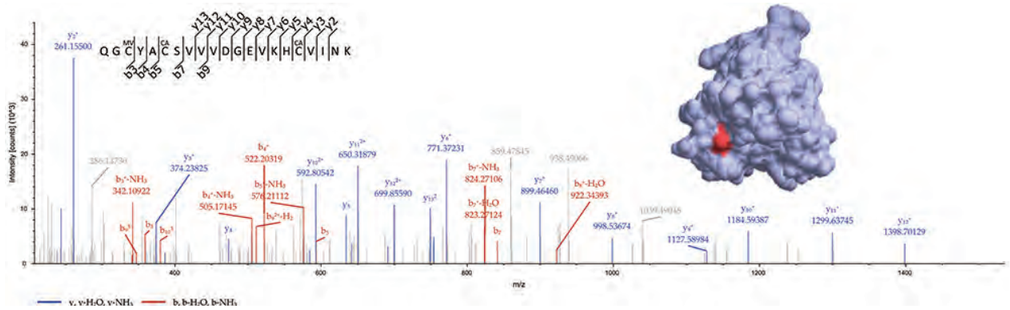
生命分子解析ユニット
Biomolecular Characterization Unit

タンパク質の構造を調べて、生命現象の謎にせまります

研究テーマ

- 生体分子の翻訳後修飾を含めた詳細な構造解析
- 生体分子の定量的解析法の開発
- RNAの質量分析

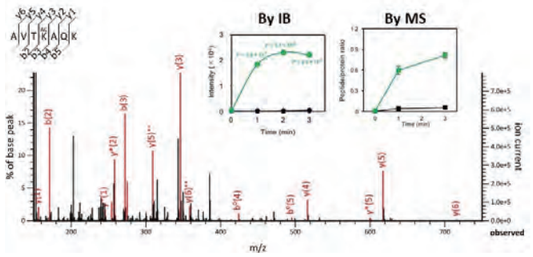
当ユニットは、生命現象の解明に向け、生体成分構造解析法の開発や構造解析の応用研究を行っている。生体成分の中でも特にタンパク質は生命現象の源であり、さまざまな生物活性がある。そのタンパク質の構造を詳細に調べることで、 活性と遺伝子との対応、生物学的活性のメカニズムや活性の制御機構を解明する。また、装置ならびに設備の設置や管理、解析方法に関する情報の整備をすることで研究支援を行っている。



Identification of PI3K p85 modification site by Methyl Vinyl Ketone (MVK)
LC-MS/MS spectrum of Cys656-containing PI3K p85 peptide modified by MVK. Inset shows the crystal structure of the cSH2 domain shown in the molecular surface model. Red residue indicates Cys656.

研究成果

- 活性カルボニルの修飾を介したPI3K抑制機構を解明するために、質量分析でメチルビニルケトン修飾部位を決定した。
- p300によるヒストンアセチル化が伝播するエピジェネティックなメカニズムを解明するために、ヒストンのアセチル化を質量分析で定量した。
- CRISPR-Cas酵素の祖先タンパク質の立体構造を解明するためにLC-MS/MSで複合体中のRNAの構造を決定した。



Identification of acetylated site of p300-reactedhistone N-terminal tails (H2B K20Ac)
LC-MS/MS spectrum of acetylated 17-23 peptide of H2B in the N-terminal tail of the p300BRPHZT-reaction histone.
The insets show the quantification of acetylation of H2B K20 in the p300BRPHZT-reaction histone by immunoblotting (left) and mass spectrometry (right). Black and green lines indicate data with the unmodified and the H4K12/K16-acetylated nucleosomes as substrates (1μM), respectively.

To resolve the mystery of biological phenomena, we examine the protein structure

Research Subjects

- Development and application of analytical methods for structural details on biological molecules
- Development of quantitative analysis of biomolecules
- Identification and characterization of RNA by mass spectrometry

Our unit provides high quality structural characterization methods to the field of biological science, aiming to further understand the mechanism and action of biological molecules. We manage specialized and technical instruments including protein chemical analyses, mass spectrometry. Our challenge to research, develop and fine-tune novel characterization methods for biological molecules, is an endless yet rewarding process.

Research Results

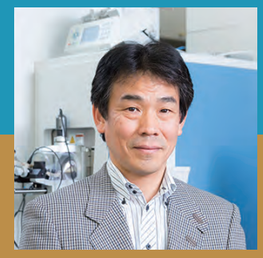
- The methyl vinyl ketone modification site of PI3K was determined by mass spectrometry to elucidate the mechanism of enzyme inhibition via modification of the active carbonyl.
- The histone acetylation by p300 was quantified by mass spectrometry to elucidate the epigenetic mechanisms to propagate histone acetylation by p300.
- The structure of the RNA in the complex was determined by LC-MS/MS to elucidate the three-dimensional structure of the ancestor protein of the CRISPR-Cas enzyme.

主要論文 / Publications

Morimoto, A. *et al.*
Methyl vinyl ketone and its analogs covalently modify PI3K and alter physiological functions by inhibiting PI3K signaling.
J. Biol. Chem. **300**, 105679 (2024)

Kikuchi, M. *et al.*
Epigenetic mechanisms to propagate histone acetylation by p300/CBP.
Nat. Commun. **14**, 4103 (2023)

Nakagawa, R. *et al.*
Cryo-EM structure of the transposon-associated TnpB enzyme.
Nature **616**, 390-397 (2023)



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