Metabolism Disease Project Part II : Diagnostic Strategy For Wilson's Disease

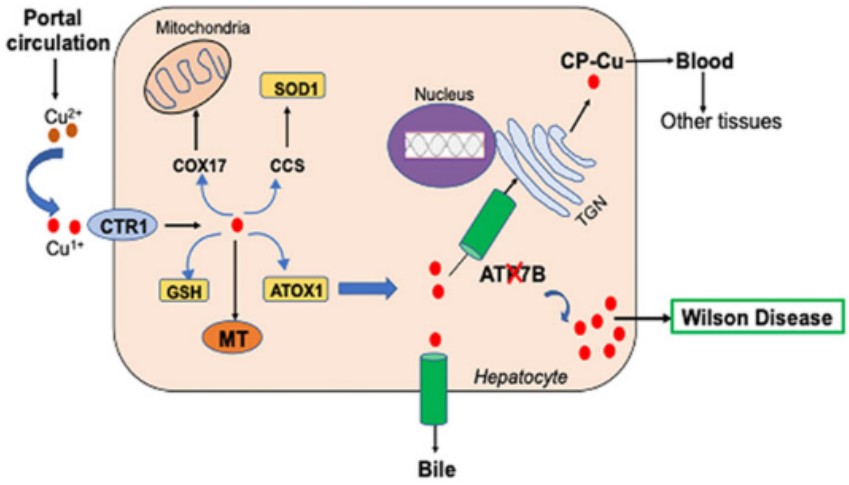

Figure 1: The inactivation of ATP7B, characterizing Wilson's disease, affects the neutralization of copper in hepatocytes. Through liver portal circulation, reduced copper is oxidized and transported across the membrane via CTR1, a high affinity copper uptake protein. Copper has five intracellular fates. SOD1 and GSH, antioxidant enzymes that regulate reactive oxidative species in the cell. COX17, a shuttle that delivers copper to cytochrome oxidase c complex in the mitochondria. Lastly, a secretory pathway involving ATOX1 transport protein to the copper transporting ATPase, ATP7B. From there, ATP7B transports Cu into the trans-Golgi network for incorporation into ceruloplasmin and to the apical membrane for excretion. A buildup of copper results in excess copper in the body and oxidative stress on the liver (Dev *et al,* 2022).

Wilson's disease may clinically manifest through tiredness and loss of appetite, eye jaundice, fluid build up in the stomach or legs, difficulties with speech, swallowing, or physical coordination, depression, muscle stiffness, and Kayser-Fleischer rings (Mayo Clinic, 2023). These symptoms begin when patients start to accumulate copious amounts of copper in the liver and eventually enter the bloodstream. The copper will circulate in the body and will deposit in different areas, including the eyes and brain. Knowing this, a good target and minimally invasive way to identify potentially impacted patients is by determining the copper content within the eyes, as Wilson disease patients tend to exhibit Kayser-Fleischer rings encircling the corneas.

The method commonly employed to determine the presence of the Kayser-Fleischer rings is via an eye evaluation known as a slit-lamp exam (U.S. Department of Health, 2018). However, Kayser-Fleischer rings may not be easily visible on routine examination in the initial stages and become more prominent as the disease progresses (Pandey, 2024). Although there are less invasive diagnostic techniques, such as urine tests to measure the concentrations of copper, for more definitive results, more invasive tests like liver biopsies where tissue damage is assessed are needed. To circumvent that and be able to determine in the initial stages, even if the ring is not prominent, is by focusing on the copper levels circulating in the eyes such that a contact lens is engineered to absorb the copper in the eyes, specifically Cu^{2+} accumulation. Current research has shown the potential development of smart contact lens sensors (SCLs) (Kazanskiy *et al,* 2023). After the allotted period of wear, it will be taken as a sample, and a colorimetric method will be employed for the detection of the metal copper using chelator bathocuproinedisulfonic acid disodium salt (BCS). BCS assay requires a standard curve to elucidate the concentration of copper, which can be determined spectroscopically at 490 nm (Wang *et al*, 2023). The copper levels obtained will be compared to a standard expected copper level in the body to determine the severity and how much it deviates from the normal range.

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