Iwate Medical University

# Protein dynamics in response to genotoxic drugs regulated by proteasome system

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# COI Disclosure Information

## Kohei Kume

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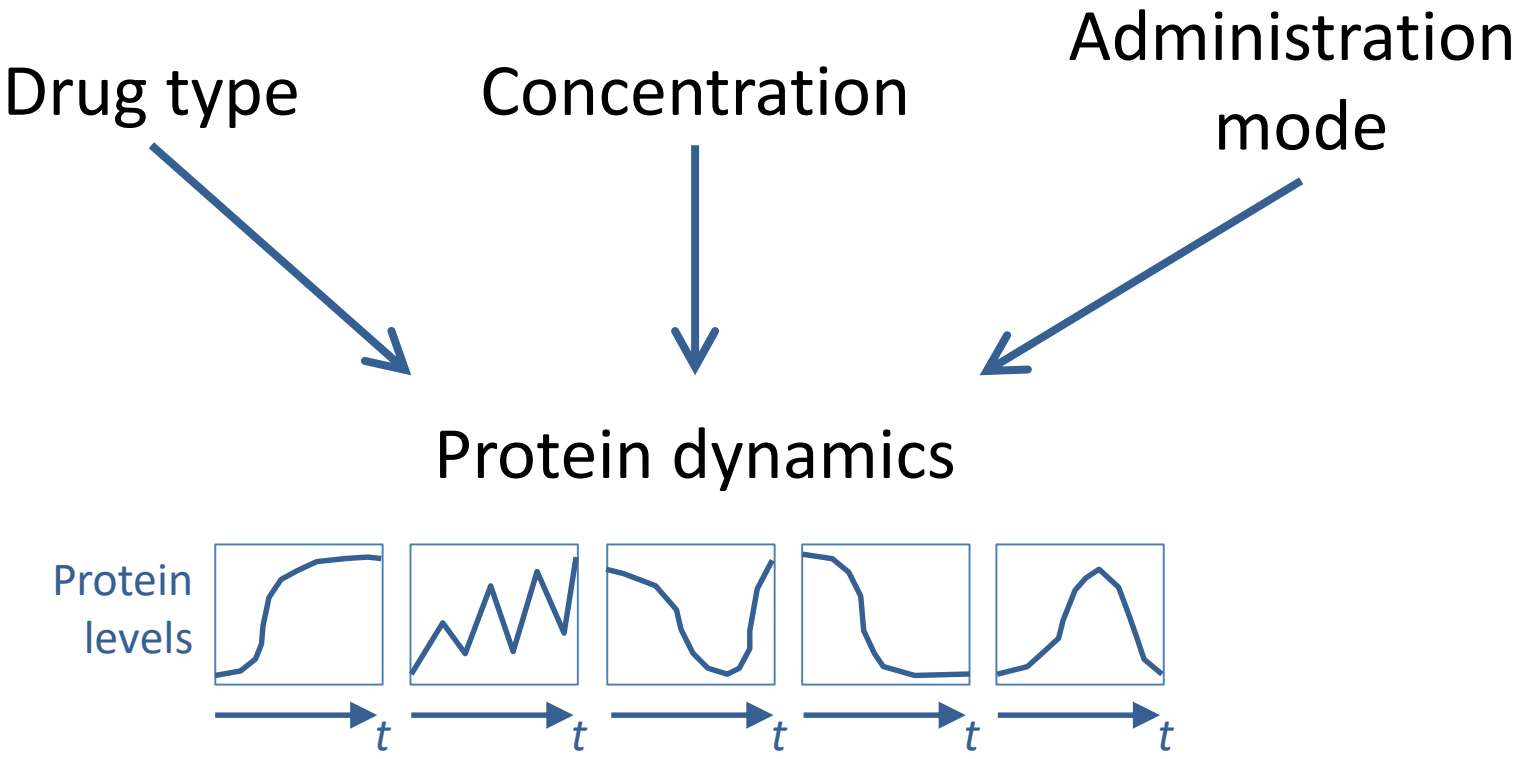
**I have no financial relationships to disclose.**

# Protein dynamics is differentially altered by various drug treatments




Little is known about systematic methods for multidimensional protein dynamics.

