School of Life Sciences

Seminar Series

No. 2019-24

Thu., **7 November**, 11:00am

Jukhyun Bio Auditorium(RM.121)

English

Environment-dependent binary protein interactome of a cell

Speaker | Dae-Kyum Kim

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광주과학기술원 생명과학부

Gwangju Institute of Science and Technology School of Life Sciences

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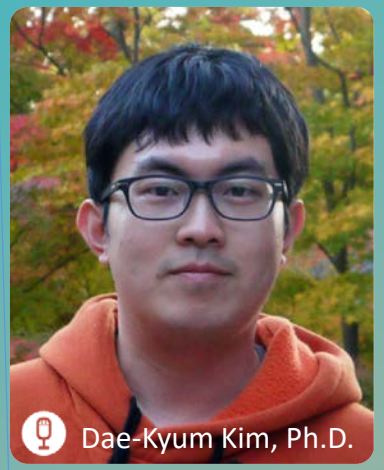

Dae-Kyum Kim, Ph.D.

Education/Experience

2006-2009	B.S. in Department of Life Sciences, POSTECH, Pohang, South Korea Summa cum laude
2009-2015	Ph.D. in Department of Life Sciences, POSTECH, Pohang, South Korea (Co-advisors: Yong Song Gho Ph.D. and Daehee Hwang, Ph.D.)
2015-present	Postdoctoral Fellow, Donnelly Centre, University of Toronto and Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada (Advisor: Frederick P. Roth, Ph.D.)

Abstract

Global insights into the impact of subcellular localization, tissue-specific expression and other dynamic cellular contexts, require systematic understanding of the protein interactome, which has remained incomplete. Here, we present the Human Reference Interactome (HuRI), consisting of 53K biophysical protein-protein interactions (PPIs) identified by yeast-two hybrid screening most of human protein genes (18K out of all 20K genes). We show this network to be highly biologically relevant, but the unbiased nature of the screen enables otherwise-confounded analyses. For example, we find limited evidence for one of the most cited results in network analysis, that essentiality is correlated with number of PPIs. By integrating transcriptome and proteome data, we exploit several cellular context-specific PPI networks to generate and support several hypotheses: i) a new cell-death protein, OTU6DA, validated by viability assay in HeLa cell line, ii) candidate extracellular vesicle (EV) recruiters mediating trafficking of interaction partners into EVs, confirmed with CRISPR knockout in U373vIII cell line, and iii) dominant negative function of an uncharacterized short isoform of NCK2 during brain development, confirmed in zebrafish. Thus, the uniform coverage of the HuRI network with high biological relevance can yield strong and subsequently-validated hypotheses about biological function.
However, HuRI is limited to ‘static’ networks in a single environment. Here, we engineered the fluorescence-Barcode Fusion Genetics-Yeast Two-Hybrid (fBFG-Y2H) assay to simultaneously query >2 million protein pairs under various contexts, including previously inaccessible environments affecting cell fitness. Applying fBFG-Y2H to nearly all possible yeast protein pairs, we generated high-quality interaction maps under four conditions of baseline, poor carbon source, oxidative stress, and DNA damage. Using stringent thresholds, we discovered ~6500 total interactions, of which ~2000 are environment specific. Our network uncovered ‘contextual hubs’ (e.g. Afg2, Gac1, and Tpk1) which gain or lose many interaction partners exclusively in specific environments. Contextual networks showed enriched connectivity between proteins with relevant functions, while also revealing dense subnetworks that enable functional predictions. Thus, we provide the first proteome-wide maps of protein interaction across multiple environments, enabling understanding of principles that underlie global cellular response to changing contexts.