Session 19 - Gluconeogenesis

"New" synthesis of glucose from noncarbohydrate precursors

**Problem:** Brain, Renal Medulla, Erythrocytes, Testis

- Require glucose as their primary metabolic fuel
- Brain uses 120 g / day
- Whole body uses 160 g / day
- Total [glucose + glycogen] reserves = 190 g → Not much!

**Solution:** GNG = efficient way to manufacture glucose to meet steady state needs

GNG happens in (a) Liver and (b) Renal Cortex

**Example:** Cori Cycle

\[ [G]_{\text{blood}} = 5\text{mM}; [L]_{\text{blood}} = 9\text{mM} \]

GNG in liver builds lactate up into glucose which is returned to muscle

**Precursors to Glucose (GNG Substrates)**

1. Lactate
2. Ala
3. Glu
4. Asp
5. Odd Chain FA
6. Met, Ile, Val
7. Glycerol
8. (Ribose) (via Pentose Phosphate Pathway)

We'll map on detailed GNG Pathway (next page)

This actually is a carbohydrate but it can get converted to glucose via GNG

**Pathway Overview**

- Looks like Glycolysis in Reverse
- But must bypass glycolysis' irreversible steps (→ )

**Sites of Pathway Control**

- Liver has GK

This is our goal (end here)

GNG specific steps

Steps common to glycolysis and GNG

**Nature invented enzymes to allow GNG:**

It's complicated

GNG precursors (1→8) enter pathway

CO₂

AcCoA

TCA

GNG precursors (1→8) enter pathway
Mechanisms of GNG Enzymes

1.) G6Pase

2.) F16BPase

3.) PC

4.) Phospho Enol Pyruvate Carboxylase (PEP-CK)
   -- The same CO₂ is lost that was put on by PC
   -- PEP-CK can be cytosolic, mitochondrial, or both (depending on species)
   -- If mitochondrial, PEP can freely go into cytoplasm via transporter to participate in GNG

Pathway Details

- Liver or renal cortex cell
- G6Pase
- Glycerol
- Glucose transporter

Key GNG enzymes
Numbers are on key on previous page – e.g., 1 = lactate

-- Going from L → G is like a ship going up river through locks on a canal
-- Energy input is needed