# 세미나 초록

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| **성명** | 정승민 |
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| **발표 주제** | The role of metabolic stress response in obesity and aging |
| **발표 내용** | The regulation of DNA damage response is an essential for preserving genome integrity and eliminating damaged cells, but the fundamental question about the cellular metabolic response to DNA damage remains largely obscure. Here, we find that DNA damage induces mitochondrial fatty acid oxidation (FAO), which is required for DNA damage-induced cell death. Mechanistically, the induction of FAO increases intracellular acetyl-CoA levels and then promotes N-alpha-acetylation of caspase-2, leading to DNA damage-induced cell death. Importantly, we find that blocking this metabolic response by tumor cells in obese mice contributes to its chemoresistance. Whereas chemotherapy increases expression of FAO related genes in a PPARα -dependent manner in tumors from lean mice, accelerated hypoxia-inducible factor-1α stabilization by obesity impedes the upregulation of FAO. Moreover, we show that improving FAO by PPARα activation ameliorates the obesity-induced chemoresistance and thus enhances the outcomes of chemotherapeutic treatment in obese mice. These findings reveal the metabolic shift to FAO induction is an important metabolic response to DNA damage and may provide effective therapeutic strategies for cancer patients with obesity. |