博士論文発表会(公聴会)のお知らせ

日時:2025 年 1 月 27 日(月) 14:30 ～ 15:30

場所:理学部棟 E104 講義室

演題:Study on the cell-killing mechanism of the potential anti-cancer agent 3,3′-Diindolylmethane using fission yeast

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要旨

Cruciferous vegetables are widely consumed and contain bioactive precursor compounds like glucobrassicin. Upon digestion, glucobrassicin is metabolized into various indoles, particularly indole-3-carbinol (I3C), which is relatively unstable. Through an acid-catalyzed reaction, I3C is dimerized to form 3,3'-Diindolylmethane (DIM). DIM has emerged as a potential anticancer agent. Studies have reported that DIM can suppress the proliferation and migration of various cancer cells including esophageal, colorectal, liver, pancreatic cancers, through multiple biological pathways, such as apoptosis, autophagy, endoplasmic response (ER) stress, and cell cycle regulation. Albeit DIM function mechanisms were distinctly found in various cancer cells, the direct in vivo target of DIM remains to be further elucidated. For exploring the impacts and its mechanisms of DIM with *Schizosaccharomyces pombe* (*S. pombe*), this study reveals that in *S. pombe*, DIM also affects additional nuclear envelope components, leading to GFP-NLS leakage, which indicates nuclear envelope rupture. Additionally, DIM alters the localization of GFP-ADEL and Ost4, suggesting a broader disruptive effect on ER function. The repair of the nuclear envelope, maintenance of its physical properties, and lipid metabolic balance are essential for cell viability when exposed to DIM. I discovered a novel finding about molecular mechanisms of DIM by working on a novel mutation in the mitochondrial translation elongation factor gene, EF-Ts (*tsf1*$^{+}$), which plays a crucial role in mitochondrial protein synthesis. This mutation was found to confer resistance to DIM in *Schizosaccharomyces pombe*. Additionally, a *tsf1*Δ deletion also resulted in DIM resistance. The observed resistance might be attributed to a reduction in mitochondrial translation, as cells treated with chloramphenicol, a mitochondrial translation inhibitor, also exhibited DIM resistance. In summary, this study uncovered new biological impacts of DIM and obtained further understanding about molecular mechanism, by which, DIM exhibits cell-killing effects in *S. pombe*, emphasizing the potential of DIM as a promising anti-cancer agent.

本セミナーは統合生命科学研究科セミナーとしてプログラム共同セミナーの対象です。

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