Journal of proteome research

Article

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# Systematic Protein Level Regulation via Degradation Machinery Induced by Genotoxic Drugs

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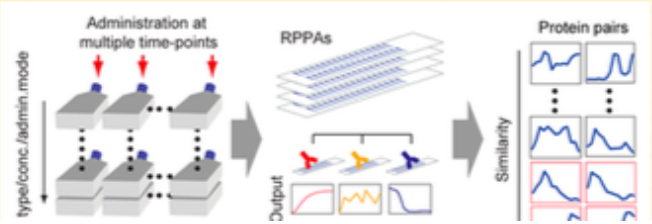
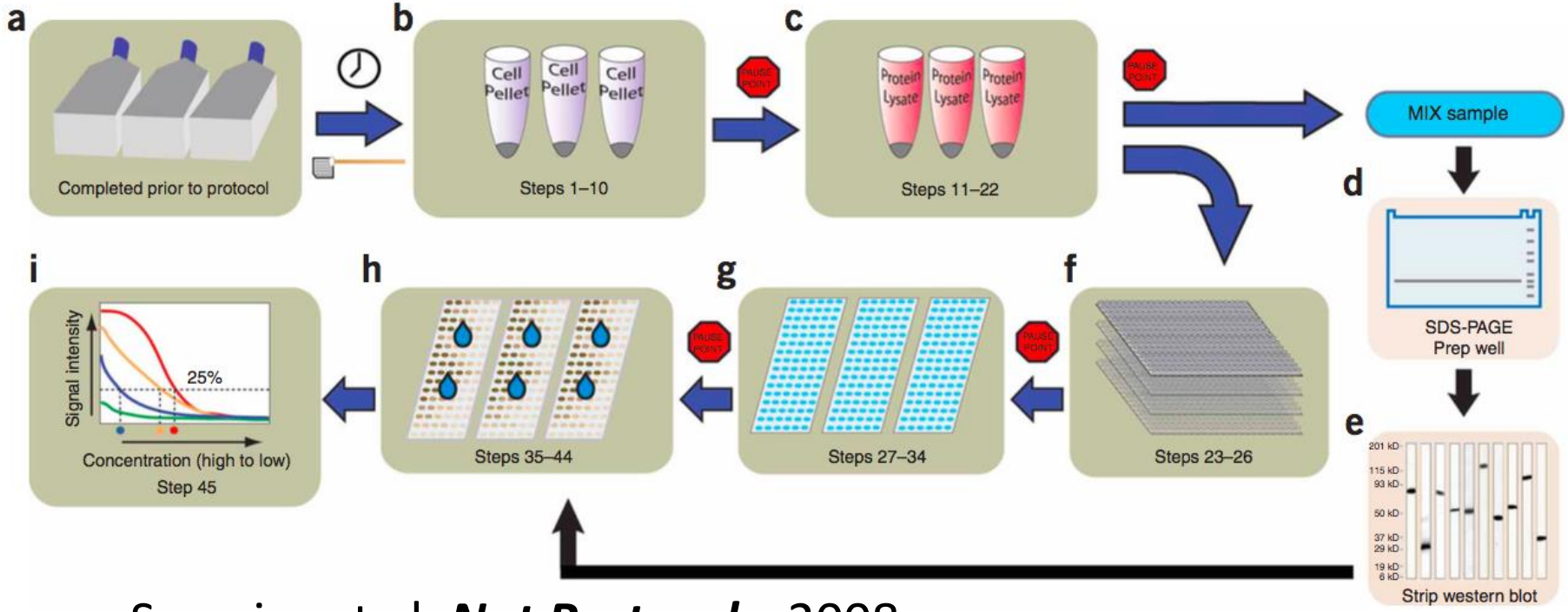
*Supporting Information*

**ABSTRACT:** In this study we monitored protein dynamics in response to cisplatin, 5-fluorouracil, and irinotecan with different concentrations and administration modes using "reverse-phase" protein arrays (RPPAs) in order to gain comprehensive insight into the protein dynamics induced by genotoxic drugs. Among 666 protein time-courses, 38% exhibited an increasing trend, 32% exhibited a steady decrease, and 30% fluctuated within 24 h after



