平成26年3月26日 March 26, 2014

実世界データ循環学リーダー人材育成プログラム特論

Lecture for Graduate Program for Real-World Data Circulation Leaders

基盤医学特論

Tokuron Special Lecture

JUN-KAN
実世界データ循環学
リーダー人材養成プログラム

ABERRANT SPLICING AS DISEASE CAUSE, DISEASE MODIFIER AND TARGET FOR TREATMENT

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Next Generation Sequencing (NGS) has dramatically changed our ability to identify genetic variation and investigate gene expression. It is therefore becoming increasingly important that our knowledge on the potential pathological consequences of the identified sequence variants is improved and there is an urgent need for development of better tools for prediction of these potential pathogenic effects. This is particularly true for variants affecting pre-mRNA splicing, since these cannot be evaluated simply on the basis of the genetic code.

Pre-mRNA splicing is a fundamental process required for correct expression of almost all protein coding genes. It is critically dependent on the balanced interplay between numerous splicing-regulatory elements (SREs) throughout our genes and on correct expression of the splicing regulatory proteins (SRPs) that bind to the SREs. Thus, sequence variations that affect SREs or changes that affect expression of SRPs, may disrupt splicing. A rapidly increasing number of diseases are now known to be caused by aberrant pre-mRNA splicing and variations in splicing efficiency may determine disease severity. Moreover, the splicing process may be targeted for treatment of human disease by employing splice shifting oligonucleotides (SSOs) that block fundamental SREs.

We employ Next Generation Sequencing of RNA (RNA-seq) to characterize global changes in splicing resulting from genetic defects, like Spinal Muscular Atrophy (SMA), changes in splicing resulting from siRNA mediated knock-down of regulatory splicing factors (SRPs) and global changes resulting from treatment with drugs, like the polyphenolic drug, Resveratrol. Moreover, we employ RNA-seq to identify human pseudoexons, which are at risk of being activated by mutations and thus cause disease.

In my talk, I will present our work on diseases where aberrant splicing plays a fundamental role. I will present our work on aberrant splicing in SMA, our work on aberrant splicing by pseudoexon activation and our recent work on aberrant splicing of the RAS oncogenes as a disease modifier and as targets for SSO-based splicing directed therapy against cancer.

日時：	2014 年 3 月 26 日（水）　午後 5 時から午後 6 時半
Date:	March 26, 2014 (Wed), 17:00 – 18:30
場所：	鶴友会館大会議室（鶴友会館２階）
Venue:	Main Conference Hall, 2nd Floor of the Kakuyu Kaikan (the Alumni Hall)
言語：	英語
Language：	English
連絡先：	神経遺伝情報学　大野欽司 (内線 2447)
Contact:	Kinji Ohno, Neurogenetics (ext. 2447)
注意：	事前連絡は不要です。基盤医学特論単位認定ができます。
Note：	No registration is required. A Tokuron lecture credit may be requested at the venue.