



オートファジー研究会セミナー

Development of modified RavZ proteins selectively delipidating mATG8-PE on autophagosome using LC3-, GABARAP- selective LIRs identified from a novel method to characterize binding property of LIR motifs for mATG8s in live cells

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During selective or non-selective autophagy, autophagosome biogenesis, recognition/ recruitment of cargo is tightly regulated by mammalian ATG8 proteins (mATG8s) and their selective binding partners with a LC3-interacting region (LIR) motif. Although several putative LIR motifs have been identified, their selective binding property for each mATG8 and the functional significance on autophagy remain elusive. Here, we developed a novel method to characterize selective LC3- or GABARAP-binding LIR motifs in live cells using nuclear localization signal. Using our method, we could identify selective LC3C-, GABARAP/-L1- or GABARAP-L2-binding LIR motif. Our structural analysis identified the critical residues in LIR motif or in LC3/GABARAP protein required for their selective interaction. Furthermore, by replacement of LC3 or GABARAP-selective LIR motifs into modified RavZ protein, we developed a new tool to selectively cleave PE conjugated mATG8 to understand specific roles of lipidation of mATG8 on autophagy/selective autophagy. Therefore, our modified RavZ will be very useful tool to study the functional significance of each PE-mATG8 on selective autophagy in various cellular contexts.

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