# Reverse-phase protein arrays (RPPAs)

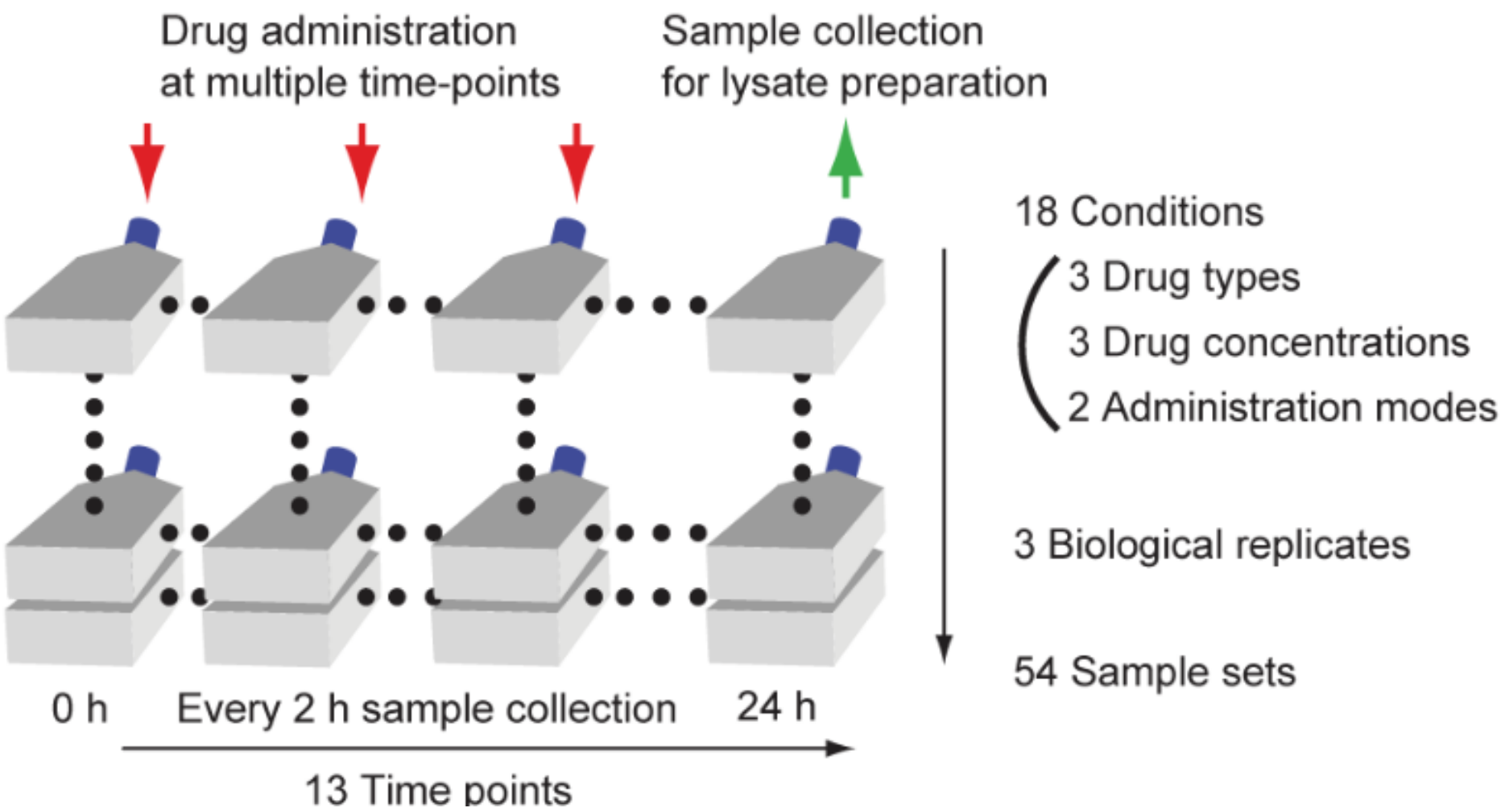



Spurrier et al. ***Nat Protocols***, 2008

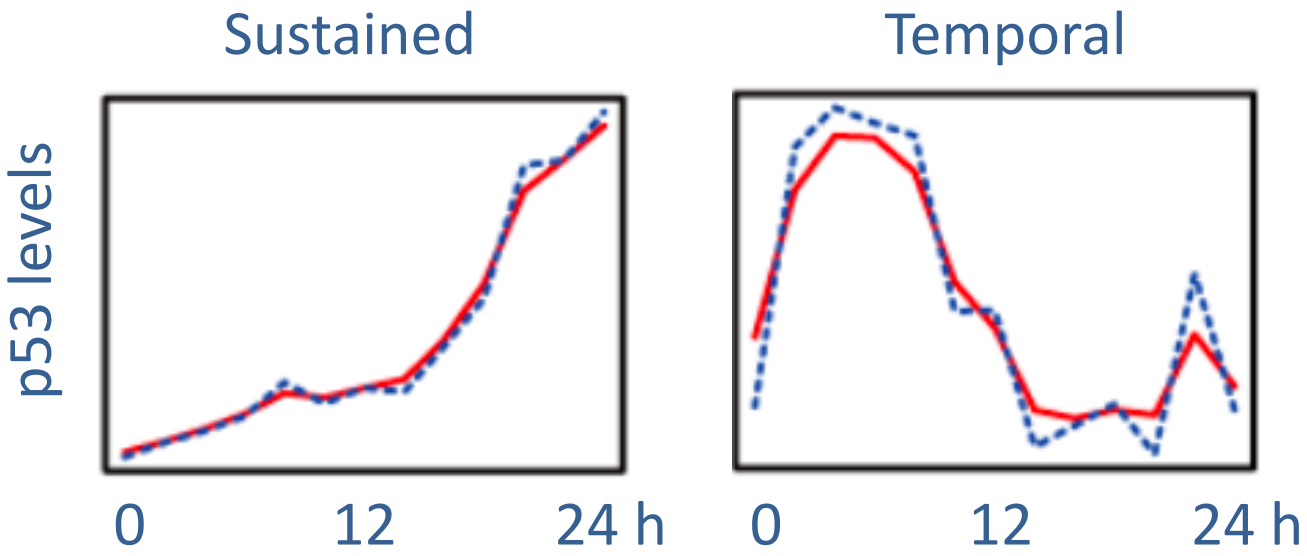
Nishizuka SS, inventor; Japanese patent 2010-081879

A micro-scale dot blot that can monitor protein levels across >10,000 data points.

