Department of Computer Science, The University of Hong Kong

CS Seminar

Using nanopore sequencing to interrogate the genome, epigenome and transcriptome

Prof. Winston Timp
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Date:
Oct 28, 2019
Monday
10:00 am

Venue:
Room 308
Chow Yei Ching Building
The University of Hong Kong

Abstract:

Nanopore sequencing is a single molecule characterization method, allowing direct sequencing of DNA or RNA with read lengths ranging from kilobases to even megabases. Unlike traditional sequencing-by-synthesis methods, it can distinguish covalently modified nucleotides directly through their modulation of the electrolytic current. And the long reads allow for straightforward detection of structural variations, large insertions, deletions or transpositions that are often difficult to detect with short-read sequencing.

We demonstrate the power of this technique, as applied with DNA, combined with exogenous labeling, to perform an integrative, single molecule characterization of the epigenome. We used M.CviPI, a GpC methyltransferase, to label accessible chromatin in cancer and normal cell lines. This allowed us to simultaneously correlate nucleosome positioning and native CpG methylation along long (~10kb) single molecules.

We investigated methods of targeted sequencing for deeper nanopore sequencing at specific genomic loci. Using ligation only to DNA freshly cut by Cas9, we demonstrated deep coverage at 10 different sites selected for their relevance to breast cancer. We used this focussed coverage of long (>20kb) native nanopore sequencing reads to measure single molecule methylation patterns, SVs and SNVs.

Finally, we have applied native RNA sequencing to interrogate poly(A) tail lengths and modifications to RNA which may be involved in post-transcriptional regulation. RNA base modifications are detectable via modulation of the nanopore current; our initial focus is on the METTL3 motif (GGm6ACU). Poly-A tail lengths inform mRNA lifetime; we can measure these lengths from how long the molecule takes to transit the pore. With these methods we have measured gene specific and even isoform specific poly(A) tail lengths and modification signals.

About the Speaker:

Winston Timp is an assistant professor in Biomedical Engineering at Johns Hopkins University. His lab's focus is in the development and application of sequencing technologies to gain a deeper understanding of biology and a more accurate set of clinical tools for human disease. Timp's research integrates the principles of biophysics, molecular biology, and computational biology to create new tools for exploring the epigenomes and genomes of different lifeforms, ranging in size from the flu virus to hummingbirds to California redwoods. Based on the knowledge gained from these studies, Timp and his lab apply their toolsets to clinical samples for the diagnosis, surveillance and treatment of human disease. Recent projects in Timp's lab include new sequencing methods to diagnose infectious disease, new methods to characterize RNA biology, and examining single molecule epigenetics of cancer.

All are welcome!
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