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フォールディングとアンフォールディングの自在操作の実現
Recent Advances in Operating Protein Folding

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Understanding the dynamic assembly of protein disulfide isomerase enzymes during their catalytic reaction ([1]*Frontier Research Institute for Interdisciplinary Sciences, Tohoku University*)○Masaki Okumura[1]

ヒト小胞体内は、ジスルフィド結合の形成を伴った立体構造形成を触媒する 20 種類以上もの酵素群 PDI family が存在し、抗体等が品質管理される。本発表では、PDI family 酵素群の生物学的理解に立脚しデザインし化合物が酵素と匹敵する機能について紹介し、バイオ医薬品の品質を支えるスマートケミストリーの今後について議論したい。

In the human endoplasmic reticulum, there are more than 20 types of enzymes, the Protein Disulfide Isomerase (PDI) family, which catalyze the disulfide-coupled protein folding. Therefore, PDI family control the quality of a large number of proteins such as IgG and insulin. In this presentation, I would like to introduce the de novo designed compounds based on biological understanding of the PDI family enzymes, and discuss the future of smart chemistry that supports the quality of biopharmaceuticals.

1) A unique leucine-valine adhesive motif supports structure and function of protein disulfide isomerase P5 via dimerization. M. Okumura, S. Kanemura, M. Matsusaki, M. Kinoshita, T. Saio, D. Ito, C. Hirayama, H. Kumeta, M. Watabe, Y. Amagai, Y.H. Lee, S. Akiyama, K. Inaba K, *Structure.* **2021**, *29*, 1357.
2) Dynamic assembly of protein disulfide isomerase in catalysis of oxidative folding. M. Okumura, K. Noi, S. Kanemura, M. Kinoshita, T. Saio, Y. Inoue, T. Hikima, S. Akiyama, T. Ogura, K. Inaba K, *Nat Chem Biol.* **2019**, *15*, 499.
3) Semi-enzymatic acceleration of oxidative protein folding by N-methylated heteroaromatic thiols. S. Okada, Y. Matsumoto, R. Takahashi, K. Arai, S. Kanemura, M. Okumura, T Muraoka, *Chem. Sci.* **2023**, *14*, 7630.

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