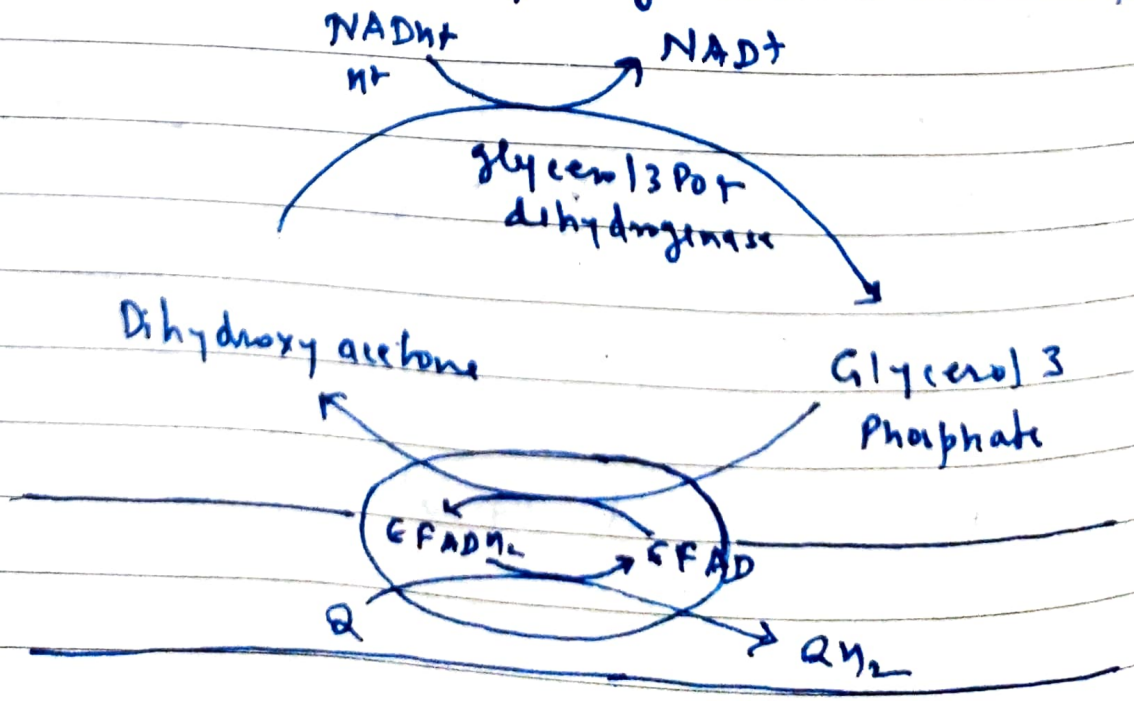
# Shuttles

- One function of the respiratory chain is to regenerate $NAD^+$ for use in glycolysis. NADH cannot simply pass into mitochondria for oxidation by the respiratory chain, because the inner mitochondrial membrane is impermeable to NADH and $NAD^+$.
- The soln is that $e^-$ from NADH, are carried across the mitochondrial membrane. One of the several means of introducing $e^-$ from NADH into ETC is the glycerol 3-$PO_4$ shuttle

The first step in this shuttle is the transfer of a pair of $e^-$ from NADH to dihydroxy acetone phosphate, a glycolytic intermediate to form glycerol 3 $PO_4$. This rxn is catalysed by a glycerol 3 Phosphate dehydrogenase in the cytoplasm

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the reduced flavin transfers its e⁻ to the e⁻ carrier Q, which then enters the respiratory chain as $QH_2$. When cytoplasmic NADH transported by the glycerol 3 Phosphate shuttle is oxidized by the respiratory chain, 1.5 rather than 2.5 molecules of ATP are formed. The yield is lower because FAD rather than $NAD^+$ is the electron acceptor in mitochondrial glycerol 3 Phosphate dehydrogenase.

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→ The glycerol 3 Phosphate shuttle is especially prominent in muscle and enables it to sustain a very high rate of oxidative phosphorylation.

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→ Some insects lack lactate dehydrogenase and are completely dependent on the glycerol 3 phosphate shuttle for the regeneration of cytoplasmic $NAD^+$.

→ In the heart and liver, e⁻ from cytoplasmic NADH are brought into mitochondria by the malate-aspartate shuttle, which is mediated by two membrane carriers and four enzymes.

e⁻ are transfered from NADH in the cytoplasm to oxaloacetate, forming malate, which traverses the inner mitochondrial membrane in exchange of a ketoglutrate and then reoxidized by $NAD^+$ in the matrix. to form NADH.

