic, adipogenic, or chondrogenic lineages. This is consistent with

the view that the adipose lineage arises from the same multipotent stem cell population of mesodermal origin that gives rise to the muscle and cartilage lineages (Huang et al., 2009).

When appropriately induced with hormonal agents (*e.g.* glucocorticoid, insulin-like growth factor-1, and cyclic AMP or factors that mimic these agents) committed preadipocytes differentiate into adipocytes in culture. A large body of evidence shows that differentiation of 3T3 preadipocytes faithfully mimics the *in vivo* process giving rise to cells that possess virtually all of the biochemical and morphological characteristics of adipocytes. Following hormonal induction, confluent preadipocytes undergo mitotic clonal expansion, become growth arrested, and then coordinately express adipocyte gene products.

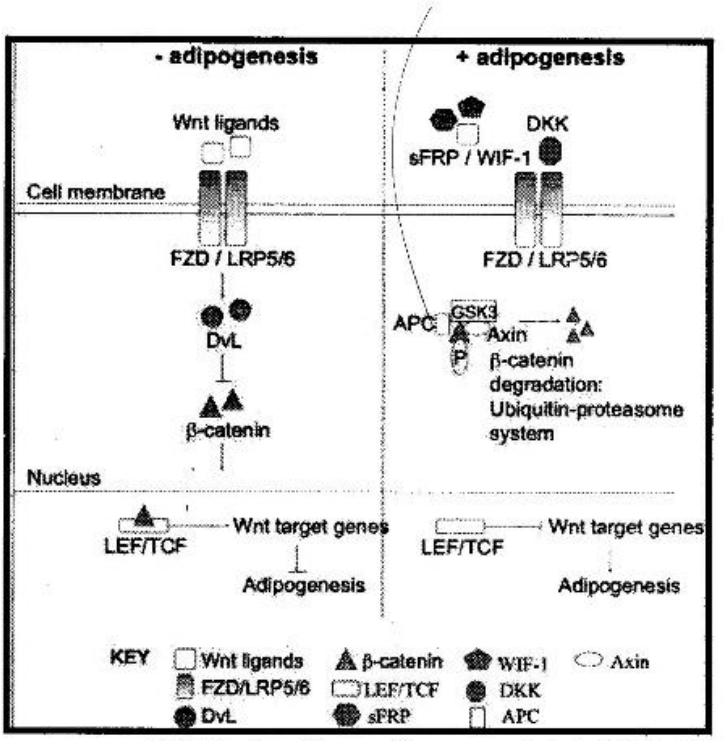

Figure 2. The presence of Wnt signaling, adipogenesis is inhibited through β-catenin-mediated expression of Wnt target genes (Choi et al., 2010)

Observation Technique

Rumokoy (1995) used the *compteur-β* to realized a measurement of ADN replication of preadipocyte cultures that were incorporated with the radioactive ^{3}H marker. The cultures were used also to learn the lipogenesis activities at differentiated cells. The

understanding of adipocyte differentiation and proliferation derives largely from studies with preadipose cell lines in culture, notably the C3H10T1/2 and NIH 3T3 fibroblastic cell lines and the 3T3-L1 and 3T3-F442A preadipocyte lines. *Defined media* of adipose cell culture generally based on the DME/F12 as basal medium supplemented with some antibiotics like penicillin, streptomycine.

