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# Thesis Outline
# Anantya Pustimbara

5-Aminolevulinic acid (ALA) is a natural amino acid that widely used in medicine for both diagnostic and therapeutic applications. The combination of ALA with additional ferrous iron has shown particular promise, giving encouraging outcomes in cancer treatment and addressing other health concerns. ALA's safety profile is well-known, as it is naturally produced within the human body.

This study explores the effects of ALA combined with two different ferrous iron sources - sodium ferrous citrate (SFC) and hemin. The results demonstrate significant improvements across various applications, including iPS MELAS syndrome, adipogenesis in pre-adipocyte 3T3-L1 cells, and the treatment of TMK-1 gastric cancer cells.

In the context of iPS MELAS syndrome, the combination of ALA and SFC enhances mitochondrial function. It is shown that the increased relative expression levels of OXPHOS system complex proteins and HO-1 occurs, both of which are critical for MELAS syndrome and heme catabolism, respectively. The improvement in heme biosynthesis observed after ALA and ALA-SFC treatment suggests that the increased expression of OXPHOS system complex proteins may be linked to the elevated rate of heme production, as several of these protein complexes contain heme.

Furthermore, the research reveals the potential combination of ALA with hemin, another source of ferrous iron, to enhance the effectiveness of photodynamic therapy (PDT) on TMK-1 gastric cancer cells. This combination reduces cell viability and increases PpIX accumulation in TMK-1 cells. The addition of hemin significantly induces ROS production and $Fe^{2+}$ accumulation, promoting lipid peroxidation and iron-mediated cell death through the Fenton reaction. Additionally, the increased iron supply influences the expression of iron homeostasis-related genes and mitochondrial-related proteins.

Both SFC and hemin function as iron providers in this study. The degradation of free iron ions ($Fe^{2+}$), together with ALA administration, can impact the heme biosynthesis pathway within cells. Consequently, the combination of ALA with ferrous iron supplementation offers substantial benefits in various applications, including iPS MELAS syndrome, adipogenesis in 3T3-L1 pre-adipocytes, and the treatment of TMK-1 gastric cancer cells.

In conclusion, this study highlights the therapeutic potential of ALA in combination with ferrous iron. The positive outcomes observed in diverse applications focus on the importance of further research into this promising approach. Future investigations may focus on elucidating the precise mechanisms underlying these effects and exploring the potential of ALA-ferrous iron combinations in other therapeutic areas.