

## Chapter 16

10/21 8:00 am

### Lipids, Lipoproteins and Apolipoproteins

- ⊕ Most cholesterol is transported in a lipoprotein, made up of a mycelle-like lipid sphere with apolipoproteins embedded. The apolipoproteins determine the properties of the lipoproteins (e.g. what receptor to bind etc). Also make them soluble.
- ⊕ Chylomicrons and VLDLs are lipoproteins that mainly transport TGs, HDL and LDL focus on cholesterol.
- ⊕ Three pathways
  - Exogenous (from intestine) } employ ApoB
  - Endogenous (from liver) } }
  - Reverse (back to liver) } employs ApoA
- ⊕ Dyslipidemic triad:  $\uparrow$ VLDL,  $\uparrow$ LDL,  $\downarrow$ HDL
- ⊕ The quintet of causes for high LDL:
  - ⊕ Apolipoprotein of LDL can't bind receptor
  - ⊕ LDLR is defective
  - ⊕ ARH (anchor for LDLR) is defective
  - ⊕ ABCG5/8 cholesterol transporter w/ gain of function: too much out of liver and in from intestine
  - ⊕ Upregulation of PCSK9 reduces # of LDLR
- ⊕ HDL picks up cholesterol from the tissues, especially from macrophages. It might also have antibacterial functions.

Chapter 17  
10/21 11:00 am

## Metabolic strategies in cancer

As previously discussed, the Warburg effect is the tendency of cancers to derive most their ATP from glycolysis despite the fact that  $O_2$  is available. The higher the glucose metabolism, the faster the cancer grows.

Glycolysis can be upregulated by having more glycolytic enzymes ~~or~~ b/c of defective TCA. At the same time, fast growing cancers downregulate gluconeogenic enzymes.

Fast growing tumors need building blocks (some provided by glycolysis intermediates). DNA/RNA synthesis is upregulated, so is FA synthesis while  $\beta$ -oxidation is repressed. This makes sense from the building block perspective. Also, ketogenesis is repressed. Synthesis of cholesterol is enhanced. Since both FA and cholesterol synthesis are running full speed, the PPP must be upregulated as well to provide all the NADPH needed. Overall, a lot of glucose is needed.

Glucose is the preferred energy source b/c the cancer can "rely" on a steady supply from the body.

Cancer cells often use Hexokinase II for the reaction  $\text{glucose} \rightarrow \text{G6P}$ . When bound to mitochondria, HK II is no longer inhibited by G6P and is right at the source for ATP. Usually, only one half of HK II is active, but cancer cells have them both active at the same time. HK II also opposes cell death.

Since glycolysis produces a lot of lactate, cancer cells have lactate channels. 3-Bromopyruvate can use those channels to get into the cell and bind to HK II and  $O_2$   $\Phi$ as machinery in the mitochondria. This kills all energy supply and thereby the cancer cell. Reduced and eradicated tumors in 19 out of 19 rats.