P14-11 [E/J] ／ 小児がん・その他／Pediatric cancer and others

[座長]

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印 刷

[P-1177] 16:30〜17:15
PHLDA3遺伝子とMEN1遺伝子による膵臓神経内分泌腫瘍抑制機構の解明Unraveling the mechanisms of pancreatic neuroendocrine tumorigenesis using a new mouse model

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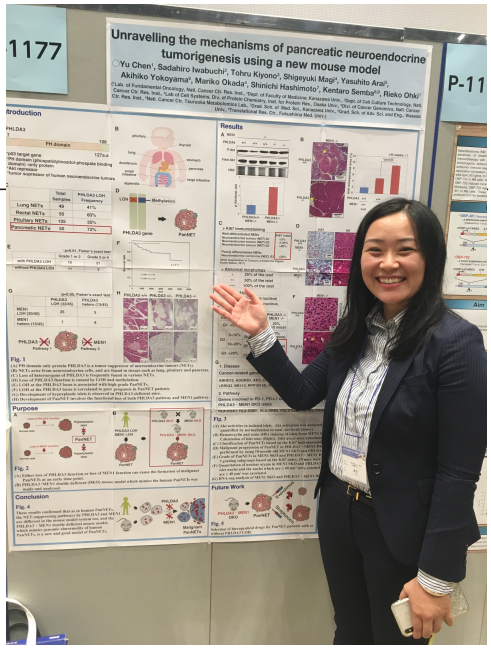

We previously demonstrated that PHLDA3 is a novel tumor suppressor of pancreatic neuroendocrine tumor (PanNET), and showed hyperplasia of the pancreatic islets is found in PHLDA3 deficient mice. We also showed that in addition to PHLDA3, functional loss of MEN1, which is a tumor suppressor gene associated with multiple endocrine neoplasia type 1, is required for the development of PanNET (PNAS, 2014).
The mechanisms of PanNET tumorigenesis remain unclear to date because of the shortage of proper experimental model systems. Therefore, we established a new PanNET mouse model that is deficient in both PHLDA3 and MEN1 (DKO) and analyzed the development and progression of PanNET. While less malignant PanNET were found in MEN1 single-deficient mice at a later age as previously reported, more malignant PanNET were found at an earlier age in DKO mice. These data suggest that the PanNET-suppressing pathway of PHLDA3 and MEN1 are independent and the functional loss of PHLDA3 is the critical determinant of PanNET progression. Using the DKO mice, we are now investigating the detailed molecular mechanism of PanNET tumorigenesis and the effects of the anti-PanNET drugs.