# Monitoring protein dynamics in response to genotoxic drugs using RPPA



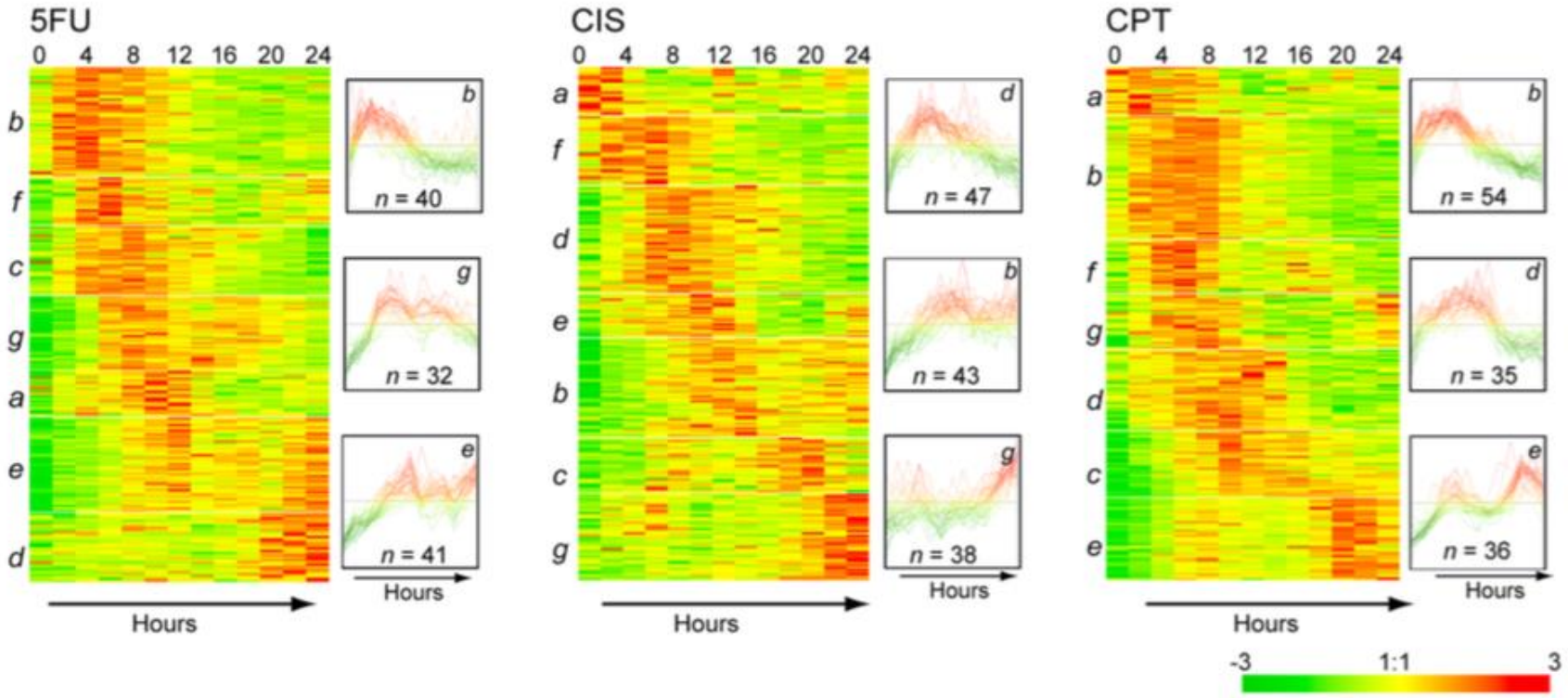
# The genotoxic stress response was immediately reset following drug removal.



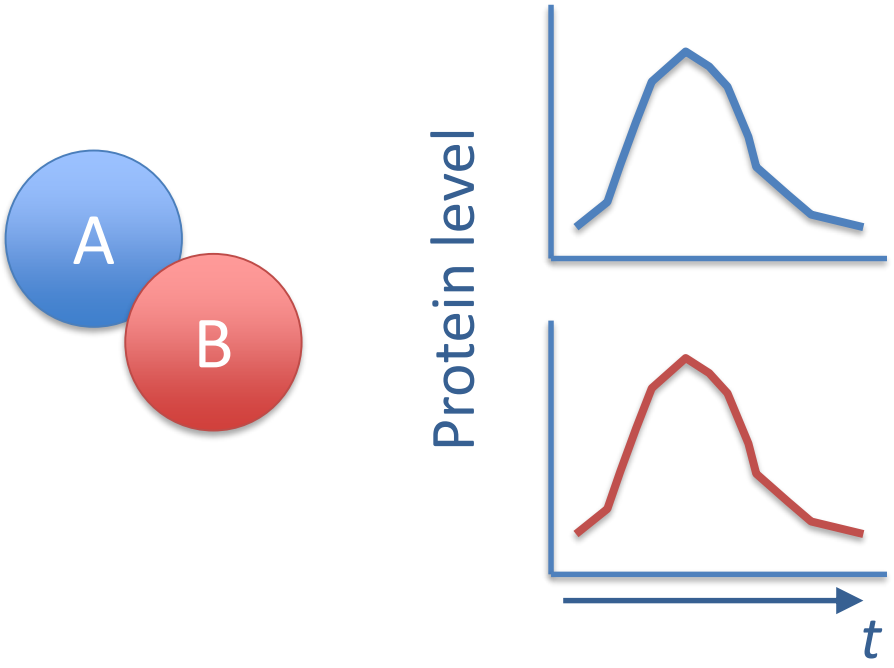

RPPA system is suitable for evaluating the protein dynamics of drug response.