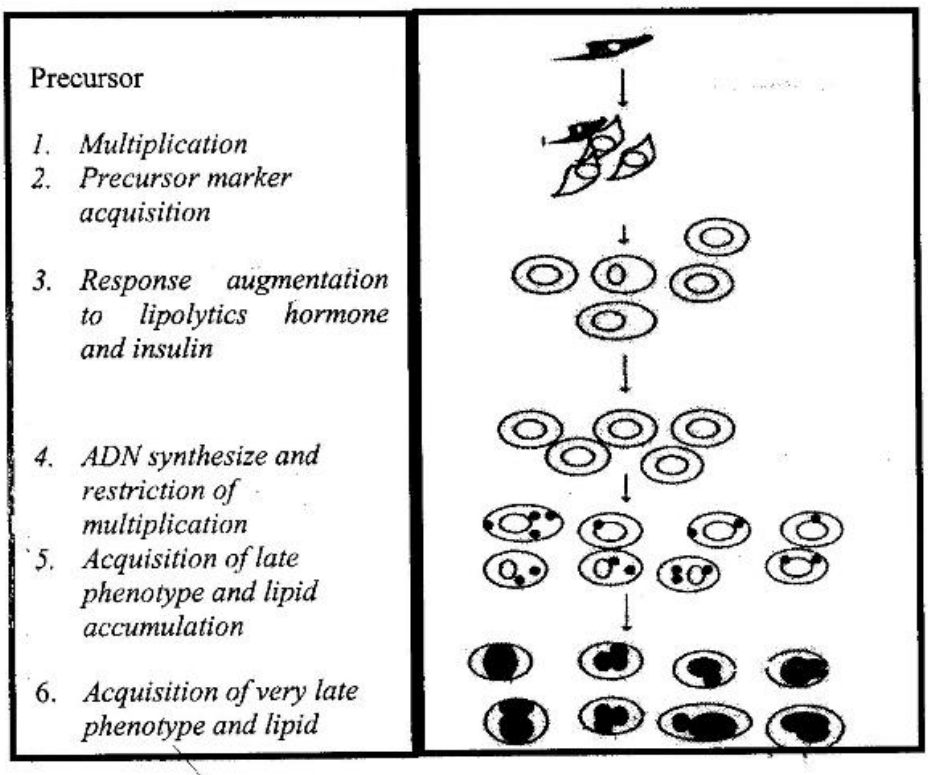

Figure 3. Observation of Adipogenesis Development

The others supplements in media culture for precursor development observation are FBS (*fetal bovine serum*), vitamins, insulin, nystatin, cortisol and L-glutamine. Treatment of multipotent C3H10T1/2 cells with 5-azacytidine gives rise to cells committed to the myogenic, adipogenic, or chondrogenic lineages. This is consistent with the view that the adipose lineage arises from the same multipotent stem cell population of mesodermal origin that gives rise to the muscle and cartilage lineages. When appropriately induced with hormonal agents (*e.g.* glucocorticoid, insulin-like growth factor-1, and cyclic AMP or factors that mimic these agents) committed preadipocytes differentiate into adipocytes in culture. A large body of evidence shows that differentiation of 3T3 preadipocytes faithfully mimics the *in vivo* process giving rise to cells that possess virtually all of the biochemical and morphological characteristics of adipocytes. Following hormonal induction, confluent

preadipocytes undergo mitotic clonal expansion, become growth arrested, and then coordinately express adipocyte gene products (Camp et al 1997).

References

Alexander T. H., S. Varghese, J. Petsche, M.J. Shamblott, Jennifer H. 2009. Elisseeff. Embryonic Germ Cells Are Capable of Adipogenic Differentiation In Vitro and In Vivo. *Tissue Engineering Part A. March 2009, 15(3): 479-486.*

Camp H.S. and S.R. Tafuri. 1997. Regulation of peroxisome proliferator-activated receptor γ activity by mitogen-activated protein kinase. *J. Biol. Chem.* **272:** 10811-10816

Choi J.H., J.M. Gimble, K. Lee, K.G. Marra, P. Rubin, J.J. Yoo, G. Vunjak-Novakovic, and D.L. Kaplan. 2010. Adipose Tissue Engineering for Soft Tissue Regeneration. *Tissue Engineering. Part B. Volume 16, Number 4, 2010.*

Gregoire F.M. 2001. Adipocyte Differentiation: From Fibroblast to Endocrine Cell *Experimental Biology and Medicine* 2001, 226:997-1002.

Huanga H., T. Songa, X.L.L. Hua, Q. Hea, M. Liua, M.D.L., and Q-Q. Tanga. 2009. BMP signaling pathway is required for commitment of C3H10T1/2 pluripotent stem cells to the adipocyte lineage. *Journal PNAS.* 106 (31) : 12670 -12675.

Rumokoy L.J.M. Etude de la différenciation de cellules précurseur adipocytaires chez le porc. 1995. Ecole National Supérieure Agronomique – Institut National de la Recherche Agronomique. Rennes. France.

Rumokoy L.J.M. 2010. Identifikasi Replikasi ADN Dalam Proliferasi Seluler Prekursor Adiposa Postnatal. Seminar Nasional. Hasil Penelitian Multitahun. Dikti Kemendiknas. Jakarta.

Sonoda E, S. Aoki, K. Uchihashi, H. Soejima, S. Kanaji, K. Izuhara, S. Satoh, N. Fujitani, H. Sugihara, and S. Toda. 2008. A New Organotypic Culture of Adipose Tissue Fragments Maintains Viable Mature Adipocytes for a Long Term, Together with Development of Immature Adipocytes and Mesenchymal Stem Cell-Like Cells. *Endocrinology 149(10):4794–4798.*