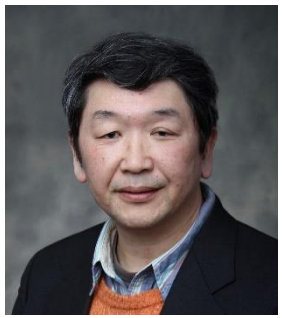
大学院特別講義のご案内



- 日時：2024年7月8日　17:00-18:30
- 場所：歯学部D棟4階 大講義室
- 講師：**三品　裕司　先生**　（ミシガン大学歯学部生命材料科学科 教授）

- **演題**:「BMP as a bridge between genetics and epigenetics - involvement in the facial morphogenesis」

- **要旨**: Midline facial defects are one of the most common birth defects. During development, cranial neural crest cells (CNCCs) delaminate from the dorsal end of the neural tube, and migrate to populate nasal processes, where they contribute to form midline facial structures. Here we identified a small increase of Bone Morphogenetic Protein (BMP) signaling via one of the BMP receptors ACVR1 with a constitutively activated mutation (ca-Acvr1) induces multi-level metabolic and epigenetic remodeling in cranial neural crest cells (CNCCs) thus causing midfacial defects, including midline facial cleft (MFC) and bifurcation of nasal septum.

  The mutant embryos started to show abnormal facial morphology at embryonic day 10.5 (E10.5). They developed an enlarged midfacial structure with abnormal medial nasal and lateral nasal processes leading to MFC. Unbiased gene expression analyses revealed that an increase of Aryl hydrocarbon receptor (AHR) in the mutant embryos. Interestingly, administration of alpha-naphthoflavon, an antagonist for AHR signaling, restore normal facial development in the half of the mutant embryos. These facts suggest that AHR signaling activity is positively regulated by BMP signaling and this may be one of the mechanisms of facial anomalies caused by increased BMP signaling. These also suggest that levels of BMP signaling may act as a risk factor for environmental insults.

  In the second line of ca-Acvr1 transgenic model, mutant mice developed ectopic cartilages in the midfacial region at embryonic day 14.5 (E14.5). We compared gene expression profiles in cranial NCCs between control and mutant mice at E10.5 by single-cell RNA sequence to identify 11 genes, of which expressions are specifically changed in mutant cranial NCCs. Xist, a long noncoding RNA and a leading player for X chromosome inactivation (XCI), is one of the 11 genes. I will discuss potential physiologic meanings of this finding of how XCI contributes to normal and pathological chondrogenesis in cranial neural crest cells.

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