学会賞受賞記念講演

Fri. Nov 14, 2025 3:45 PM - 4:15 PM JST | Fri. Nov 14, 2025 6:45 AM - 7:15 AM UTC Room 1

[AL] 学会賞受賞記念講演

司会：山本 聖一郎(東海大学消化器外科)

[AL-3] Analysis of treatment-resistant lineages in POU5F1-expressing colorectal cancer cells as a therapeutic target

Shiki Fujino[1], 三吉 範克[2,3], 林 理絵[2,3], 大植 雅之[4], 長江 歩[1], 澤田 元太[1], 森田 俊治[1], 植村 守[3], 土岐 祐一郎[3], 江口 英利[3] (1.Gastroenterological Surgery, Itami City Hospital, 2.大阪国際がんセンターがん医療創生部, 3.大阪大学大学院医学系研究科消化器外科学, 4.大阪国際がんセンター消化器外科)

Recurrence and metastasis after curative treatment remain major challenges in colorectal cancer (CRC). Distant metastasis via the bloodstream is a major barrier to cure, and current management relies on chemotherapy or radiotherapy, either prophylactically for high-risk patients or after progression. Delivering “optimal therapy” only to patients who will relapse could minimize overtreatment and improve outcomes. We established patient-derived cancer cells (iCCs) that preserve tumor heterogeneity and microenvironmental interactions. Unlike conventional lines, iCCs show gene expression similar to clinical samples and reflect patient drug responses, serving as a potential avatar model. Among mechanisms of aggressiveness, POU5F1 emerged as a key regulator of chemoresistance. POU5F1-positive cells generated heterogeneous progeny, resisted therapy, and mimicked circulating tumor cells (CTCs) driving metastasis. They displayed strong potential to form liver metastases and were enriched in recurrent tumors, correlating with poor prognosis. Using a POU5F1-EGFP reporter, we isolated POU5F1-positive/negative cells, enabling live tracking. scRNA-seq revealed Wnt signaling enrichment in POU5F1-positive cells, which also showed high CTLA4 expression, confirmed by immunocytochemistry. Epigenetic analysis identified CpG demethylation at POU5F1 and CTLA4 promoters, suggesting coordinated regulation. Importantly, the Wnt/β-catenin inhibitor XAV939 suppressed adhesion and survival of POU5F1-positive cells in vitro, and early treatment prevented liver metastasis in vivo. These findings highlight POU5F1-positive CTCs as critical drivers of recurrence and support therapeutic targeting of this subpopulation to block metastasis in CRC and potentially other cancers.