} ¡

triacylglycerol β
-oxidation .
20

,

.[1] 1970 Edwin Krebs
cAMP Protein Kinase A(PKA)
lipase

.[2] 20 b-
cAMP
PKA Hormone sensitive lipase(HSL)
.[3]

cAMP pathway,
cGMP pathway,

AMPK pathway TNF-a MAPK
pathway HSL
(Figure 1).
.
3 , ,
feeding .

1. cAMP pathway

.
HSL cAMP
(, , , ACTH)
, .

cAMP .
.
phosphodiesterase(PDE)
cAMP
.[4] HSL
.[5]

Figure 1. Lipolysis pathway in adipocytes

2. cGMP pathway

1981
Atrial natriuretic peptide(ANP)
natriuretic peptide
. ANP
.

2000 Sengenes [7] Natriuretic peptide cGMP pathway
.
cAMP HSL
PDE-3B cAMP PDE-3B
cGMP PDE-3B
. ANP
cGMP-dependent protein kinase(PKG) . PKG HSL .

ANP
ANP cGMP
.[8]

3. MAPK pathway

TNF-a
. TNF-α Knok-out
.[9]
Rosiglitazone 3T3-L1 TNF-a
.
2002 Zhang [10] TNF-a
Mitogen Activated protein Kinases(MAPK)
. TNF-a
TNF-a MAPK pathway
PDE-3B cAMP
PKA .

4. AMPK pathway

AMP-activated protein kinase(AMPK) pathway . AMPK energy sensor

AMP/ATP AMPK .
AMPK ATP
ATP .[11]
AMPK leptin
adiponectin .
2003 Yin [12] AMPK
isoproterenol
. AMPK α-subunit Adenovirus
isoproterenol
AMPK
. AMPK Hormone sensitive lipase Ser-565
.

1.
(
), , , ,
, .[13]

α-2 β .
Gs protein adenylyl cycclase
cAMP . α-2 Gi
Gi adenylyl cyclase
ATP cAMP . cAMP
PKA HSL
.

α-2
.[14] , isoproterenol 0.1-1μM
α-2
. ,
isoproterenol
. isoproterenol
.[15-16]
.[17]

2.

β-

α-2

. Bulow [6]

re-esterification

, Enoksson

Nitropruside [18]

(Figure 2).

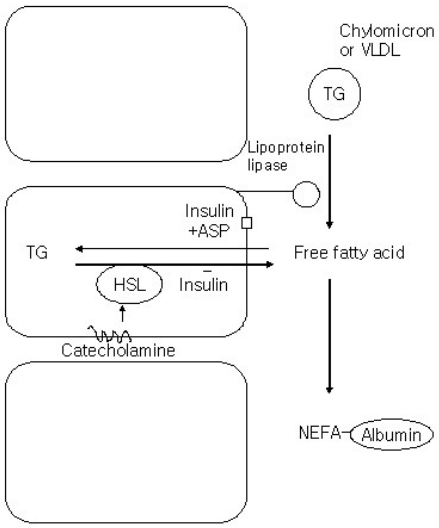

Figure 2. Regulation of fatty acid movement in and out of adipose tissue

pH [19] [20-21]

3.

, ,

15

epinephrine

87

[22] [23-24]

15 4

4

[25]

adenylyl cyclase

48-72

cAMP phosphodiesterase 72

[26]

[27]

7

[28]

[29]

[30]

.