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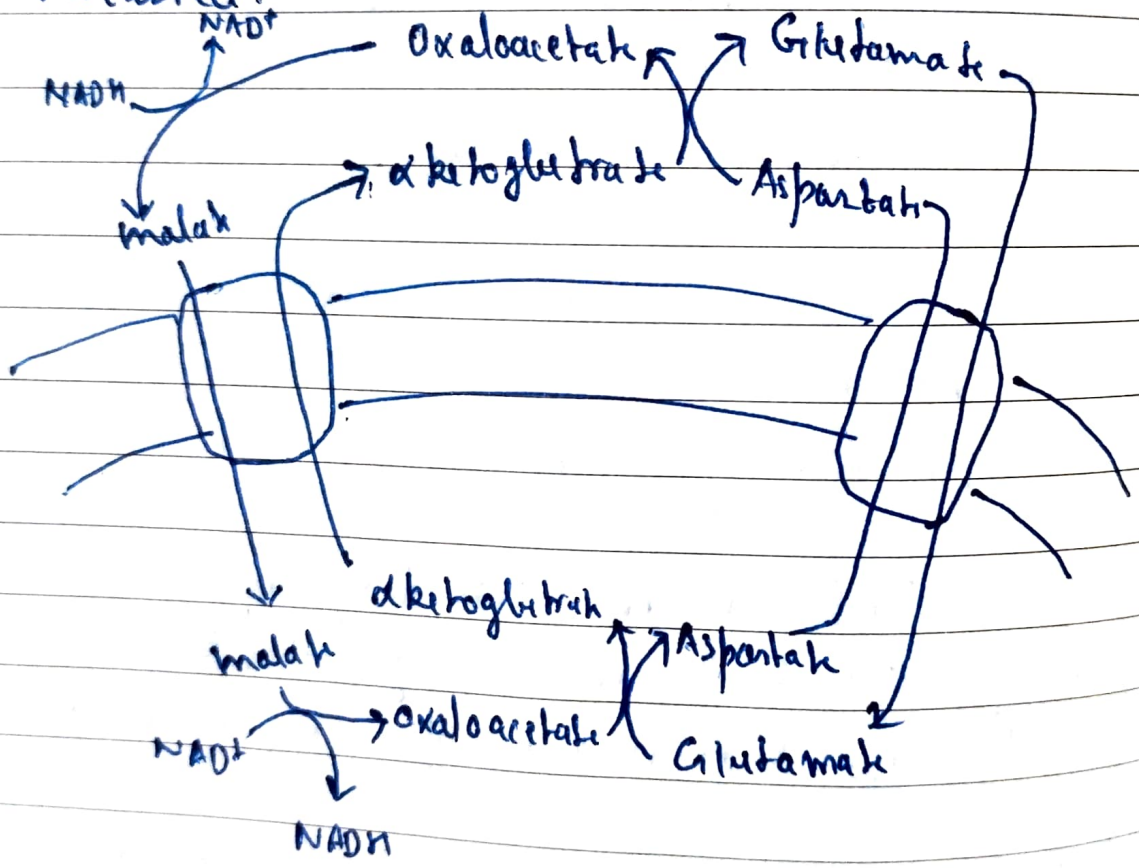
→ The resulting oxaloacetate does not readily cross the inner mitochondrial membrane and so a transamination rxn, is needed to form aspartate which can be transported to the cytoplasmic side in exchange for glutamate.

In the cytoplasm, aspartate is then deaminated to form oxaloacetate and the cycle is restarted.



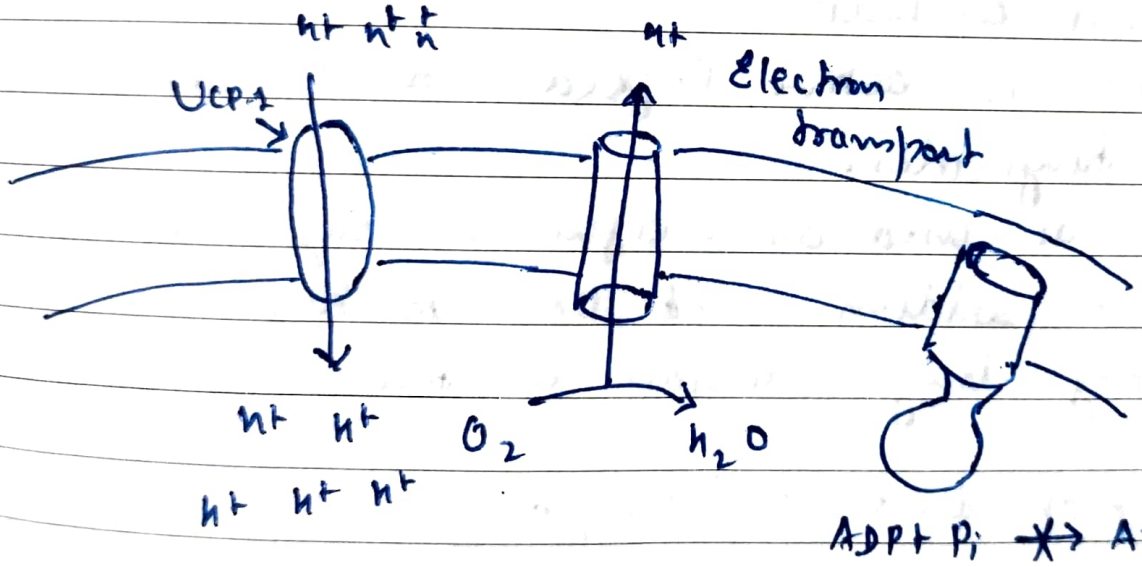

## Uncouplers

Some organism possess the ability to uncouple oxidative phosphorylation from ATP synthesis to generate heat. Such uncoupling is a means to maintain body temp. in hibernating animals, in some newborn animals (including human beings) and in mammals adapted to cold.

In animals, brown fat (brown adipose tissue) is specialized tissue for this process of nonshivering thermogenesis.

→ Brown adipose tissue is very rich in mitochondria.
- The tissue appears brown from the combination of greenish colour cytochromes in the numerous mitochondria and the red Hb present.
- The inner mitochondrial membrane of these mitochondria contain a large amount of uncoupling protein (UCP-1) or thermogenin.

UCP-1 forms a pathway for the flow of protons from the cytoplasm to the matrix.




UCP-2 which is 56% identical in seq with UCP-1 is found in variety of tissues.

UCP-3 57% identical with UCP-1 and 73% identical with UCP-2 is localized to skeletal muscle and brown fat.