S09-6 A Microgram-Scale Labeling of Biomolecules via Rapid 6π-Azaelectrocyclization: Application to PET Imaging

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Positron emission tomography (PET) is a non-invasive method that quantitatively visualizes the locations and levels of radiotracer accumulation with high imaging contrast. In the present study, we focused on biomolecular-based tracers, which are composed of peptides and proteins. A new DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid)-labeling probe was designed and synthesized, DOTA-(*E*)-ester trienal, based on our previous findings of the "reverse electron-demanded 6π-azaelectrocyclization" due to the significant Frontier-orbital overlap by the obvious substituents effects. The high reactivity of the new probe enabled the modification of lysine residues in peptides and proteins at very low concentration ($< 10^{-8}$ M) within a short reaction time to result in selective labeling of the more accessible lysine residues. Only small amounts of peptides, proteins, and antibodies (1~100 μg) were efficiently labeled with the incorporation of 2~3 units of DOTA by incubating with the probe for 10 min at room temperature; the present electrocyclization protocol is also applicable to the rapid fluorescent labeling.

MicroPET of [^{68}Ga]DOTA-somatostatin, labeled by the present method, detected this tracer being accumulated in the pancreas. Furthermore, the first PET of glycoproteins, [^{68}Ga]DOTA-orosomucoid and asialoorosomucoid successfully visualized the differences in the circulatory residence of glycoproteins, in the presence or absence of the sialic acids.

The first "direct" whole cell-labeling and its application to the *in vivo* imaging, as well as the "cell-surface chemical engineering", all of these based on the rapid azaelectrocyclization chemistry, will also be discussed in the symposium.