Synopsis of Original Research Paper

Elucidating the Molecular Mechanism of Metal Acquisition Critical for the Activation of Tyrosinase Enzymes

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Melanin is an essential pigment involved in pigmentation and UV protection. Its biosynthesis depends on the tyrosinase protein family, which includes tyrosinase (TYR), tyrosinase-related protein 1 (TYRP1), and tyrosinase-related protein 2 (TYRP2). These proteins share a high sequence identity but exhibit distinct biochemical properties. TYR contains two copper ions at its active center, supplied by the copper transporter ATP7A, which is crucial for its enzymatic activity. In contrast, TYRP1 contains two zinc ions coordinated at its active center, supplied by the zinc transporter complexes ZNT5-6 and ZNT7. Despite the importance of metal coordination, the regulatory mechanisms governing these processes within cells remain unclear.

In this study, we investigated TYR activation, a key step in melanin production. We confirmed that pigmentation requires copper supplied via ATP7A by demonstrating that ATP7A-deficient cells lost TYR activity, causing cell pellets to change from black to white. Furthermore, we identified a unique sequence in the carboxyl-terminal region of TYR that is essential for its activation. These findings provide new insights into the molecular mechanisms underlying TYR activation. Understanding ATP7A-mediated copper delivery to TYR and its specific activation may contribute to further research on melanin biosynthesis and pigmentation disorders.