PATHOPROFILE

Type 2 Diabetes

What Went Wrong with Insulin?

AUTHOR
KIMIA SOROURI

ARTIST
ELLEN LIANG

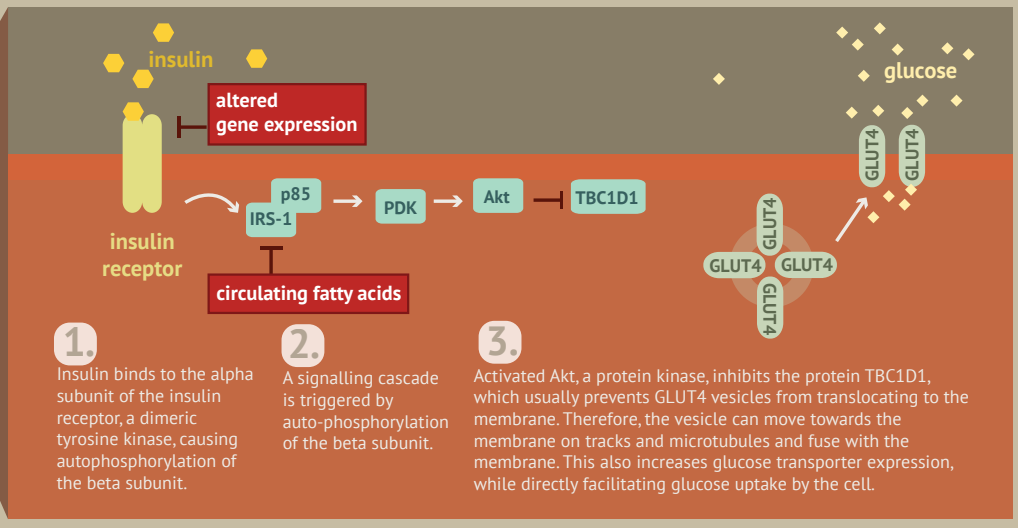
Type 2 diabetes mellitus, or non-insulin dependent diabetes mellitus (NIDDM), is a pathological condition characterized by an inadequate response to insulin, a hormone responsible for regulating blood glucose levels. NIDDM comprises of 90-95% of all cases of diabetes.[1]

Normally, insulin is released by pancreatic beta cells into the bloodstream, acting on receptors found in tissues such as skeletal muscle and the liver.[2] The binding of insulin to insulin receptors stimulates glucose uptake into cells and the storage of glucose as glycogen (glycogenesis).[3] Evidence suggests that genetic mutations may increase susceptibility to NIDDM. Specifically, a reduction of insulin receptor gene expression may be partly responsible for insulin resistance in NIDDM.[4] While molecular pathways are not very well understood, evidence suggests high blood fatty acid levels may inhibit insulin receptor substrates (IRS) in the insulin-signalling cascade.[4]

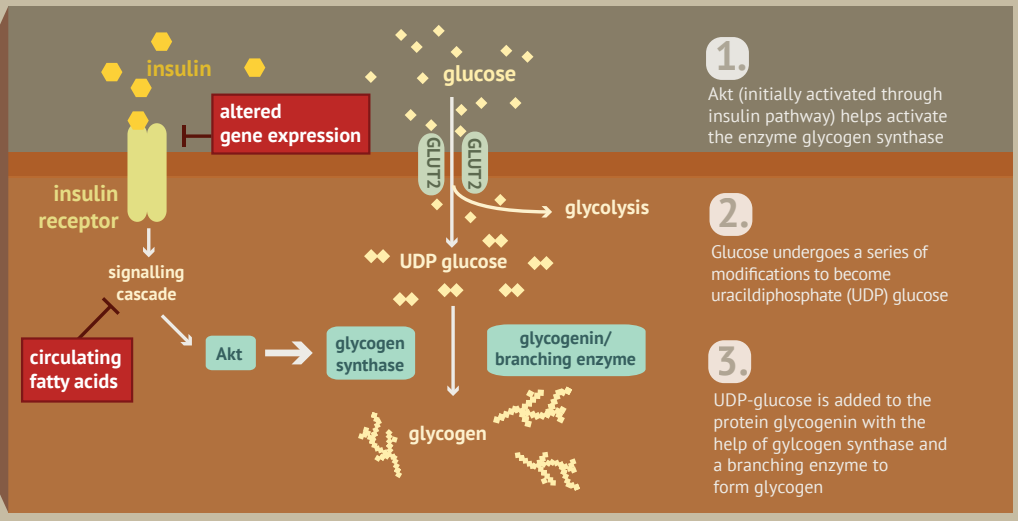
The isoforms of the glucose transporters (GLUTs) primarily involved in diabetes are GLUT2 and GLUT4.[5] There is currently limited data linking specific genes to diabetic pathology, warranting for genome-wide analyses.[6] Despite an increasing prevalence of diabetes, there is encouraging evidence supporting the ability of exercise to reduce insulin resistance.[7]

The following two diagrams depict aspects of the normal insulin signalling pathway in myocytes and hepatocytes, respectively. Potential disruptions to any components of this pathway can increase the risk of NIDDM, and are highlighted in red.[3]

MUSCLE
MYOCYTES



LIVER
HEPATOCYTES



1. American Diabetes Association. Diagnosis and classification of Diabetes Mellitus. Diabetes Care. 2012 Dec 20;36(Supplement_1):S67–S74.
2. Seino S, Shibasaki T, Minami K. Pancreatic -cell signaling: toward better understanding of diabetes and its treatment. Proceedings of the Japan Academy, Series B. 2010;86(6):563–77.
3. Gropper SS. Advanced nutrition and human metabolism. 6th Ed. Belmont, OH: Cengage Learning; 2012.
4. Saini V. Molecular mechanisms of insulin resistance in type 2 diabetes mellitus. World J Diabetes. 2010 Jul 15;1(3):68–75.
5. Schinner S, Scherbaum WA, Bornstein SR, Barthel A. Molecular mechanisms of insulin resistance. Diabetic Medicine. 2005 Jun;22(6):674–82.
6. McCarthy MI, Zeggini E. Genome-wide association studies in type 2 diabetes. Curr Diab Rep. 2009;9:164–171.
7. Steinberg GR, O'Neill HM, Dzamko NL, Galic S, Naim T, Koopman R, et al. Whole body deletion of AMP-activated protein kinase {beta}2 reduces muscle AMPK activity and exercise capacity. J Biol Chem. 2010 Nov 26;285(48):37198–209.