日本電気泳動学会 電子メール通信 No.107

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【J Electrophoresis_J-STAGE論文公開のお知らせ】

日本電気泳動学会会員の皆様

本日, Journal of Electrophoresis Vol. 63(2019) No. 1 p1-7, p9-14 (J-STAGE 電子版) に,
以下の論文2件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.2019;63:1-7.

Title: Screening of a growth inhibitor library of sarcoma cell lines to identify potent anti-cancer drugs

Authors: Zhiwei Qiao, Tadashi Kondo

Abstract: There is a need for novel drugs for sarcoma treatment. In the present study, to identify inhibitors with potential therapeutic utility in sarcomas, we screened the growth inhibitory effects of 361 inhibitors, including experimental reagents and anti-cancer drugs approved for use in non-sarcoma malignancies and those under clinical trials. The inhibitors were initially tested using 10 osteosarcoma cell lines. The half-maximal inhibitory concentration (IC50) of leptomycin B, actinomycin D, chetomin, and staurosporine was <100 nM in all the cell lines. As the promiscuous effects of staurosporine on kinases make it unsuitable for clinical applications, the other three inhibitors were tested in an additional 15 sarcoma cell lines derived from synovial sarcoma, fibrosarcoma, liposarcoma, rhabdomyosarcoma, malignant peripheral nerve sheath tumor, leiomyosarcoma, and Ewing's sarcoma. The IC50 of leptomycin B and actinomycin D was <100 nM in all cell lines and that of che!
tomin was <100 nM in all but three synovial sarcoma cell lines. Although the clinical development of leptomycin B, a chromosomal region maintenance (CRM)1/exportin (XPO)1 inhibitor, was discontinued because of toxicity, a previous clinical trial revealed that other CRM1/XPO1 inhibitors, such as selinexor, have anti-tumor effects in sarcomas. Actinomycin D has proven clinical utility in the treatment of sarcomas. Chetomin disrupts the interaction of hypoxia-inducible factor-1 with the transcriptional coactivator p300 and its clinical utility has not been established in sarcomas. Chetomin exhibited growth inhibitory effects on sarcoma cells with different histological subtypes. Library screening is a powerful approach to detect the potential utility of anti-cancer drugs in sarcoma treatment.

J Electrophoresis.2019;63:9-14.

Title: Identification of cantharidin as a drug candidate for glioblastoma by using a Connectivity Map–based approach

Authors: Zhiwei Qiao, Tadashi Kondo

Abstract: Glioblastoma (GBM) is the most common brain tumor in adults. Although the surgical and chemoradiotherapy approaches for treatment have improved, the prognosis of patients with GBM is still poor and novel drugs are urgently required. Therefore, we investigated small molecular inhibitors to target GBM on the basis of gene expression data by using a Connectivity Map (CMAP)–based approach. Using meta-analysis performed with publically available gene expression data, we identified the gene expression signature of GBM. The CMAP analysis identified 15 candidate drugs for GBM treatment. We confirmed the anticancer

cell proliferation activity of cantharidin as one of the top 15 drugs with high negative enrichment scores in CMAP analysis by using GBM cell lines. Our results indicate the potential utility of CMAP to discover the potent drugs in the GBM treatment. This approach can be applied to other malignancies than GBM.

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