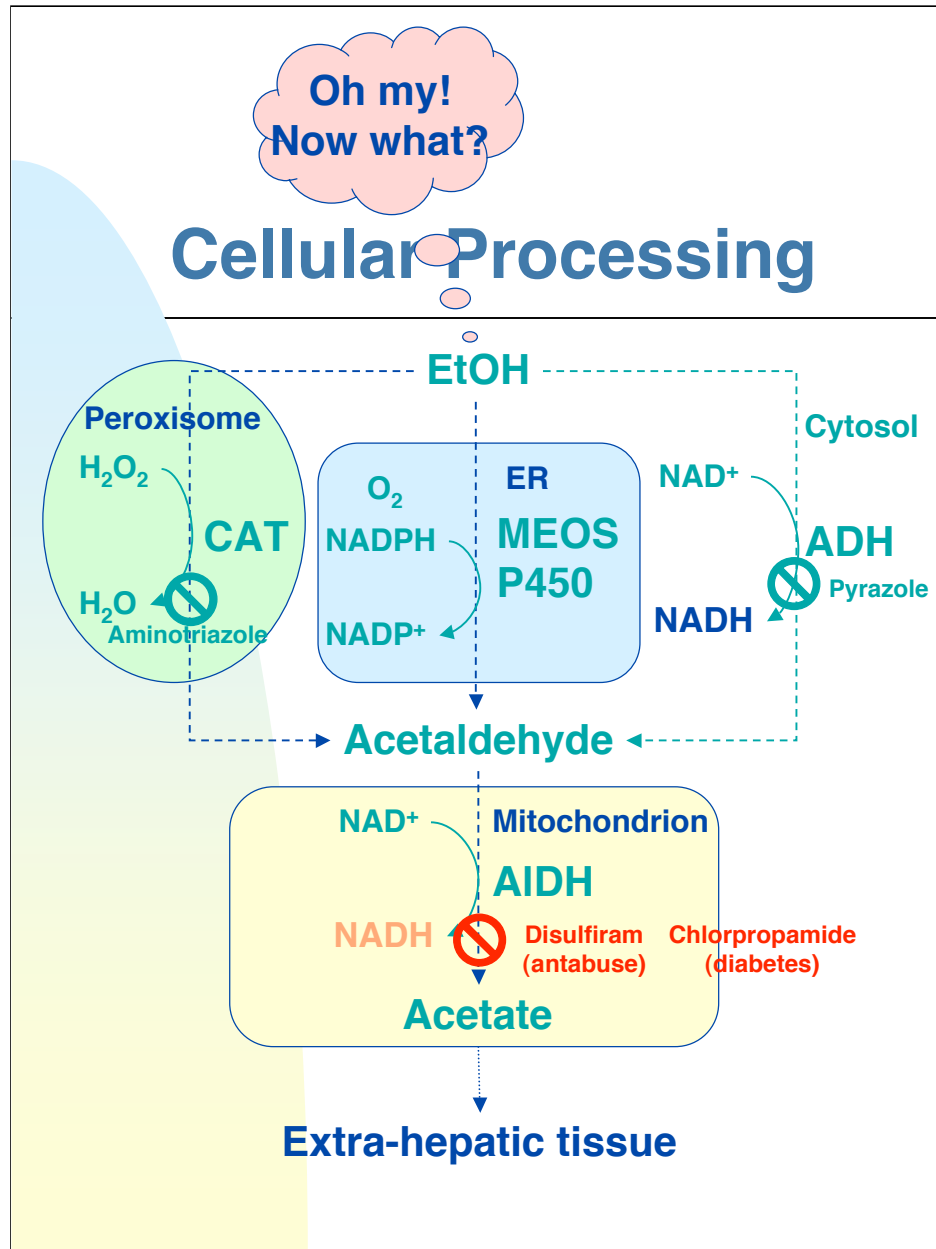


Alcohol Metabolism

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

Eric Niederhoffer
SIU-SOM



EtOH: ethanol

NAD⁺/NADH: nicotinamide adenine dinucleotide

ADH: alcohol dehydrogenase; genetic polymorphisms lower response to EtOH; ~80% of processing