# 666 protein dynamics for 37 proteins over 24 h

222 dynamics of 37 proteins

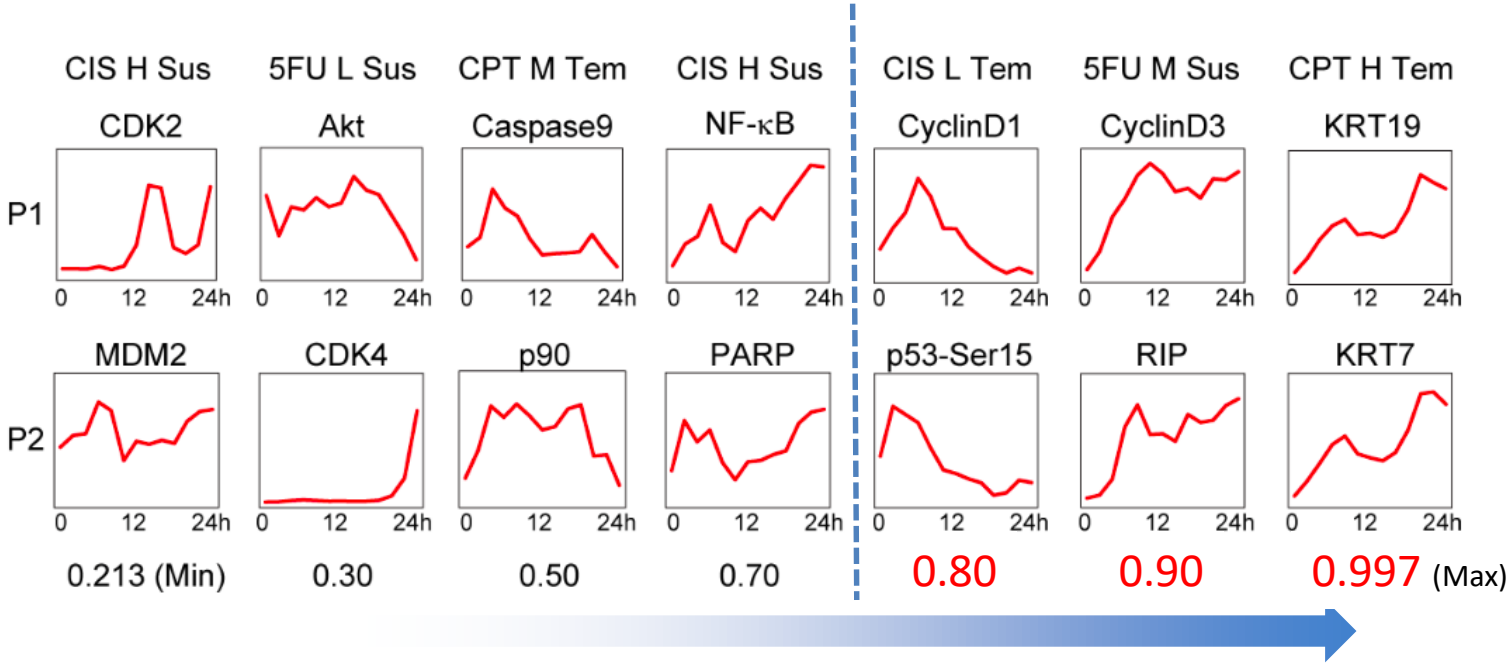


# Similarity measurement of protein dynamics using *dCor*

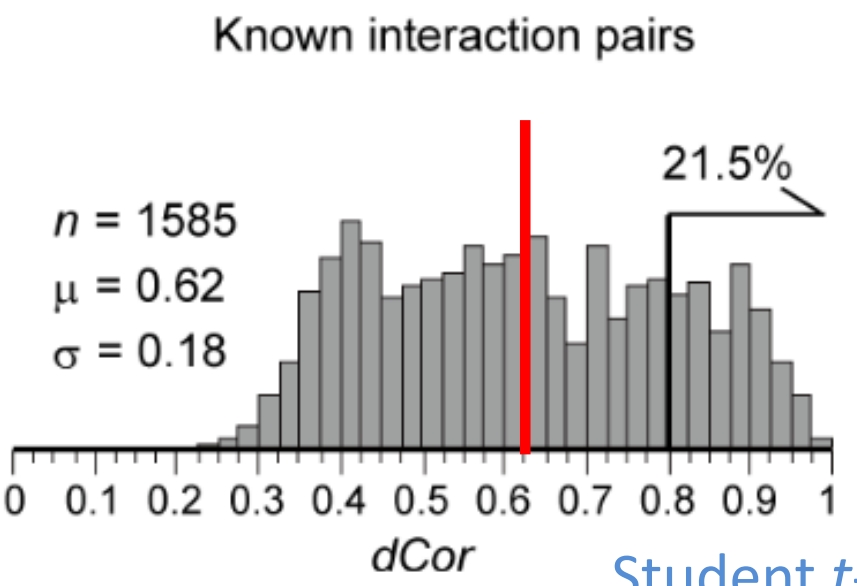


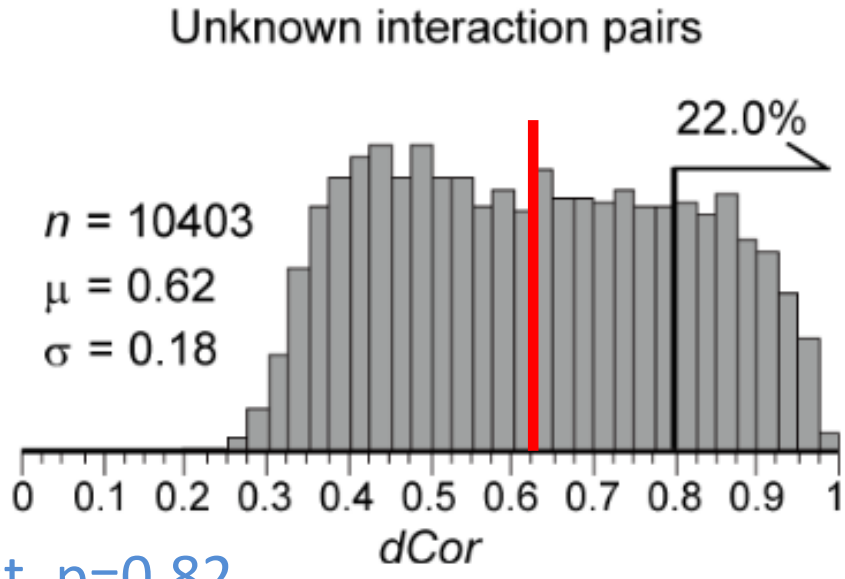

