# PROGRESS IN NEUROSCIENCE PINS

**Seminar Series of the**
**Brain & Mind Research Institute**
**Weill Cornell Medical College (WCMC)**
**&**
**The Graduate Program in Neuroscience of**
**WCMC and Sloan Kettering Institute**

**Thursday, 9/29/16, 4 PM, coffee at 3:45 PM**

**A-950**

## "Getting the Full Message: Long-Read Sequencing Reveals Coordination Events on RNA Molecules"

Hagen Tilgner, Ph.D.,
Assistant Professor of Neuroscience, Brain and Mind Research Institute,
Weill Cornell Medicine

**Abstract:**

It is well established that the vast majority of mammalian genes can generate multiple RNA and protein isoforms. Yet, the majority of publications consider a "one-gene-one-protein" model, in which each gene's expression is represented by a single number. If we view that genes can talk - the "one-gene-one-number" approach is akin to judging each gene by how much it talks; not by what it is actually saying. We have made considerable progress (both on the informatic and experimental side) on the way to actually judging genes by "what-they-say", yet important challenges still remain to be mastered. Using the long-read RNA sequencing approaches we have recently established, we generally find that 14-20% of the RNA molecules in a typical sample (human organs, lymphoblastoid cell lines, human and mouse brain) represent isoforms that cannot be found in state-of-the-art databases, with long non-coding RNA molecules standing out as the most poorly described so far. Furthermore, we now can observe pairs of alternative exons whose inclusion is coordinated, despite being located at a distance of one another on the molecule.

Our laboratory will be aiming to advance science in the following domains: (i) develop the molecular biology and informatics technologies needed to investigate isoforms and coordination events at several different levels, (ii) understand the rules that govern cell type specific isoform usage in the mammalian brain, (iii) understand isoform changes during development and aging and (iv) understand isoform switches that drive disease of the central nervous system.

**Recent Relevant Publications:**

1. **Tilgner H*,** Jahanbani F*, Blauwkamp T, Moshrefi A, Jaeger E, Chen F, Harel I, Bustamante CD, Rasmussen M, Snyder MP. Comprehensive transcriptome analysis using synthetic long-read sequencing reveals molecular co-association of distant splicing events. Nat Biotechnol. 2015 Jul;33(7):736-42.
2. Sharon D*, **Tilgner H*,** Grubert F, Snyder M. A single-molecule long-read survey of the human transcriptome. Nat Biotechnol. 2013 Nov;31(11):1009-14.
3. **Tilgner H**, Knowles DG, Johnson R, Davis CA, Chakrabortty S, Djebali S, Curado J, Snyder M, Gingeras TR, Guigó R. Deep sequencing of subcellular RNA fractions shows splicing to be predominantly co-transcriptional in the human genome but inefficient for lncRNAs. Genome Res. 2012 Sep;22(9):1616-25. doi: 10.1101/gr.134445.111

Weill Cornell Medicine

MEMORIAL SLOAN-KETTERING CANCER CENTER · ESTABLISHED 1884 ·