CAT: catalase; ~5% of processing

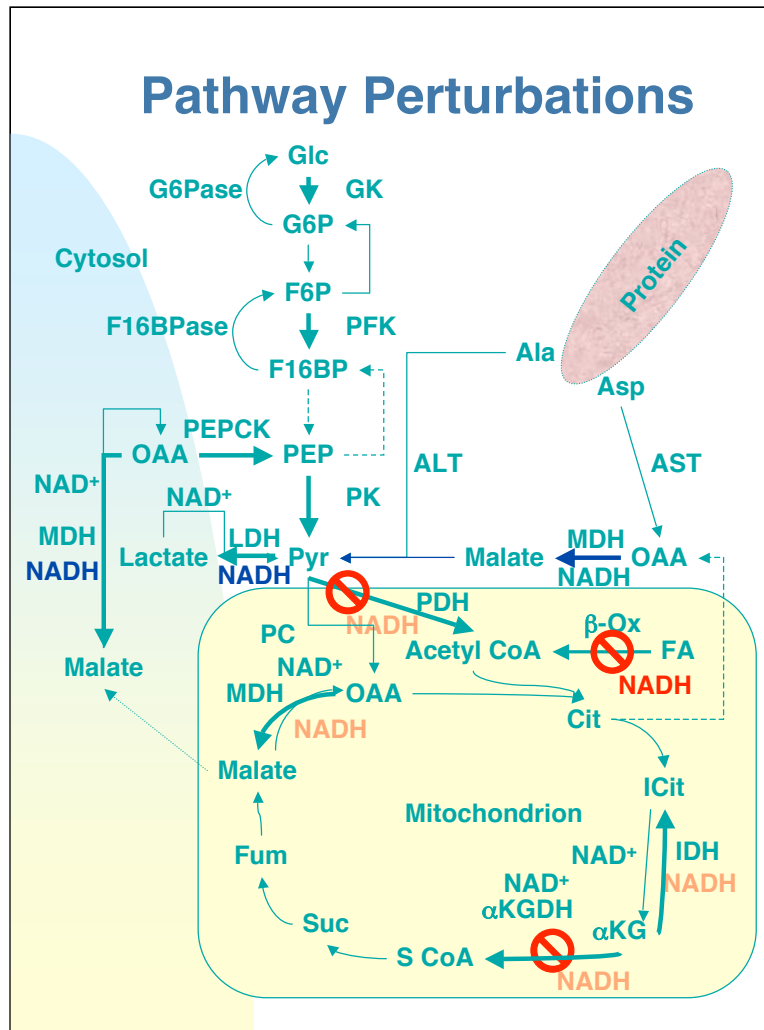
P450: cytochrome P450

MEOS: microsomal ethanol-oxidizing system; ~15% of processing

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.



