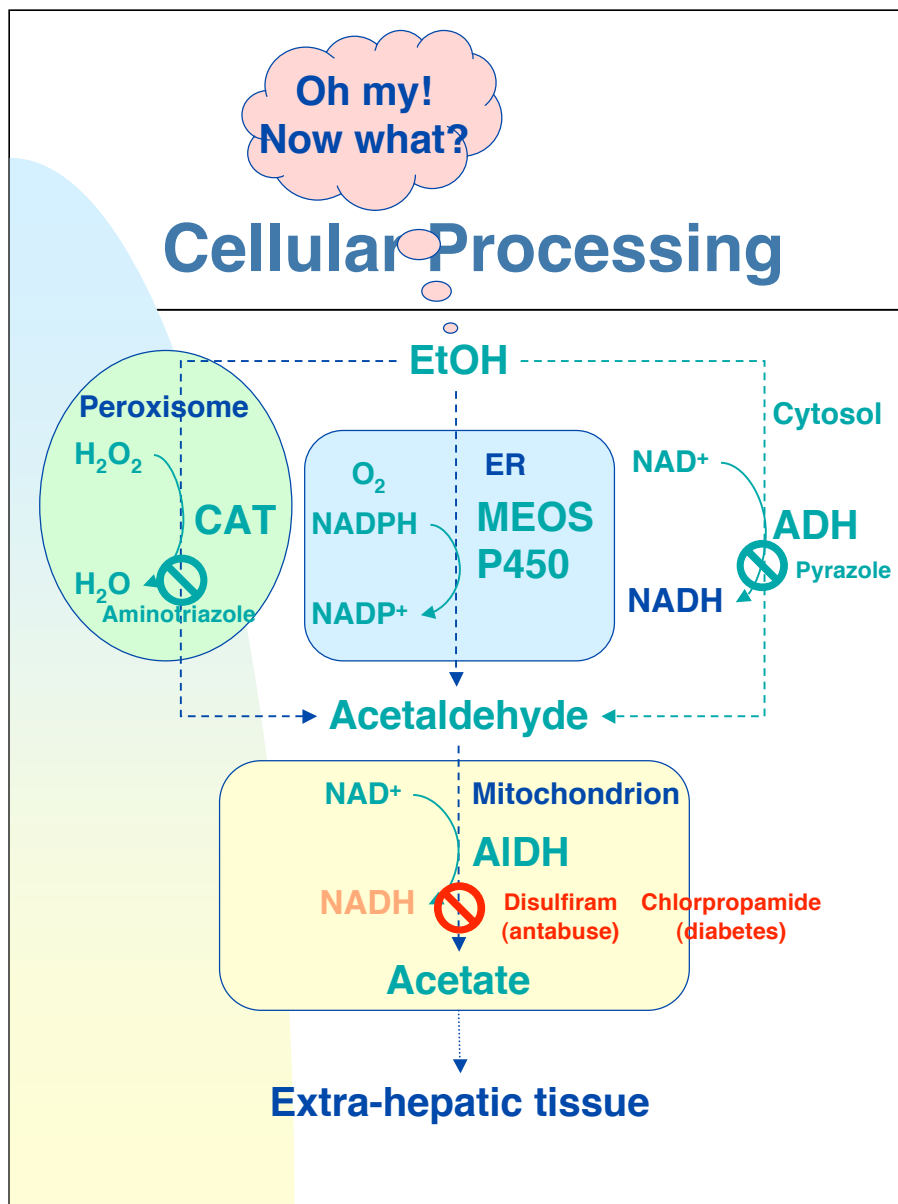


Alcohol Metabolism

- Cellular processing
- Pathway perturbations
- Malate-aspartate shuttle
- Glycerol-3-phosphate shuttle

