


## 【Grant-in-Aid for Transformative Research Areas (A)】

### Chronoproteiology: Protein Machinery that drives "time" on various time scales

	Principal Investigator	Tokyo Metropolitan Institute of Medical Science , Circadian Clock Project ,Project Leader YOSHITANE Hikari	Researcher Number : 70569920
	Project Information	Project Number : 24A304 Keywords : circadian rhythm, seasonal response, protein, posttranslational modification, translation	Project Period (FY) : 2024-2028

#### Purpose and Background of the Research

##### ● Outline of the Research

We sleep at night and wake up in the morning. In addition to this sleep-wake cycle, various physiological functions such as body temperature, hormone secretion, organ function, and gene expression show daily patterns. This circadian rhythm maintains even without environmental cues such as light and dark. The internal mechanism that counts the 24 hours is called the circadian clock. Other rhythms are also observed on different ranges of time scales from seconds to years (or centuries), such as heartbeat, segmentation clock, seasonal response, and bamboo mass flowering. In this research area, we focus on rhythmic phenomena and timer-like mechanisms and aim to elucidate the molecular mechanisms that count the "times" in various processes. Particular attention is paid to protein dynamics, such as physical properties of specific proteins, enzyme activities, protein-protein interactions, post-translational modifications, conformational changes, and translational controls; given that, we have named this research area "Chrono-Proteiology". Researchers working on this topic across diverse species and a wide range of time scales are welcome to join.

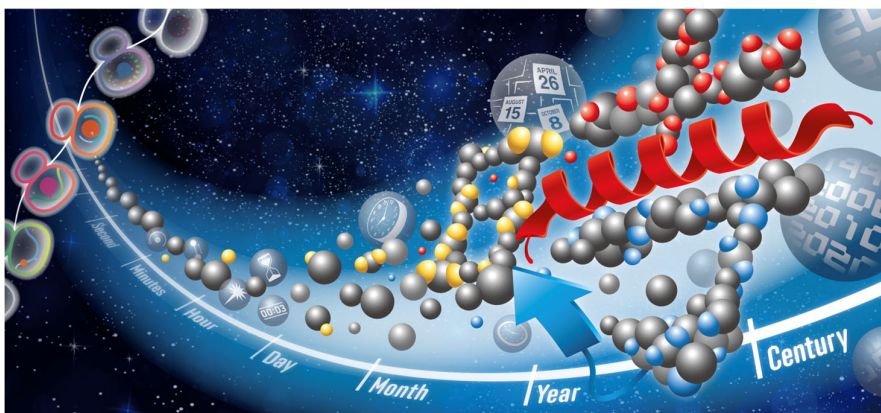


Figure 1. Image of Chrono-Proteiology

##### ● The Transformative Research Areas (A) "Chrono-Proteiology" is based on the two former TR Areas (B) "Chrono-Proteiology" and "Parametric Translation".

In Fig. 1, the Kanji character for the "time" is represented by the three-dimensional structure of a protein as the area logo of "Chrono-Proteiology". On the other hand, the area logo of "Parametric Translation" contains four symbols in the translation machinery "ribosome", generating the "time" of Chrono-Proteiology. By giving it a horizontal axis from seconds to centuries, this image indicates that various time scales are included in our research targets.

##### ● Analytical support

The Chrono-Proteiology provides a wide range of analytical supports.

- 1, Sequence determination of genome, RNA, and protein in non-model organisms.
- 2, RNA-Seq, Ribo-Seq, ATAC-Seq, DNA methylation analysis, etc.
- 3, Protein quantification using the next-generation mass spectrometer "ASTRAL".

Compared with RT-PCR for a limited number of genes, RNA-Seq technology has advanced our knowledge about gene expressions. In some cases, however, protein levels do not correlate with RNA levels, due to some mechanisms such as regulation of translation efficiency without changes in RNA levels. Therefore, a comprehensive omics approach at the protein level has been awaited. The "ASTRAL" accurately quantifies more than 10,000 proteins at ultra-high speed, and the time has come to describe the whole forest with the resolution to see the details of each tree and get the whole picture.



Figure. 2 Next-generation mass spectrometer "ASTRAL"

#### Expected Research Achievements

The Transformative Research Area (A) "Chrono-Proteiology" will reveal the principles of autonomous oscillations and period determination of biological clocks by focusing on protein dynamics, such as physical properties of specific proteins, enzyme activities, protein-protein interactions, post-translational modifications, conformational changes, and translational controls, through the following three research projects.

##### ● project 1: Chrono-Proteiology for circadian rhythms

We aim to identify the molecules that count the "time" and determine the 24-hour period in the circadian clockwork. Based on autonomous photosynthetic rhythms in enucleated *Acetabularia* (without transcriptional rhythms), we will test the possibility that protein oscillators, like cyanobacterial KaiC, drive autonomous rhythms also in eukaryotes. We aim to understand the principle of autonomous oscillation by applying the understanding and research strategies developed by the KaiC research to eukaryotes such as enucleated *Acetabularia* and mice.

##### ● project 2: Chrono-Proteiology for non-24-hours rhythms

Focusing on rhythmic phenomena on various time scales, such as the seasonal responses driven by the 365-day circannual clock and the bamboo flowering with a cycle of 5-120 years, we aim to elucidate the molecular mechanisms that count the "time" on various time scales and the mechanisms that determine their periods, by applying our knowledge and strategies developed by the circadian clock research.

##### ● project 3: Parametric Translation for supporting Chrono-Proteiology

The unique approach of measuring and controlling translation efficiency provides a technical basis for research projects in this area. It is generally accepted that transcription factors and RNA levels determine the amount of protein synthesis. However, recent studies have shown that the protein amount produced from a single copy of RNA is dynamically regulated at the translation level. Considering that clocks counting days and years receive to temporal and seasonal cues from noisy and slowly changing environmental cycles, the translation control can tune the clocks to respond to the cues, as shown by Transformative Research Area (B) "Parametric Translation". We will elucidate the role of the translational control in the rhythms across time scales.

Homepage  
Address, etc.

Homepage <https://chronoproteiology.org>