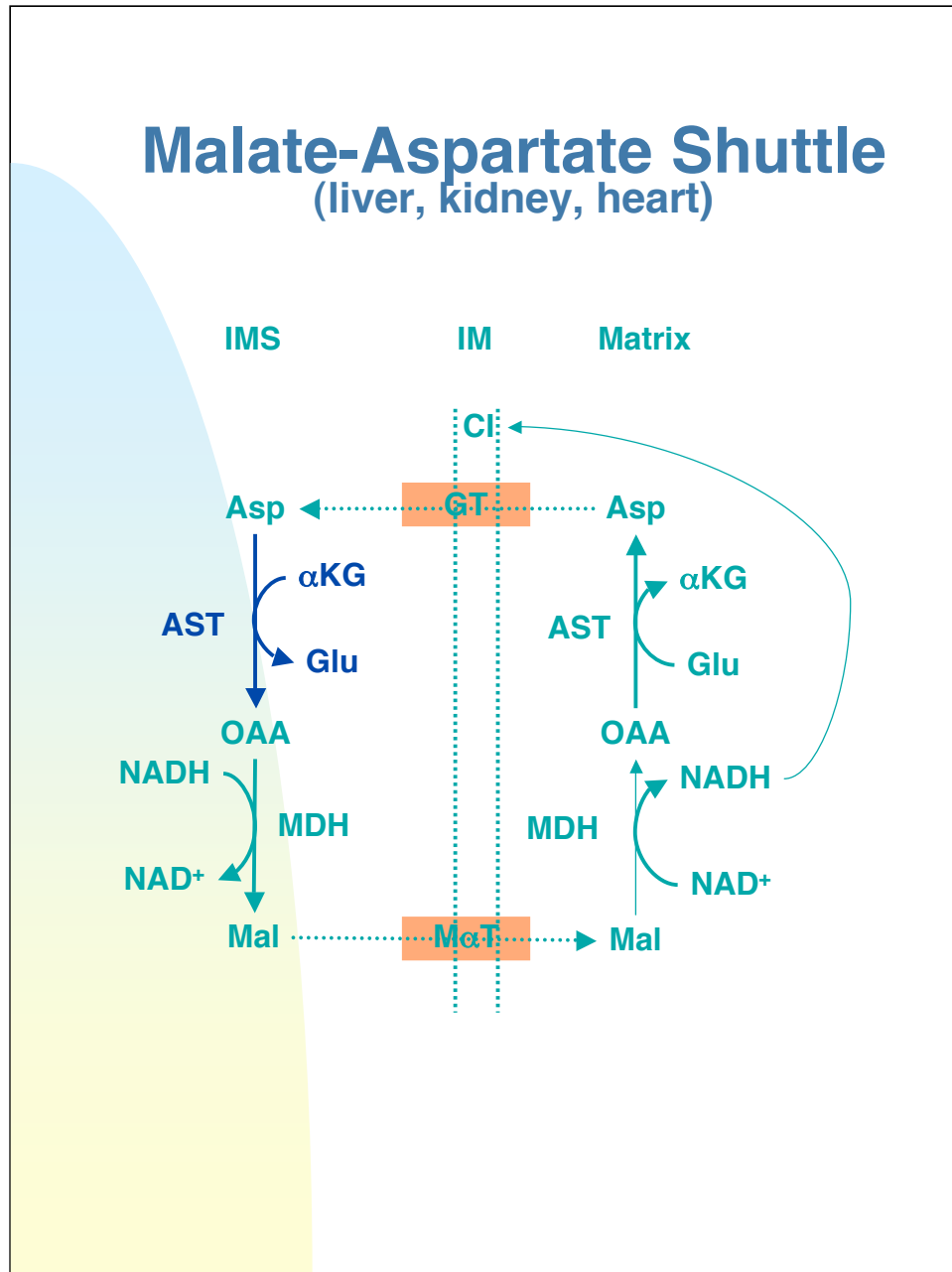
Glc: glucose	GK: glucokinase	G6P: glucose-6-phosphate
F6P: fructose-6-phosphate	PFK: phosphofruktokinase	F16BP: fructose-1,6-bisphosphate
PEP: phosphoenolpyruvate	PK: pyruvate kinase	Pyr: pyruvate
PDH: pyruvate dehydrogenase	Cit: citrate	ICit: isocitrate
IDH: isocitrate dehydrogenase	alpha-KG: alpha-ketoglutarate	
NAD⁺/NADH: nicotinamide adenine dinucleotide	alpha-KGDH: alpha-ketoglutarate dehydrogenase	
S CoA: succinyl coenzyme A	Suc: succinate	Fum: fumarate
MDH: malate dehydrogenase	OAA: oxaloacetate	PC: pyruvate carboxylase
LDH: lactate dehydrogenase	PEPCK: phosphoenolpyruvate carboxykinase	
F16BPase: fructose-1,6-bisphosphatase	G6Pase: glucose-6-phosphatase	
Ala: alanine	Asp: aspartate	ALT: alanine transaminase
AST: aspartate transaminase		

