Non-Insulin Dependent Diabetes Mellitus

(NIDDM)

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Period 6
SBS11QHG-02

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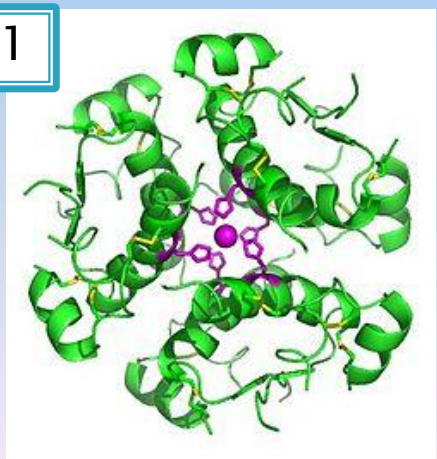

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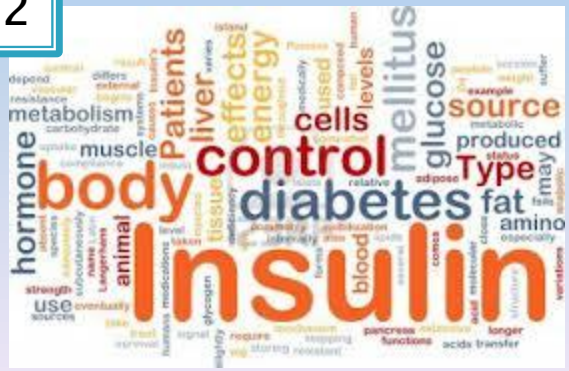

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Physiology

- Non-Mendelian Polygenic Inheritance
- Most common form of Diabetes, 80-90 percent of all cases
- Also known as Diabetes Type 2
- 7% of cases share both Type 1 and Type 2 symptoms
- Late onset, but higher obesity rates have increased its prevalence among teenagers and young adults
- As of 2011, it has been recorded that 8.3% of the United States is suffering from NIDDM
- Can affect all cells of the body
- Inadequate insulin receptors do not allow cells to uptake glucose, though in most cases, this process is only slowed
- Malfunctions affect the liver, pancreas, and blood vessels
- Increased chance of heart attacks and strokes from high glucose levels in the blood

Molecular Cause

- NIDDM is a polygenic disease; it can be caused by a multitude of genes, including *CAPN10*, *GCGR*, and *INSR*.
- There is no clear inheritance pattern, and manifestation is also dependent on environmental factors, such as weight
- *INSR* is located on Chromosome 19; loci 19p13.3-p13.2
- A substitution of the methionine amino acid to isoleucine at codon 119 adds a random start codon in the translation of the insulin receptor
- This would lead to a fault in its insulin binding domain, resulting in a receptor that would not properly signal the glucose transporters to work

Pathway

- MAPK pathway: communicates information from the insulin receptor to the DNA of the cell
- Lipid, Protein, and Glycogen Synthesis
- Inhibition of Gluconeogenesis: stops the making of more glucose from non-carbohydrate substances such as amino acids

