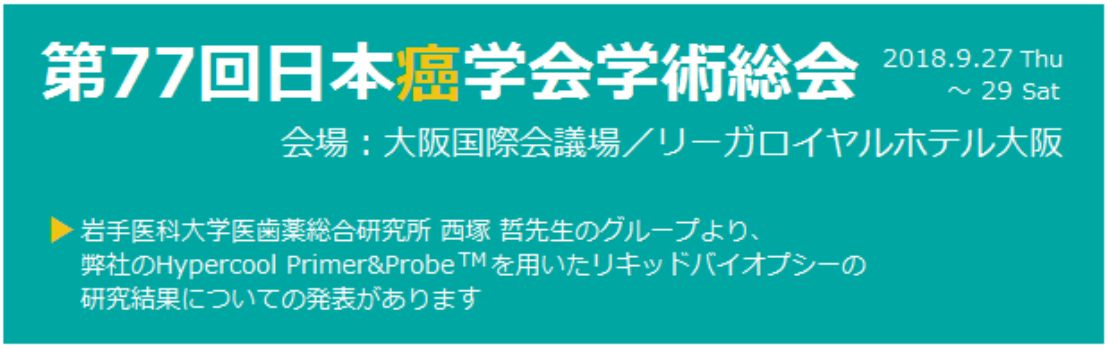

2018 年 9/27（木）～9/29（土）
第 77 回日本癌学会学術総会
会場：大阪国際会議場／リーガロイヤルホテル大阪
アクセス：
・電車
京阪電車中之島線「中之島（大阪国際会議場）駅」(2 番出口)すぐ
JR 大阪環状線「福島駅」から徒歩約 15 分
JR 東西線「新福島駅」(3 番出口)から徒歩約 10 分
阪神本線「福島駅」(3 番出口)から徒歩約 10 分
大阪メトロ「阿波座駅」(中央線 1 号出口・千日前線 9 号出口）から徒歩約 15 分
・バス
JR「大阪駅」駅前バスターミナルから、大阪シティバス(53 系統 船津橋行)または(55 系統 鶴町四丁目行)で約 15 分、「堂島大橋」バス停下車すぐ

本学会で、岩手医科大学医歯薬総合研究所 西塚 哲先生のグループより、弊社の Hypercool Primer & Probe™ を用いたリキッドバイオプシーの研究結果について発表されます。
Hypercool テクノロジー™ は、短い DNA・RNA の検出を可能にする技術です。

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第 77 回日本癌学会学術総会における、３演題の抄録をご紹介します。

▶▶▶P15-11 [English/Japanese] ／ 新規バイオマーカー (1) New biomarker (1)
[座長]井上 雅智 (近畿大・医・奈良病院 消化器外科)
2018/09/27 16:30～17:15 Room P(D) 大阪国際会議場 10 階 1010+10-1&2

[P-1359] 16:30～17:15
大腸癌 heterogeneity が ctDN A に及ぼす影響について
The effect of primary tumor heterogeneity on circulating tumor DNA detection in colorectal cancer patients

[演者]八重樫 瑞典 (岩手医大・外科)
[共著者]岩谷 岳 (岩手医大・外科)／佐藤 慧 (岩手医大・外科)／遠藤 史隆 (岩手医大・外科)／藤田 征志 (理研 統合生命医科学研究セ)／中川 英刀 (理研 統合生命医科学研究セ)／西塚 哲 (岩手医大・医歯薬総合研)

To verify the effect of tumor heterogeneity in regard to circulating tumor DNA (ctDNA), multiregional (three sites) sequencing of 14 primary colorectal tumors using a 151-gene ClearSeq panel followed by the ctDNA detection using digital PCR (dPCR) was performed. Among 76 mutations in 14 tumors, clonal mutations, common in the three regions, were observed in 78.6% (11/14); whereas all tumors exhibited at least one subclonal mutation. Mutant allele frequencies (MAF) of the clonal mutations were significantly higher than those of subclonal mutations ($p < 0.01$; 32.7% vs 20.9%). In preoperative patient plasma, ctDNA was detected in 85.7 % (12/14) of patients with the mean MAF of 2.1%. ctDNA was more frequently detected with clonal mutations than that of subclonal mutations ($p < 0.05$; 78.2% vs 50%). Of note, a tumor-unique mutation from one of the two tumors in a single patient with liver metastasis was detected in plasma. Proteomic analysis using reverse-phase protein array showed that the tumor with the mutation exhibited more aggressive cell proliferating patterns. These results suggest that clonal mutations with high MAF in a primary tumor are suitable for ctDNA analysis using dPCR.

