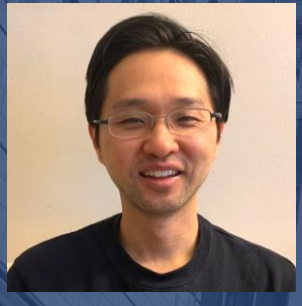
NEW YORK KOREAN BIOLOGISTS
NYKB

2023 NYKB Special Seminar

Tuesday, October 24, 2023, 7 pm – 8 pm (EST)

On-line meeting (zoom)



Whijae Roh, Ph.D.

Senior Computational Biologist
Pfizer

Forward and reverse translation between preclinical models and patient samples for iterative drug development process

Jung-Min Kee, Ph.D.

Associate Professor
Department of Chemistry
Ulsan National Institute of Science and Technology (UNIST)

Chemical tools for protein histidine and arginine phosphorylation

Talk 1 (7:00–7:30 pm)

Forward and reverse translation between preclinical models and patient samples for iterative drug development process

Whijae Roh
Pfizer Inc, San Diego, CA, USA

Forward translation of preclinical findings to clinical samples offers potential improvements in patient stratification based on biomarkers. It also supports the discovery of effective drug combinations and the investigation of resistance mechanisms in patients. Conversely, reverse translation enhances the alignment of tumor models with patient context through genomics-guided preclinical model selection. To this end, we introduce a non-negative matrix factorization (NMF) computational engine, designed for both forward and reverse translations for drug discovery and development. This framework performs integrative analyses of gene expression profiles from preclinical models and patient tumor tissues. Forward translation of preclinical *CDK4* and *CDK6* CRISPR knock-out cell line data to TCGA breast cancer patient samples shows *CDK4* gene dependency in S4 subtype and *CDK6* gene dependency in S5 subtype. Reverse translation of TCGA lung adenocarcinoma (LUAD) expression subtypes to lung cancer cell lines shows *CDK4* gene dependency in the TCGA LUAD S3 expression subtype. This adaptable AI-driven computational framework can facilitate iterative drug development process by forward translation of a wide range of drugs from preclinical studies into the clinic by predicting drug response in patients and reverse translation of selecting preclinical models that accurately represent patients' disease phenotypes.

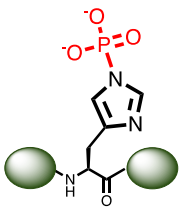
Talk 2 (7:30–8:00 pm)

CHEMICAL TOOLS FOR PROTEIN HISTIDINE AND ARGININE PHOSPHORYLATION

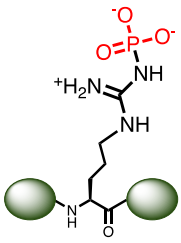
Jung-Min Kee
Department of Chemistry, Ulsan National Institute of Science and Technology (UNIST), Ulsan, Korea

Despite the well-recognized biological importance of protein phosphorylation, non-conventional forms of phosphorylation on histidine and arginine residues have evaded our attention and scrutiny for a long time. This gap in our understanding stems from the inherent chemical instability of phosphohistidine (pHis) and phosphoarginine (pArg), making the investigation of these forms of phosphorylation notoriously challenging.[1]

We present novel chemical tools to tackle these historically elusive protein modifications here. First, we describe convenient activity assays to monitor the phosphorylation and dephosphorylation of His/Arg in real-time. Our assays were successfully employed for the biochemical characterization and inhibitor discovery of the corresponding kinases and phosphatase. We also report our progress on developing chemoproteomic probes for these enzymes.



pHis



pArg

- ❑ Chemically unstable and difficult to study
- ❑ Key modulators of metabolism and protein degradation
- ❑ Novel tools for His/Arg phosphorylation
  - ✓ Convient enzyme activity assay methods
  - ✓ Novel kinase/phosphatase inhibitors
  - ✓ Affinity- and activity-based probes for proteomics

References

[1] Kee, J.-M.; Muir, T. W. *ACS Chem. Biol.*, **2012**, *7*, 44–51.
[2] Ahn, S.; Jung, H.; Kee, J.-M. *ChemBioChem*, **2021,** *22*, 319–325.
[3] Jung, H.; Choi, Y.; Lee, D.; Seo, J. K.; Kee, J.-M.* *Chem. Commun.* **2019,** *55*, 7482–7485.
[4] Choi, Y.; Shin, S. H.; Jung, H.; Kwon, O.; Seo, J. K.*; Kee, J.-M.* *ACS Sens.*, **2019**, *4*, 1055–1062.
[5] Lee, D.; Lee, Y.; Shin, S. H.; Choi, S.; Lee, S. H.; Jeong, S.; Jang, S.*; Kee, J.-M.* *Bioorg. Chem.* **2023**, *130*, 106232.
[6] Kim, H. J.; Jung, H.; Kim, S.; Seo, J. K.; Kee, J.-M.* *ACS Med. Chem. Lett.* **2022**, *13*, 1911–1915.