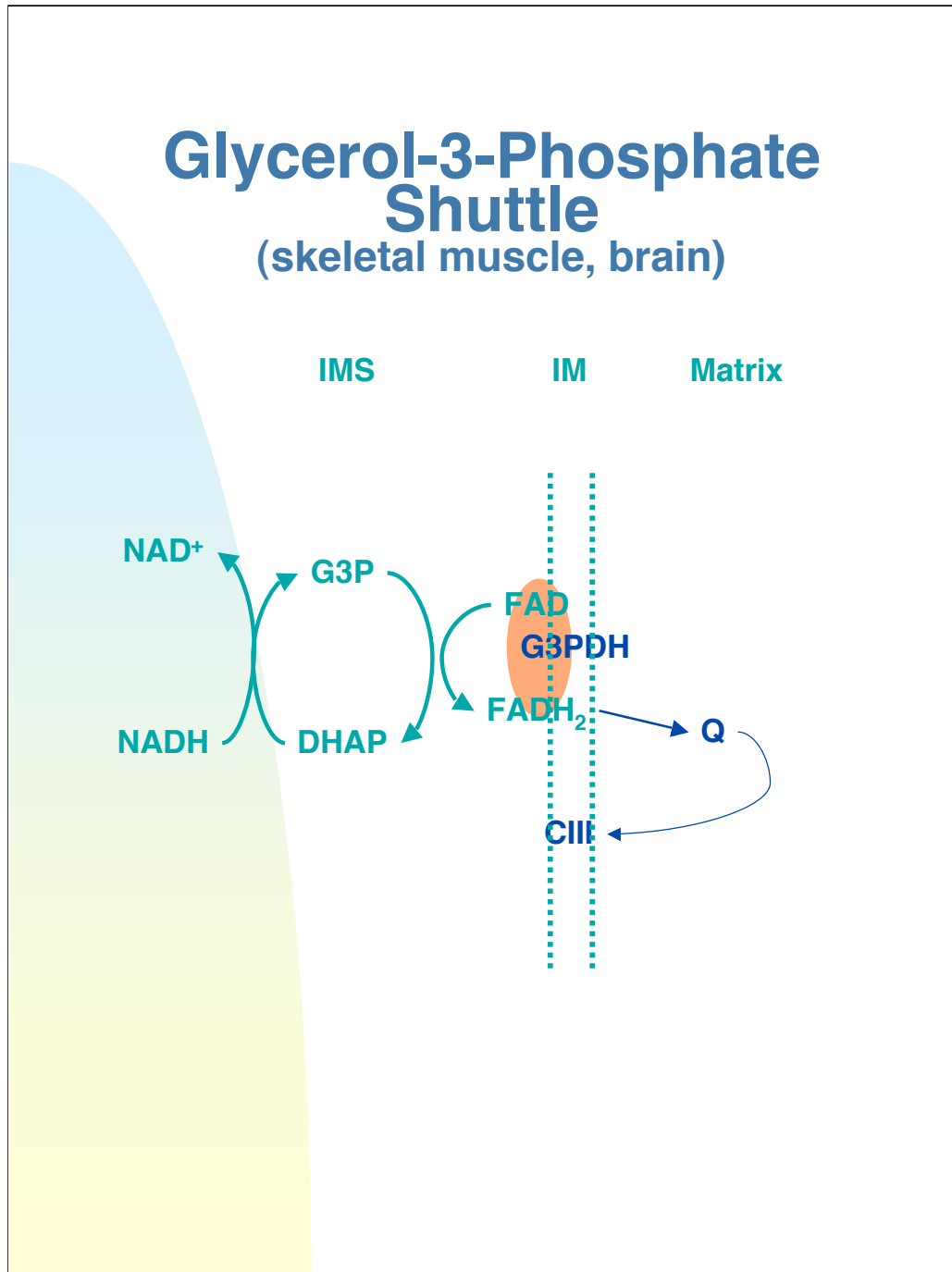
Recall NADH/NAD⁺ controls PDH activity (PDH - active, PDH-P_i - inactive) also through action of PDH kinase (active when [NADH]/[NAD⁺] is high) and phosphatase; PDH inhibition leads to increased [lactate], [pyruvate], [alanine].

Acetaldehyde inhibits PDH by modifying thiamin pyrophosphate (TPP) of the E₁ component.

Abrupt halt of EtOH can lead to alcoholic ketoacidosis; clinical test looks for acetoacetate but not 3-hydroxybutyrate, ketosis and ketouria underestimated

beta-oxidation inhibited by high [NADH]/[NAD⁺]





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/FADH₂: 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)?**
- **What are useful (important) clinical markers?**
- **How does the cell process NADH?**