

2021年4月16日

【お知らせ_電気泳動第65巻1号のJ-STAGEからの公開】

日本電気泳動学会会員の皆様

本日、Journal of Electrophoresis Vo. 65 (2021) No.1 (J-STAGE 電子版)に、以下の2報の論文が掲載されましたのでお知らせ致します。

(<https://www.jstage.jst.go.jp/browse/jelectroph>)

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J Electrophoresis. 2021; 65:1-11.

Title: Proteogenomic approach to drug targets in osteosarcomas with different original sites

Authors: Rei Noguchi, Yuki Yoshimatsu, Takuya Ono, Akane Sei, Tadashi Kondo

Abstract: Regulation of kinase activity plays a crucial role in carcinogenesis and cancer progression. Mutations in the activity domain of kinases are extensively investigated as therapeutic targets. We examined anti-proliferative anti-cancer drugs and drug targets via the multi-omics approach: (i) comprehensive kinase activity assay, (ii) high-throughput drug screening, and (iii) genomic sequencing. Two osteosarcomas cell lines, NCC-OS1-C1 and NCC-ESOS1-C1 derived from bone and soft tissue respectively, were used. Genetic alterations were examined by NCC Oncopanel based on the next-generation sequencing technology and SNP array. One hundred kinases were monitored by the PamStation 12, an in vitro kinase assay. The anti-proliferative effects of 214 FDA-approved anti-cancer drugs were examined. Mutation of PIK3CA and deletion of CDKN2A were identified in NCC-ESOS1-C1 and druggable genetic alterations were not identified in the NCC-OS1-C1. PI3K-AKT pathway or CDKN2A inhibitors did not show significant effects on these cell lines. Comprehensive kinomic assay revealed no remarkable differences on these osteosarcoma cells ($R^2=0.99$). The two cells shared similar kinase activity profiles for FES, FER, PDGFR- β , VEGFR2, and Wee1. Anti-proliferative effects of anti-cancer drugs on NCC-OS1-C1 and NCC-ESOS1 cells showed remarkable differences. Significant responses to romidepsin and trabectedin were observed for both. Eribulin was effective on NCC-OS1-C1; ifosfamide and

dacarbazine were effective on NCC-ESOS1-C1 only. Hence, investigating kinase activities and genetic alterations will lead to predict the effects of kinase inhibitors. The different status of kinase mutations, activities, and response to inhibitors should be integrated. Multi-omics experiments and data integration are crucial in understanding cancer progression and developing novel therapies.

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J Electrophoresis. 2021; 65:13-22.

Title: Comprehensive miRNA expression analysis for histological subtypes of soft tissue sarcoma

Authors: Ryuto Tsuchiya, Yuki Yoshimatsu, Naoto Tsuchiya, Seiji Ohtori, Akira Kawai, Tadashi Kondo

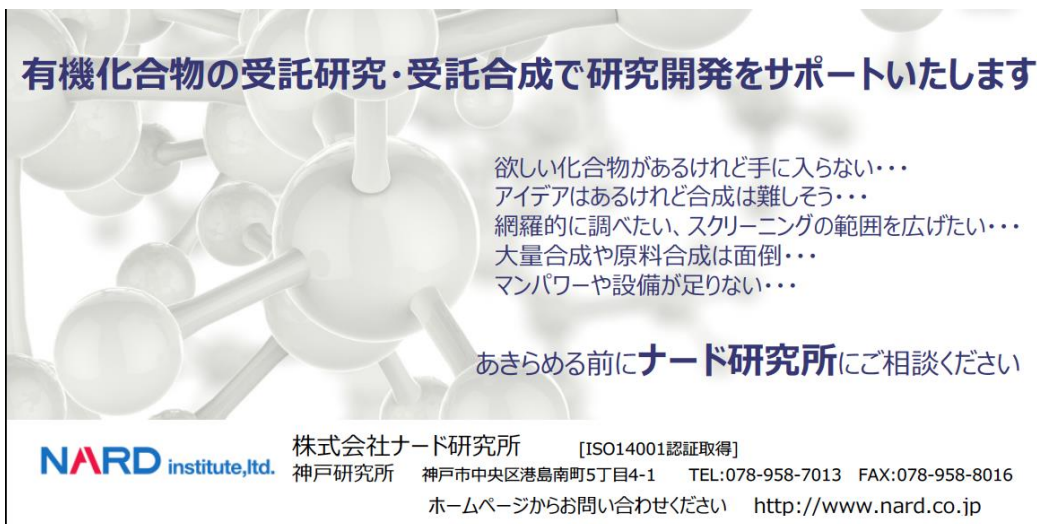
Abstract: Sarcoma is a rare mesenchymal malignancy that comprises more than 50 histological subtypes. Because of the rarity and diversity of sarcomas, their differential diagnosis is difficult, and there is still a need for biomarkers to support pathological diagnoses. Micro RNAs (miRNAs) are small noncoding RNAs that regulate the behavior of tumors, such as invasion and metastasis. The expression patterns of miRNAs reflect the origin of malignancy and are considered to be candidate biomarkers. To understand the molecular background of those histological subtypes, we investigated the miRNA expression in 89 tumor tissues of eight subtypes. The correlation coefficients between each sarcoma subtype on the basis of miRNA expression values were mostly higher than 0.7, reflecting the common mesenchymal origin. By contrast, hierarchical clustering and principal component analysis showed that three types of sarcoma with chromosomal translocation (i.e., dermatofibrosarcoma protuberans, myxoid liposarcoma, and synovial sarcoma) were grouped according to their histological subtypes, whereas five types with complex karyotypes (i.e., myxofibrosarcoma, malignant peripheral nerve sheath tumor, undifferentiated pleomorphic sarcoma, dedifferentiated liposarcoma, and pleomorphic liposarcoma) were not. Notably, the number of miRNAs whose expression pattern was unique to histological subtypes with statistical significance was higher in sarcomas with chromosome translocation than in those with complex karyotypes. Hence, it can be concluded that the miRNAs unique to histological subtypes are candidate biomarkers for the differential diagnosis of sarcomas, particularly in those with chromosomal translocation.

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日本電気泳動学会 編集委員長
亀山 昭彦

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