▶▶▶J15-1 [Japanese] ／ 新規バイオマーカー (1) New biomarker (1)
[座長]新谷 康 (大阪大・医・呼吸器外科)
2018/09/28 09:00～10:15 Room 8 大阪国際会議場 10 階 1008

[J-2017] 09:00～10:15
Digital PCR を用いた食道癌患 者における症例特異的血漿中遊離 DNA モニタリング
Patient-specific circulating tumor DNA monitoring using digital PCR in esophageal squamous cell cancer patients

[演者]岩谷 岳 (岩手医大・外科)
[共著者]遠藤 史隆 (岩手医大・外科)／佐々木 泰史 (札幌医大・フロンティア研・ゲノム医科)／八重樫 瑞典 (岩手医大・外科)／佐藤 慧 (岩手医大・外科)／佐々木 教之 (岩手医大・外科)／秋山 有史 (岩手医大・外科, 国立がん研究セ・細胞情報学分野)／佐々木 章 (岩手医大・外科, 札幌医大・フロンティア研・ゲノム医科)／増田 万里 (国立がん研究セ・細胞情報学分野, 岩手医大・医歯薬総研・治療開発研究部門)／時野 隆至 (札幌医大・フロンティア研・ゲノム医科)／西塚 哲 (岩手医大・医歯薬総研・治療開発研究部門)

This study aimed to monitor therapeutic response of esophageal squamous cell carcinoma (ESCC) using circulating tumor DNA (ctDNA) by digital PCR (dPCR) with individual ESCC tumor-specific mutations. A mutation screening of primary tumors from 27 ESCC patients (Stage I/II/III/IV: 5/3/12/7) was performed by amplicon

sequencing using the ESCC panel targeting 31 genes. First-line therapies included surgery, chemoradiotherapy, and chemotherapy. With the median follow-up was 459 days, 288 blood samples were examined for ctDNA. Among 45 mutations identified from primary tumors were analyzed in pre-treatment blood, 34 (83%) were detectable as a ctDNA. In 35 mutations from Stage II or higher cases, ctDNA was detectable in 97% (34/35). The Mutation allele frequency (MAF) of good responders could decrease to 0 after one cycle of chemotherapy, whereas the MAF of non-responders stayed high levels. A patient who had a recurrence after resection for stage II ESCC showed that ctDNA had been detected six months before the recurrence was noticeable by CT scan. The patient-specific ctDNA monitoring readily indicates the disease Stage and possibly facilitates an early recurrence detection of ESCC.

▶▶▶S19 [English] ／ 次世代の医療を切り拓く Liquid Biopsy Liquid biopsy paves the way for next-generation medicine
[座長]三森 功士 (九州大・別府病院・外科)／江口 英利 (大阪大・院医・消化器外科)
2018/09/29 13:40～16:10 Room 3 大阪国際会議場 10 階 1003

[S19-6] 13:40～16:10
治療後体内腫瘍量動態モニタ リングツールとしての腫瘍由来循環
DNA Circulating tumor DNA as a tool for monitoring gastrointestinal tumor burden dynamics in the therapeutic context

[演者]西塚 哲 (岩手医大・医歯薬総合・医療研究開発)
[共著者]岩谷 岳 (岩手医大・医・外科・分子治療研)

The greatest challenge to advanced gastrointestinal cancer treatment is to fully prevent post-therapeutic relapse. To monitor post-therapeutic tumor burden, we conducted cancer-related gene panel sequencing of esophageal, stomach, and colorectal primary tumors, followed by the identification of patient-unique mutations that can be used for circulating tumor DNA (ctDNA) detection. A high success rate of ctDNA detection was achieved using primer/probe synthesis with Hypercool technology for digital PCR (dPCR), in which the stable detection level for SNVs were 0.01%. The dynamics of the ctDNA were largely consistent with the tumor burden defined by the CT scan, except that the ctDNA's elevation level had been seen six months earlier than the visual detection of the relapsed lesion. Multi-region tumor sequencing revealed that clonal mutations had a higher chance of being detected as ctDNA, while their functional effects at the protein level remain to be determined. By combining panel sequencing and dPCR, tumor burden dynamics that are monitored using ctDNA can readily be a sensitive indicator for earlier detection of post-the rapeutic relapse of gastrointestinal cancers.