S7 [E] ／ マウスモデルを用いた発がん研究を再考する／Carcinogenesis experiments revisited

[座長]

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座長のことば

2019/09/26 13:00〜15:30 Room 5 (1F Room D)

印 刷

[S7-2] 13:00〜15:30
p53が制御する新規の神経内分泌腫瘍抑制経路の解明Identification of a novel p53 downstream pathway important in neuroendocrine tumor development

[演者]大木 理恵子 (国立がん研セ・研・基礎腫瘍学)

The most important function of p53 is the transcriptional regulation of p53 target genes. We have performed an exhaustive screen of p53-inducible genes and reported the molecular function of several novel p53 target genes, including Noxa, Reprimo, AEN, FUCA1, IER5 and PHLDA3. These genes are involved in fundamental tumor suppression pathways; including apoptosis, growth suppression and stress response. Here, we report on PHLDA3, a tumor suppressor gene encoding a repressor of Akt. PHLDA3 functions as a negative regulator of Akt (Cell, 136, 535-550, 2009) and a tumor suppressor gene that undergoes 2-hit inactivation in various neuroendocrine tumors (NETs) (PNAS, 111, E2404-E2413, 2014, and unpublished data). Furthermore, loss of PHLDA3 function in NETs is mutually exclusive with loss of p53 function, suggesting that PHLDA3 is a pivotal downstream mediator of p53 in NET suppression. We also demonstrated that PHLDA3 represses Akt activity in endocrine cells and that PHLDA3-deficient mice develop abnormalities in endocrine tissues. Collectively, these results indicate the existence of a novel p53-PHLDA3-mediated pathway of tumor suppression that is important for the development of NETs.