Eric Niederhoffer
SIU-SOM



EtOH: ethanol

ADH: alcohol dehydrogenase; genetic polymorphisms lower response to EtOH

NAD⁺/NADH: nicotinamide adenine dinucleotide

CAT: catalase

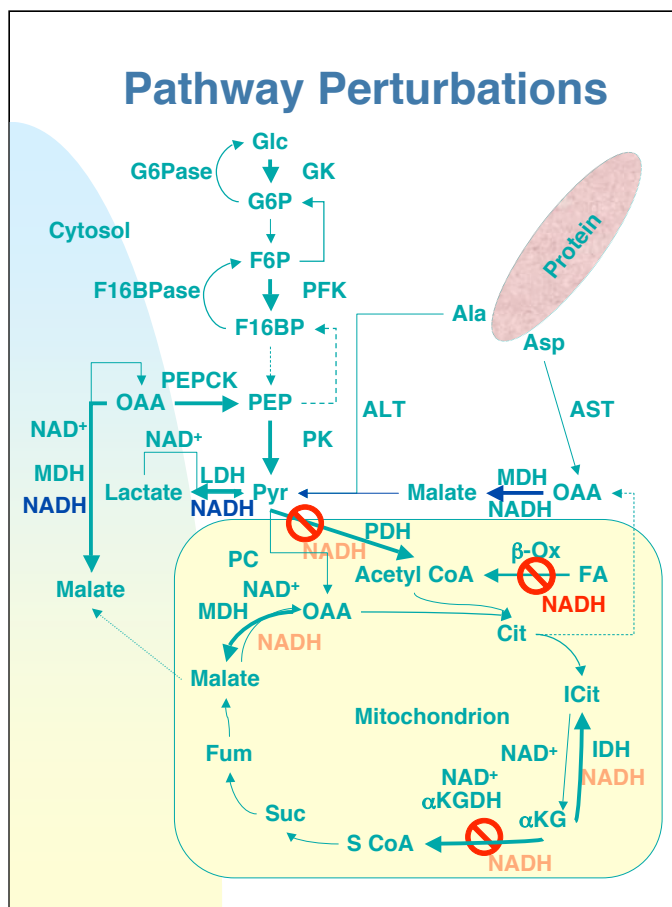
MEOS: microsomal ethanol-oxidizing system

P450: cytochrome P450

NADP⁺/NADPH: nicotinamide adenine dinucleotide phosphate

AIDH: aldehyde dehydrogenase; ~50% ethnic Chinese lack gene

Thiamine is consumed during hepatic metabolism of EtOH, hypothalamus responds to thiamine deficiency by ordering increase in hepatic ADH activity that gives enhanced EtOH degradation.



Glc: glucose

G6P: glucose-6-phosphate

PFK: phosphofruktokinase

PEP: phosphoenolpyruvate

Pyr: pyruvate

Cit: citrate

IDH: isocitrate dehydrogenase

NAD⁺/NADH: nicotinamide adenine dinucleotide

αKGDH: α-ketoglutarate dehydrogenase

S CoA: succinyl coenzyme A

Fum: fumarate

OAA: oxaloacetate

LDH: lactate dehydrogenase

PEPCK: phosphoenolpyruvate carboxykinase

F16BPase: fructose-1,6-bisphosphatase

Ala: alanine

ALT: alanine transaminase

GK: glucokinase

F6P: fructose-6-phosphate

F16BP: fructose-1,6-bisphosphate

PK: pyruvate kinase

PDH: pyruvate dehydrogenase

ICit: isocitrate

αKG: α-ketoglutarate

Suc: succinate

MDH: malate dehydrogenase

PC: pyruvate carboxylase

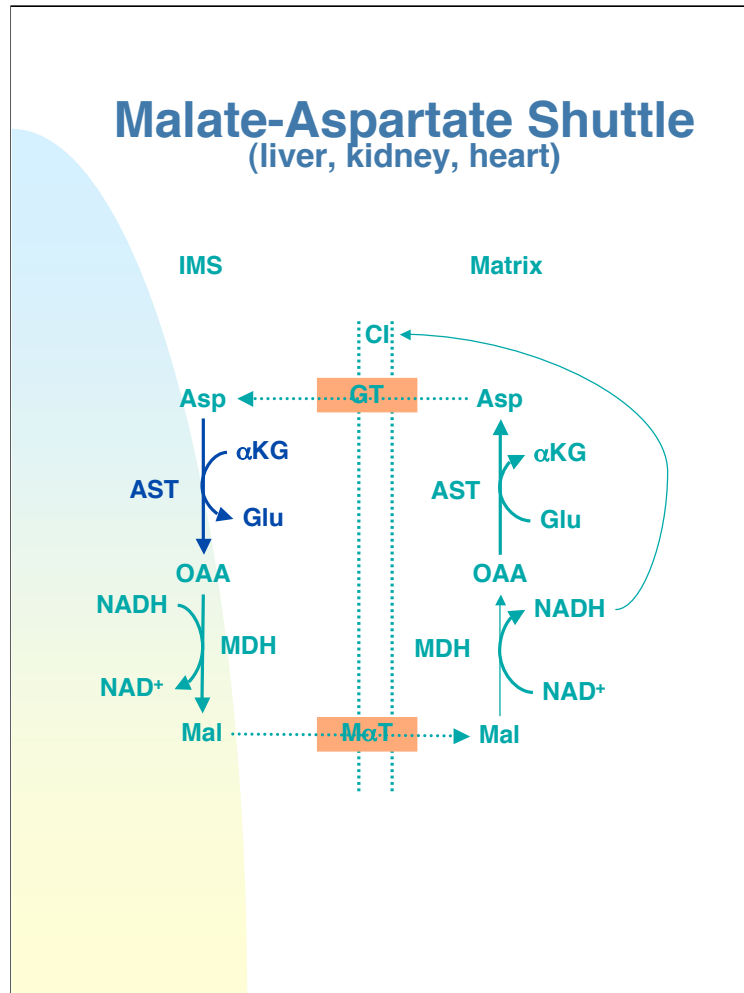
G6Pase: glucose-6-phosphatase

Asp: aspartate

AST: aspartate transaminase

Recall NADH/NAD⁺ controls PDH activity also through action of PDH kinase and phosphatase; PDH inhibition leads to increased [lactate], [pyruvate], [alanine].

