平成29年11月19日

核酸を標的とした低分子創薬研究会

「米国スクリップス研究所　Matthew　Disney 博士講演会」

臨時受講のご案内

米国スクリップス研究所 Matthew Disney 博士講演会について、当日限りの臨時受講者を下記の通り募集いたします。下記申込書にご記入の上、事務局までお申込み下さい。

記

１．主催：　　　一般財団法人　大阪大学産業科学研究協会

２．臨時受講会費：　会員企業 20,000円／人

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３. 期　　日: 　　　平成２９年１２月１５日 午後２時より

４．場　　所：　　　富国生命ビル　５F　立命館大学大阪梅田キャンパス　演習室２

４．懇 親 会：　　　富国生命ビル　３F　立食形式。一律2,000円を申し受けます。

大阪大学産業科学研究協会 事務局

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―――――――――――――＜12月15日臨時受講申込書＞――――――――――――

一般財団法人　大阪大学産業科学研究協会　事務局宛

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「核酸を標的とした低分子創薬研究会」にて12月15日に開催されます米国スクリップス研究所　Matthew David Disney 博士講演会の臨時受講を申し込みます。

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講演要旨

Sequence-Based Rational Design of Precise Small Molecules Targeting RNA

Matthew D. Disney

Department of Chemistry

The Scripps Research Institute

A challenge in biomedical research is to rapidly convert genome sequence into lead drugs. In this talk, I describe a series of synergistic approaches that allows one to quickly and accurately convert genome sequence, namely the RNA products of the genome, into lead therapeutic targets. The general approach described herein is very different from typical drug discovery efforts that often rely on screening of a single drug target to identify lead compounds. Rather, it is an attempt to advance a rational, predictable approach to drug disease-causing RNAs with small molecules. I will describe various aspects of this technology that includes the development of rapid screening assays to assess and score the binding of small molecules to RNA folds. The approach is target agnostic but by using this binding information, one can mine the transcriptome (RNA sequence) for these folds to rationally identify druggable RNA targets for small molecules via an approach named Inforna (see: *Nat Chem Biol.* 2014 Apr;10(4):291-7. doi: 10.1038/nchembio.1452.).

Amongst several advances in this area, we will describe efforts to design bioactive small molecules that target cancer-causing non-coding RNAs and, if time permits, RNA repeat expansions that cause incurable rare disease. For example, small molecules have been rationally designed to target oncogenic microRNA-96 (see: *Nat. Chem. Biol. 2014. 10(4):291-7. doi: 10.1038/nchembio.1452 and Proc. Natl. Acad. Sci. U.S.A. 2016. 113(21):5898-903. doi: 10.1073/pnas.1523975113*.), -210 (*J. Am. Chem. Soc. 2017. 139(9):3446-3455. doi: 10.1021/jacs.6b11273*.), and -18a (*ACS Central Science. 2017. 3(3):205-216. doi: 10.1021/acscentsci.7b00009*) that are causative of various cancers including breast and prostate. In addition, chemical approaches to identify the on- and off-targets of small molecules targeting RNA will be presented, namely Chemical-Cross-Linking and Isolation by Pull Down (Chem-CLIP, *J. Am. Chem. Soc. 2017. 139(9):3446-3455. doi: 10.1021/jacs.6b11273, and others*). This approach has demonstrated selective binding of small molecules to the RNAs to which the compounds were designed to target **in cells.** Chem-CLIP and other studies havealso elucidated factors affecting the ability of small molecules to selectively and potently target microRNA precursors.Lastly, the ability of these compounds to affect tumor burden in mouse models of cancer will be presented and the activities of these small molecules compared to that of antagormirs, which recognize their target via Watson-Crick base pairing to mature microRNAs. In summary, it appears that non-coding microRNA precursors may be more druggable with small molecules via rational and predictable approaches than previously realized.