ASURA Protects Sister-Chromatid Cohesion in Mitosis

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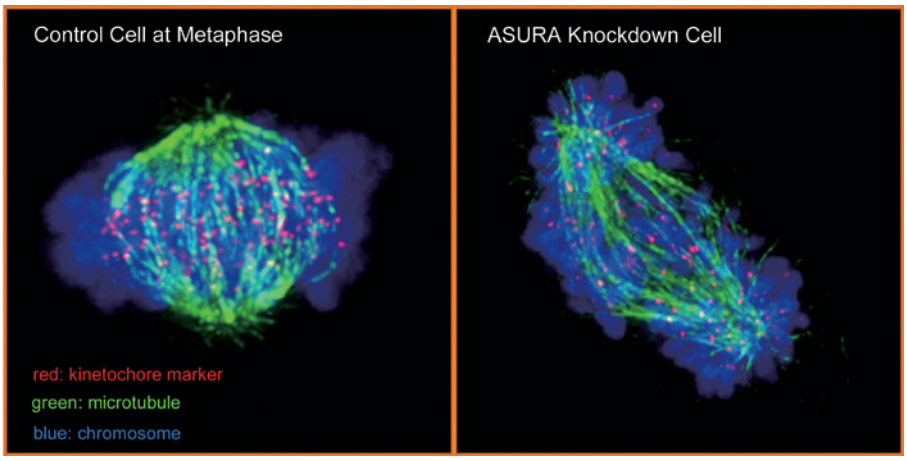
Cohesion between sister chromatids is essential for proper chromosome segregation in mitosis. In vertebrate mitotic cells, most cohesin is removed from the chromosome arms, but centromeric cohesin is protected by shugoshin until the onset of anaphase. However, the mechanism of this protection of centromeric cohesion is not well understood. Here, we demonstrate that ASURA (PHB2/REA/BAP37) is involved in the regulation of sister chromatid cohesion during mitosis in HeLa cells. ASURA is a multifunctional protein which derived from the Asura. Asura with 3 faces and 6 bodies worked most energetically in Buddhism. ASURA is an evolutionarily conserved protein in eukaryotes and has multiple functions, such as transcriptional regulation (REA; repressor of estrogen activation), mitochondria morphogenesis, apoptosis, cell viability and development, (PHB2; prohibitin2) and lymphocyte function (BAP37; B cell receptor associated protein 37). However, its functions in mitosis have not yet been determined. We show that depletion of ASURA by RNA interference (RNAi) causes premature sister chromatid separation and defects in chromosome congression accompanied with mitotic arrest by spindle checkpoint activation. In the absence of ASURA, cohesin is dissociated from centromeres during early mitosis, although the centromeric localization of shugoshin is preserved. Thus, our findings suggest that, in addition to the shugoshin, ASURA is also required to protect the centromeric cohesion from phosphorylation by Plk1 during early mitosis and that its function is essential for proper mitotic progression.



A Submicrogram-Scale Protocol for Biomolecule-Based PET Imaging by Rapid 6π-Azaelectrocyclization: Visualization of Sialic Acid Dependent Circulatory Residence of Glycoproteins

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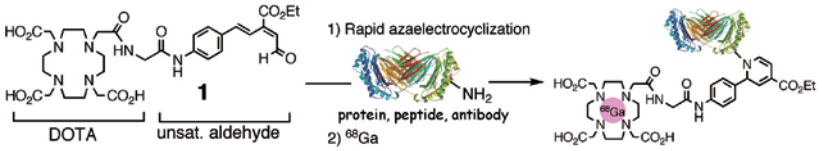
Fig. 1 Rapid labeling of biomolecules via 6π-azaelectrocyclization.



Positron emission tomography (PET) is a non-invasive method, which 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 aldehyde **1** (Fig. 1). The high reactivity of **1** enabled the modification of lysine residues in peptides and proteins to be completed in a very short time even at very low concentrations (~10^{-8} M) which resulted in selective labeling of the more accessible lysine residues. For examples, only small amounts of somatostatin, albumin, and cytokines (500 ng ~ 100 μg) were efficiently labeled with the incorporation of 2~3 units of DOTA by incubating with 10 equivalents of **1** for 10 min. The present electrocyclization protocol is also applicable to rapid fluorescent labeling; as less as 2 μg of anti-GFP antibody was successfully labeled retaining its GFP recognition activity with 90 % of the intact mAb. 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; sialic acids at the non-reducing end of the oligosaccharides significantly contribute to the metabolic stability of the glycoproteins in serum (Fig. 2).

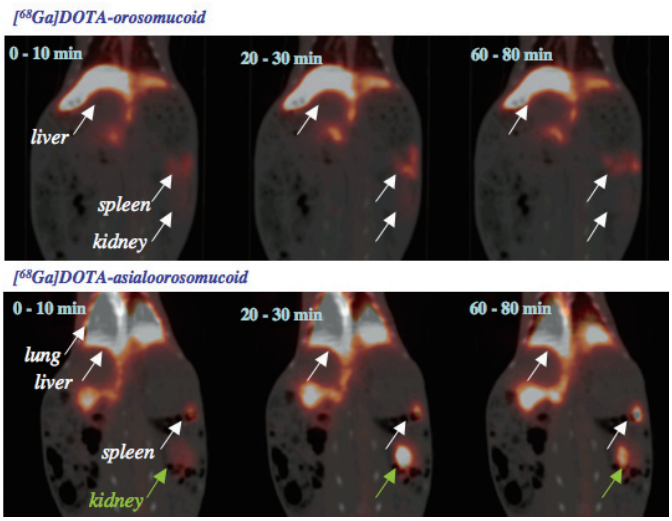


Fig. 2 Dynamic PET images of [^{68}Ga]DOTA-orosomucoid and asialoorosomucoid in rabbit.