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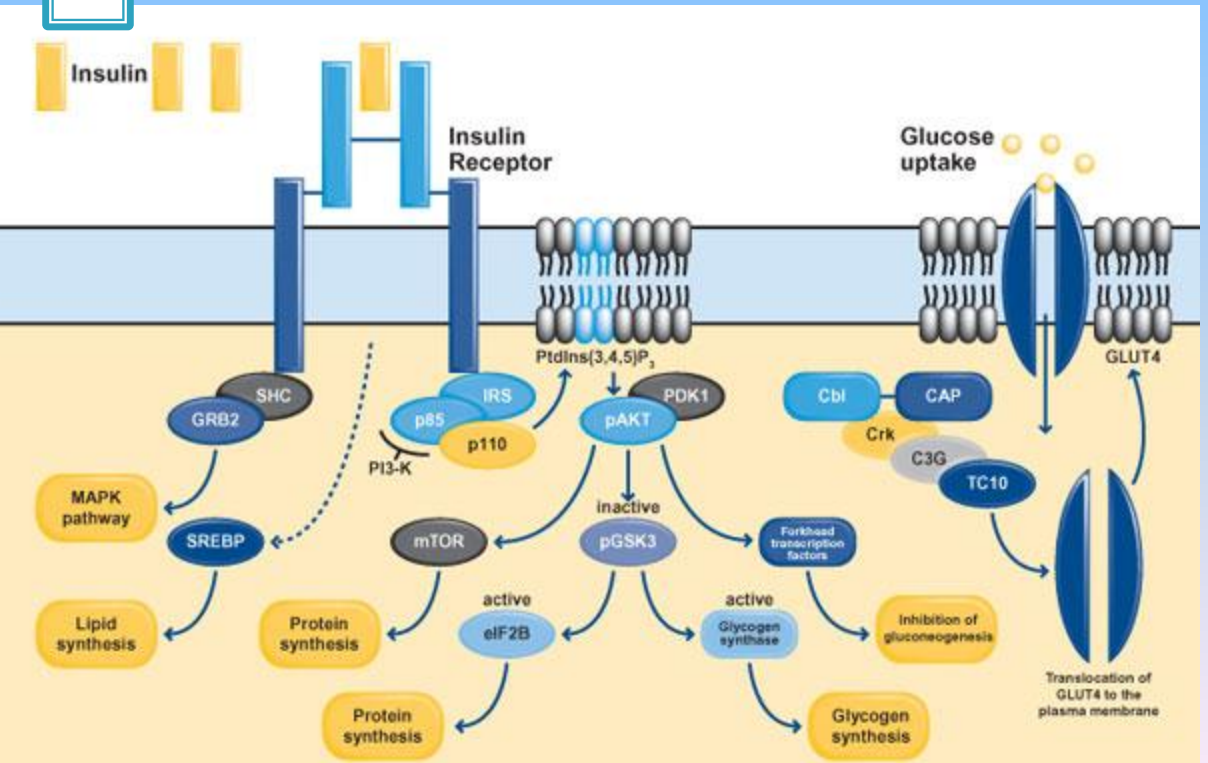

- Phosphorylation of Cbl-CAP complex, which in turn interacts with protein Crk, which is associated with the Rho-family guanine nucleotide exchange factor C3G, which activates the GTP-binding protein family TC10, which finally promotes the GLUT4 glucose transporter to the plasma membrane

Treatments

- Modification of Lifestyle:
  - Foods of soluble fibers or low glycemic indexes
  - Increased exercise, preferably taking walks, swimming, and cycling
- Medicinal Intake
  - Intake of hypoglycemic drugs, which increases insulin action
  - Drugs such as metformin can lower glucose levels by 20%
  - Long-acting insulin injections; high doses may have negative side effects
- Future Cures
  - Artificial organs; a glucose monitoring device with an insulin delivery tube to be a pancreas or usage of stem cells to recreate a pancreas
  - Cell transplantations rather than whole organs

Proposal

- GLUT 1 transporter found in most cells
- GLUT 2 transporter found in liver, beta cells, hypothalamus, basolateral membrane of small intestine
- GLUT 3 transporter found in neurons, placenta, and testes
- GLUT 4 transporter found in skeletal and cardiac muscle and body fat, the insulin activated protein
- GLUT 5 found in mucosal surface in small intestine and sperm

Plan:

- Transfer any, preferably GLUT 1, to replace the dysfunction of GLUT 4
- Artificially create proteins if receptors are deformed instead
- Manual insertion of a phosphate group (PO_4^{3-}) to induce phosphorylation of Cbl-CAP complex
- Depending on the type of defect, transcriptional activators can be replaced with artificial or imported ones

Limits:

- The transportation of the man-made products is a problem. Artificial lipid vesicles have been seen to interact with a variety of mammalian cells, such as blood cells and spleen cells. But once the package is brought into the cell, the function of the artificial protein is up to chance. This may work well with one or two cells, but when the whole body is involved, the probability of success gets increasingly less; the injection of the artificial products also do not last forever
- Phosphorous is needed for phosphorylation. But putting in phosphates is merely providing the materials for the activators to use. It promotes transcriptional activity, but a defective protein will remain defective. Furthermore, the random distribution of the phosphates throughout the cell would induce not just the transcriptional activators that is targed

References

Images:

- Fig 1: https://upload.wikimedia.org/wikipedia/commons/thumb/0/0d/InsulinHexamer.jpg/250px-InsulinHexamer.jpg
- Fig 2: http://anthonycolpo.com/insulin%E2%80%A6an-undeserved-bad-reputation/
- Fig 3: http://www.diabetesone.net/insulin/
- Fig 4: http://healthwise-everythinghealth.blogspot.com/2012/03/what-is-diabetes.html
- Fig 5: http://www.foods-healing-power.com/type-2-diabetes-symptoms.html
- Fig 6: http://www.abcam.com/index.html?pageconfig=resource&rid=10602
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- http://www.medscape.com/viewarticle/550547
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Content

Physiology

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Molecular Cause

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