Familial hypercholesterolemia: Lipid Levels Gone Wrong

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SBS11QHG pd 3
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Physiology

Fig. 1

Fig. 2

Fig. 3

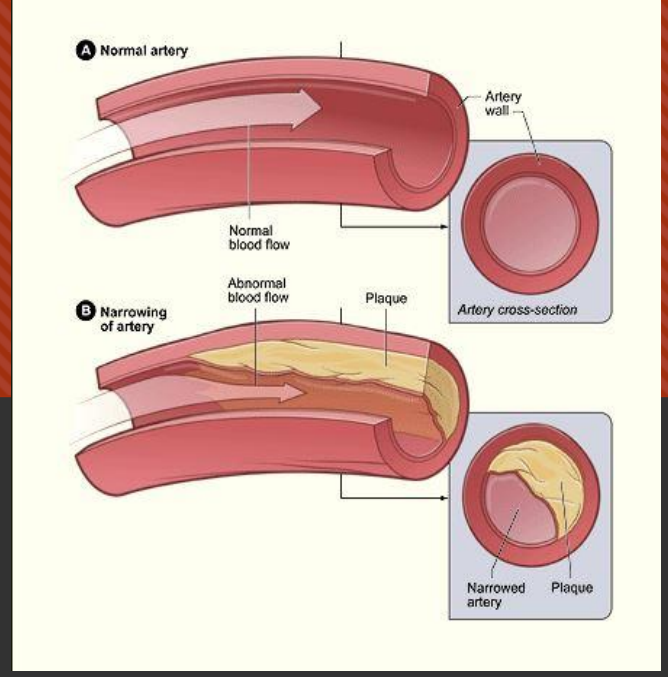

Fig. 4

- Accounts for less than 5% of people with hypercholesterolemia, or high cholesterol levels.
- Causes abnormally high levels of cholesterol in the blood (over 300 mg/dL total, over 200 mg/dL of LDL)
- High amount of LDL causes xanthomas and causes atherosclerosis
- Targets the LDL Receptor only, decreasing efficiency
- Onset at birth
- Common side effect is coronary heart disease

Molecular Cause

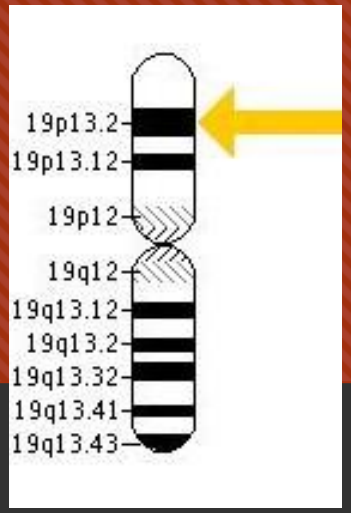

Fig 5

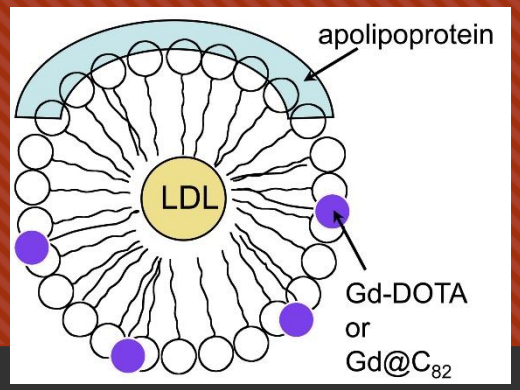

Fig 6

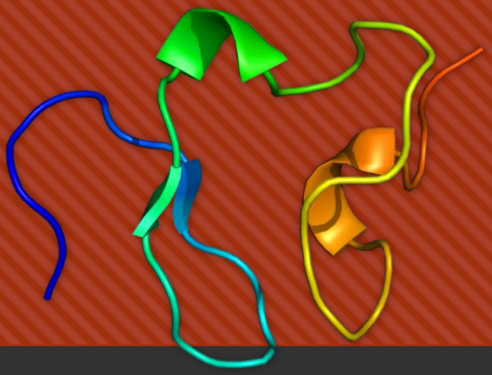

Fig 7

- LDLR is a receptor that controls amounts of LDL in the blood by endocytosis
- Transmitted Autosomal Dominantly
- Mutations involve the LDLR gene, which is on chromosome 19 location 19p13.2
- Mutations could range from large insertions, deletions, etc. Any negative changes in the could cause this disorder
- The mutation causes a change in the LDLR, which cannot remove LDL as efficiently
- Because of this inefficiency, more LDL is produced from IDL, increasing levels even higher
- Hepatic clearance also reduced.
- The inefficiency results in abnormally high levels of LDL

Current Treatments

- At the moment, there is no cure
- Treatment revolves around reducing the risk of coronary heart disease
- First step is change in diet & continued exercise
- Drugs are also viable, most commonly statins. Others, however, are available
- In severe cases, apheresis can be used
- Last resort is through liver transplantation, which is the organ responsible for LDLR.
- Other methods to cure are being looked into…

Proposed Cure/Limits

- Much research has/is being done towards stem cells for use in curing
- Two types of stem cells: adult and embryonic
- Through differentiation of embryonic stem cells, hepatic cells can be cultured.
- In 1995, JA Rhim demonstrated through transplanting nude hepatocytic genes from healthy mice to mice with diseased livers.
- Gave room for the idea of transplantation as a basis of competitive liver regeneration.
- After differentiation and removal of undifferentiated cells, grafting of healthy cells to diseased liver is the proposed cure.
- Idea comes from skin grafting and transplantation already in use

Content References

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- National Human Genome Research Institute (NHGRI). (2011). Learning About Familial Hypercholesterolemia. Retrieved from http://www.genome.gov/25520184
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- Cell Therapy for the diseased liver: from stem cell biology to novel models for hepatotropic human pathogens. In *PubMed.* Nicolas Brezillon, et al., NLM. NIH, 2008. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2562180/

Image References

- In order of appearance:
- Corneal arcus
  http://dro.hs.columbia.edu/corarcus.htm
- Xanthomas on knees
  http://dermatlas.med.jhmi.edu/image/xanthoma_1_020310
- Xanthelasma
  http://dermatlas.med.jhmi.edu/image/Xanthelasma_1_030926
- Atherosclerosis
  http://www.nhlbi.nih.gov/health/health-topics/topics/atherosclerosis/
- Chromosome 19
  http://ghr.nlm.nih.gov/gene/LDLR
- LDL model
  http://www.sas.upenn.edu/~midre/research.htm
- LDLR model
  http://en.wikipedia.org/wiki/LDL_receptor