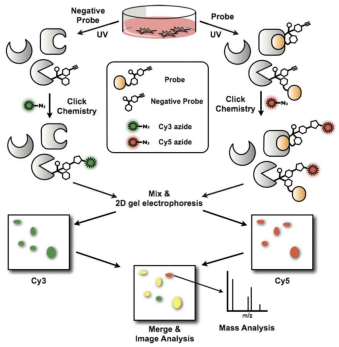
세미나 초록

발표주제	Photoaffinity Probes for the Investigation of Small Molecule–Protein Interactions
발표내용	Phenotype-based drug discovery has emerged as a promising approach for the discovery of first-in-class therapeutic agents. Even though this emerging technique enables innovation in the discovery of bioactive small molecules with novel mechanisms of action, phenotype-based approaches require successful identification of small molecule-protein interactions, which is the rate-limiting process in drug discovery. To overcome the bottle neck process, we devised a photoaffinity-based approach.[1-3] This approach employs a photoactivatable moiety that can generate reactive species upon ultraviolet (UV) irradiation and create covalent bonds with adjacent molecules. Owing to this covalent cross-linking of the probe with proteome, it becomes conceptually possible to pursue the target protein identification of bioactive small molecules with low efficacy (even micromolar activity), whereas the conventional affinity-based target identification (ID) approach requires that the probe have a single-digit nanomolar activity or better to ensure successful target ID via its high affinity toward target proteins. Therefore, photoaffinity-based target ID can significantly accelerate phenotype-based drug discovery through the target identification of early stage hit compounds. In this presentation, two successful cases of target protein ID will be discussed.[4,5,6]  **Figure 1.** Photoaffinity based target protein identification. In the second part of this presentation, electrochemical analysis of extracellular vesicles for disease diagnosis will be discussed. Extracellular vesicles, including exosomes, are nanoscale membrane particles that carry molecular information on parental cells. They are being pursued as biomarkers of various diseases, especially cancer that are difficult to detect or serially follow. To solve this issue, we developed a compact sensor technology for rapid, on-site exosome screening. The sensor is based on an integrated magneto–electrochemical assay: exosomes are immuno-magnetically captured from patient samples and profiled through electrochemical reaction. By combining magnetic enrichment and enzymatic amplification, the approach enables (i) highly sensitive, cell-specific exosome detection and (ii) sensor miniaturization and scale-up for high-throughput measurements. We demonstrated this system to screen extracellular vesicles in human body fluids such as plasma or urine samples from patients with ovarian cancer,[7,8] kidney transplant rejection[9] and colorectal cancer patients.[10] The sensor allowed for the simultaneous profiling of multiple protein markers within an hour, outperforming conventional methods in assay sensitivity and speed.

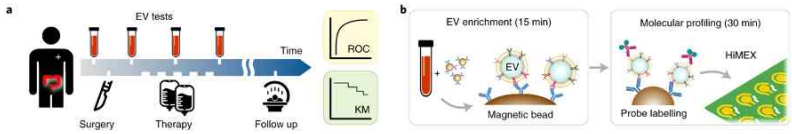


Figure 2. Extracellular vesicle analysis for disease diagnosis.

References

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