Abrupt halt of EtOH can lead to alcoholic ketoacidosis.



IMS: inner membrane space; pores in outer mitochondrial membrane allow passage of many molecules from cytosol

OAA: oxaloacetate

NAD⁺/NADH: nicotinamide adenine dinucleotide

MDH: malate dehydrogenase

Mal: malate

MaT: malate- α -ketoglutarate transporter, dicarboxylate carrier

CI: complex I

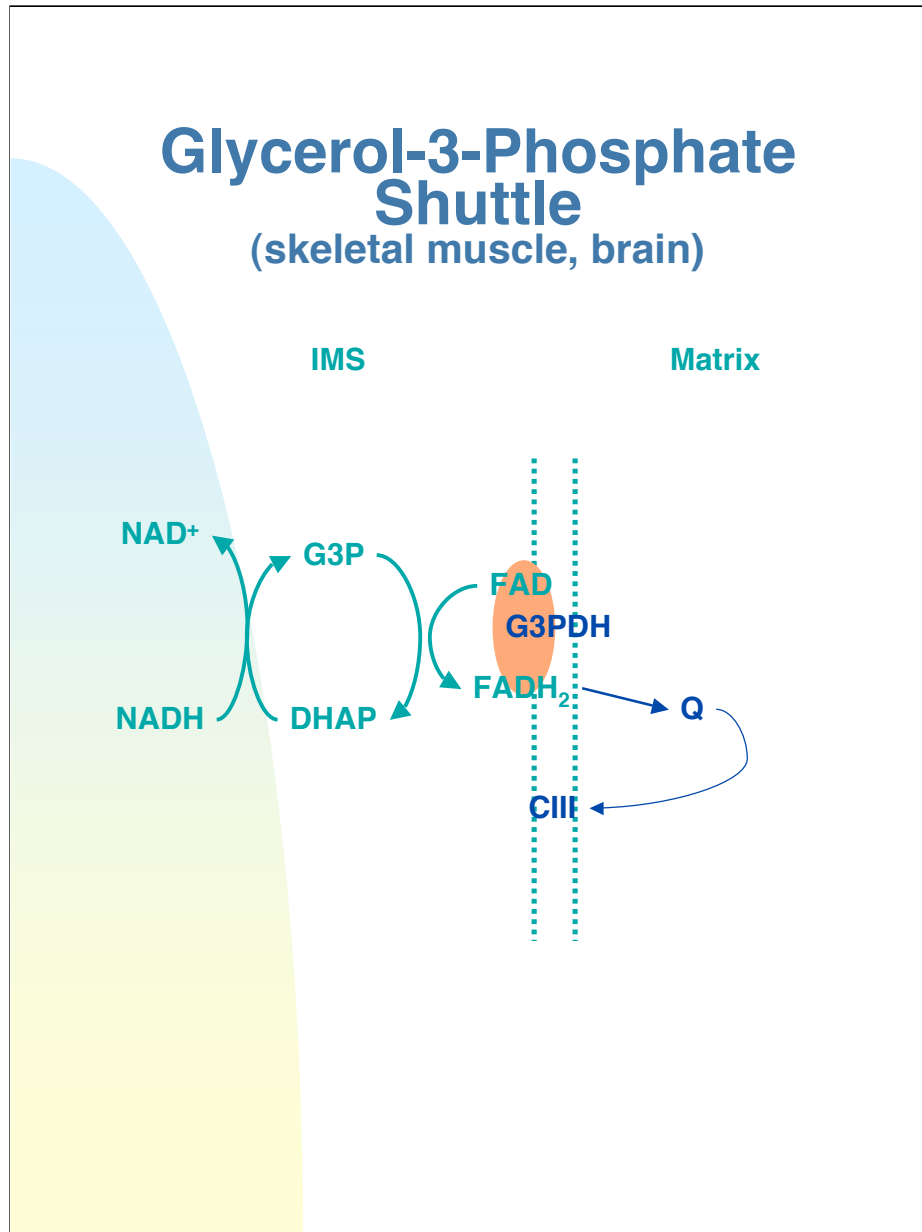
Glu: glutamate

AST: aspartate transaminase

α KG: α -ketoglutarate

Asp: aspartate

GT: glutamate transporter, glutamate-aspartate carrier



IMS: inner membrane space; pores in outer mitochondrial membrane allow passage of many molecules from cytosol

G3PDH: glycerol-3-phosphate dehydrogenase

NAD^+/NADH : nicotinamide adenine dinucleotide

DHAP: dihydroxyacetone phosphate

FAD/FADH_2 : flavin adenine dinucleotide

Q: ubiquinone

CIII: complex III

Review Questions

- **How is ethanol detoxified (enzymes, cofactors, products, location)?**
- **Which metabolic pathways are affected by alcohol-derived NADH (enzymes, metabolites)?**
- **How does the cell process NADH?**