1. Birnbaum MJ. Lipolysis: more than just a lipase. J Cell Biol 2003;161(6):1011-2.
2. Corbin JD, Reimann EM, Walsh DA, Krebs EG. Activation of adipose tissue lipase by skeletal muscle cyclic adenosine 3',5'- monophosphate-stimulated protein kinase. J Biol Chem 1970;245(18):4849-51.
3. Garton AJ, Campbell DG, Cohen P, Yeaman SJ. Primary structure of the site on bovine hormone-sensitive lipase phosphorylated by cyclic AMP-dependent protein kinase. FEBS Lett 1988;229(1):68-72.
4. Degerman E, Smith CJ, Tornqvist H, Vasta V, Belfrage P, Manganiello VC. Evidence that insulin and isoprenaline activate the cGMP-inhibited low-Km cAMP phosphodiesterase in rat fat cells by phosphorylation. Proc Natl Acad Sci U S A 1990 ;87(2):533-7.
5. Stralfors P, Honnor RC. Insulin-induced dephosphorylation of hormone-sensitive lipase. Correlation with lipolysis and cAMP-dependent protein kinase activity. Eur J Biochem. 1989;182(2):379-85.
6. Bulow J, Madsen J. Influence of blood flow on fatty acid mobilization form lipolytically active adipose tissue. Pflugers Arch 1981;390(2):169-74.
7. Sengenes C, Berlan M, De Glisezinski I, Lafontan M, Galitzky J. Natriuretic peptides: a new lipolytic pathway in human adipocytes. FASEB J 2000;14(10):1345-51.
8. Moro C, Crampes F, Sengenes C, De Glisezinski I, Galitzky J, Thalamas C, et al. Atrial natriuretic peptide contributes to physiological control of lipid mobilization in humans. FASEB J 2004;18(7):908-10.
9. Uysal KT, Wiesbrock SM, Marino MW, Hotamisligil GS. Protection from obesity- induced insulin resistance in mice lacking TNF-alpha function. Nature 1997;389(6651):610-4.
10. Zhang HH, Halbleib M, Ahmad F, Manganiello VC, Greenberg AS. Tumor necrosis factor-alpha stimulates lipolysis in differentiated human adipocytes through activation of extracellular signal-related kinase and elevation of intracellular cAMP. Diabetes 2002 ;51(10):2929-35.
11. Kemp BE, Mitchelhill KI, Stapleton D, Michell BJ, Chen ZP, Witters LA. Dealing with energy demand: the AMP-activated protein kinase. Trends Biochem Sci 1999;24(1):22-5.
12. Yin W, Mu J, Birnbaum MJ. Role of AMP-activated protein kinase in cyclic AMP-dependent lipolysis In 3T3-L1 adipocytes. J Biol Chem 2003;278(44):43074-80.
13. Vernon RG. Effects of diet on lipolysis and its regulation. Proc Nutr Soc 1992;51: 397-408.
14. Mauriege P, Galitzky J, Berlan M, Lafontan M. Heterogeneous distribution of beta and alpha-2 adrenoceptor binding sites in human fat cells from various fat deposits: functional consequences. Eur J Clin Invest 1987;17(2):156-65.
15. Van Harmelen V, Lonnqvist F, Thorne A, Wennlund A, Large V, Reynisdottir S, et al. Noradrenaline-induced lipolysis in isolated mesenteric, omental and subcutaneous adipocytes from obese subjects. Int J Obes Relat Metab Disord 1997;21(11):972-9.
16. Monzon JR, Basile R, Heneghan S, Udupi V, Green A. Lipolysis in adipocytes isolated from deep and superficial subcutaneous adipose tissue. Obes Res 2002;10(4): 266-9.
17. Dax EM, Partilla JS, Gregerman RI. Mechanism of the age-related decrease of epinephrine-stimulated lipolysis in isolated rat adipocytes: beta-adrenergic receptor binding, adenylate cyclase activity, and cyclic AMP accumulation. J Lipid Res 1981 ;22(6):934-43.
18. Enoksson S, Nordenstrom J, Bolinder J, Arner P. Influence of local blood flow on glycerol levels in human adipose tissue. Int J Obes Relat Metab Disord 1995 ;19(5):350-4.
19. Belfrage E, Hjemdahl P, Fredholm BB. Metabolic effects of blood flow restriction in adipose tissue.Acta Physiol Scand 1979;105(2):222-7.
20. Bulow J. Subcutaneous adipose tissue blood flow and triacylglycerol-mobilization during prolonged exercise in dogs. Pflugers Arch 1982;392(3):230-4.
21. Hjemdahl P, Fredholm BB. Influence of adipose tissue blood flow on the lipolytic response to circulating noradrenaline at normal and reduced pH. Acta Physiol Scand 1976;98(1):74-9.
22. Andrews J, Kashiwagi A, Verso MA, Vasquez B, Howard BV, Foley JE. Effects of four-day fast on triglyceride mobilization in human adipocytes. Int J Obes 1984;8(4):355-6.
23. Arner P, Ostman J. Changes in the adrenergic control and the rate of lipolysis of isolated human adipose tissue during fasting and after re-feeding. Acta Med Scand 1976;200(4):273-79.
24. Wolfe RR, Peters EJ, Klein S, Holland OB, Rosenblatt J, Gary

H Jr. Effect of short-term fasting on lipolytic responsiveness in normal and obese human subjects. Am J Physiol 1987;252(2 Pt 1):E189-96.

25. Jensen MD, Haymond MW, Gerich JE, Cryer PE, Miles JM. Lipolysis during fasting. Decreased suppression by insulin and increased stimulation by epinephrine. Clin Invest 1987;79(1):207-13.
26. Osegawa M, Makino H, Kanatsuka A, Suzuki T, Hashimoto N, Yoshida S. Modulation of insulin action by fasting: a study using a phosphodiesterase activation system in rat fat cells. Horm Metab Res 1985;17(12):633-6.
27. Arner P, Engfeldt P, Ostman J. Relationship between lipolysis, cyclic AMP, and fat-cell size in human adipose tissue during fasting and in diabetes mellitus. Metabolism 1979;28(3):198-209.
28. Kather H, Wieland E, Scheurer A, Vogel G, Wildenberg U, Joost C. Influences of variation in total energy intake and dietary composition on regulation of fat cell lipolysis in ideal-weight subjects. J Clin Invest 1987;80(2):566-72.
29. Tepperman HM, Dewitt J, Tepperman J. Effect of a high fat diet on rat adipocyte lipolysis: responses to epinephrine, forskolin, methylisobutylxanthine, dibutyryl cyclic AMP, insulin and nicotinic acid. J Nutr 1986;116(10):1984-91.
30. Kettelhut IC, Foss MC, Migliorini RH. Lipolysis and the antilipolytic effect of insulin in adipocytes from rats adapted to a high-protein diet. Metabolism 1985;34(1):69-73.