HTI study: Inhibition of tyrosinase induces autophagy

We discovered that inhibition of tyrosinase induces autophagy, demonstrating the direct involvement of autophagy in melanin production and challenging the conventional pigment-suppression strategies in zebrafish research model.

Autophagy (self-eating) is an important cellular degradative mechanism involves in many physiological processes (intracellular material turnover, cell death and proliferation, development etc.) and hence, implicates in many human diseases including cancer, neurodegeneration, aging, heart disease and infection.

Because of its importance, autophagy has been widely studied in recent years with different research models. In particular, externally fertilized zebrafish embryo represents a very unique whole-organism model. In general, zebrafish model is highly fertile, fast growing, similar to mammalian in many ways as well as highly amenable to genetic editing and drug treatment. With the use of fluorescent transgenic zebrafish lines or fluorescent dye, live-tracking of autophagy signal through the transparent fish body under fluorescent microscope is possible.

A chemical tyrosinase (key enzyme for pigment formation) inhibitor, phenylthiourea (PTU) is conventionally used in most zebrafish research to suppress pigment formation, thereby increasing the optical transparency during embryonic development before microscopic observation. In this study, we discovered that PTU treatment and genetic targeting of tyrosinase significantly induced autophagy within zebrafish embryos. This discovery linked autophagy directly with pigment (melanin) production and highlighted the potential role of autophagy in melanoma.

The following are the main findings and implications of the study.

(1) PTU treatment and genetic targeting of tyrosinase significantly induced autophagy within zebrafish embryos.

(2) This discovery linked autophagy directly with pigment (melanin) production and highlighted the potential role of autophagy in melanoma.

(3) This observation raises a novel concern in numerous autophagy-related studies using PTU-treated or tyrosinase-targeted zebrafish model.

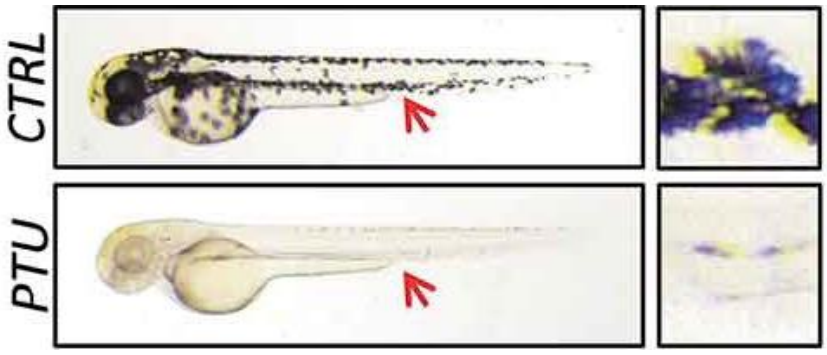

Figure 1 *indicates that Phenylthiourea (PTU) is conventionally used to suppress pigment formation in zebrafish model.*

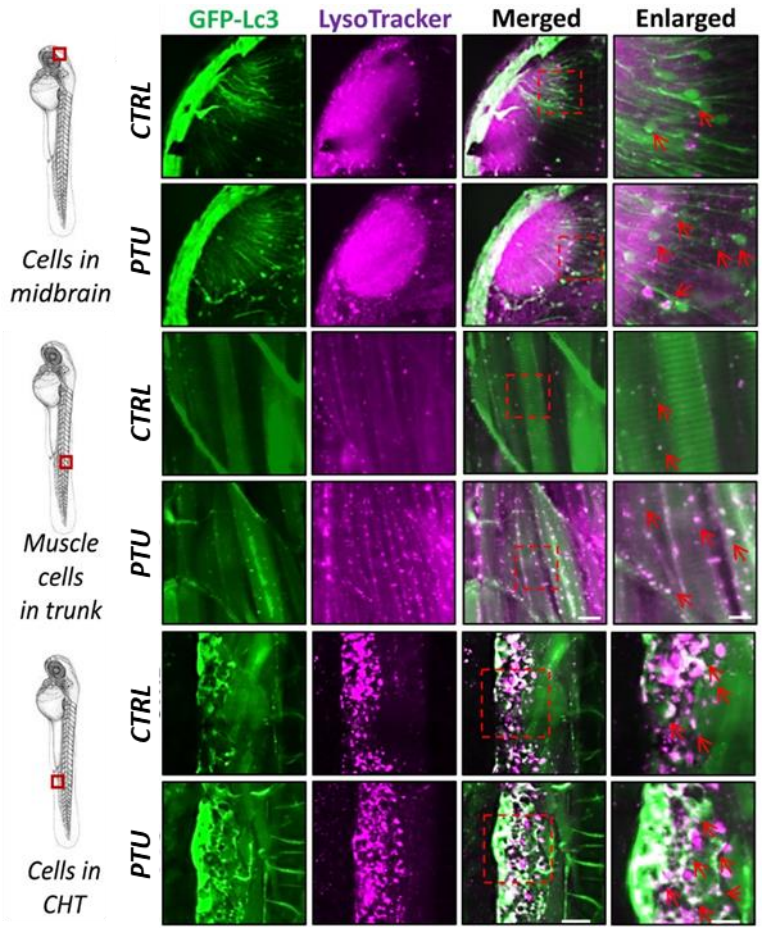

Figure 2 *demonstrates that Phenylthiourea (PTU) treatment induces autophagy in different tissues in zebrafish model. Live fluorescent images taken by LightSheet microscope in University Research Facility for Life Sciences (ULS).*

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