$$dCor(X, Y) = \frac{dCov(X, Y)}{\sqrt{dCov(X, Y)\, dCov(X, Y)}}$$

# Similarity measurement of protein dynamics using distance correlation, *dCor*



# No significant difference between protein pairs of known and unknown interactions



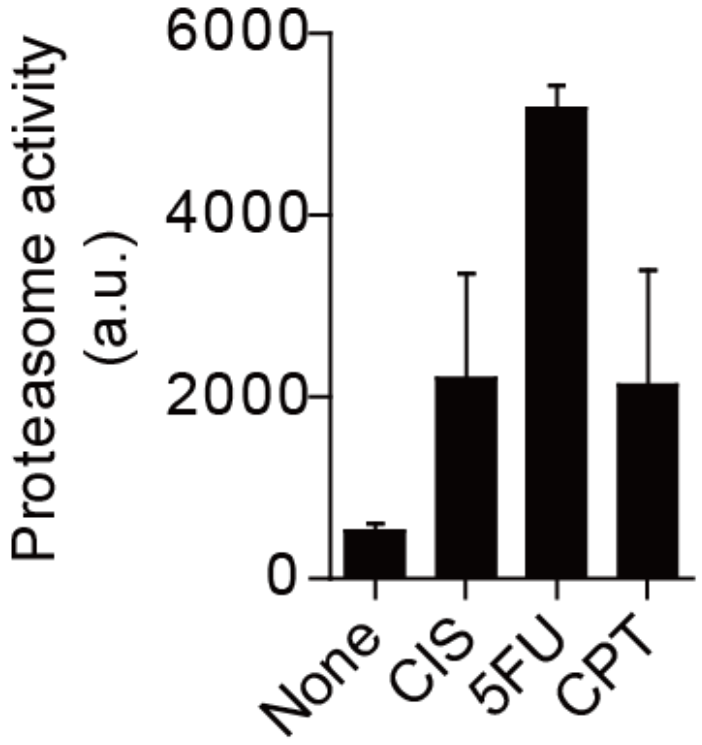




Student *t*-test, p=0.82

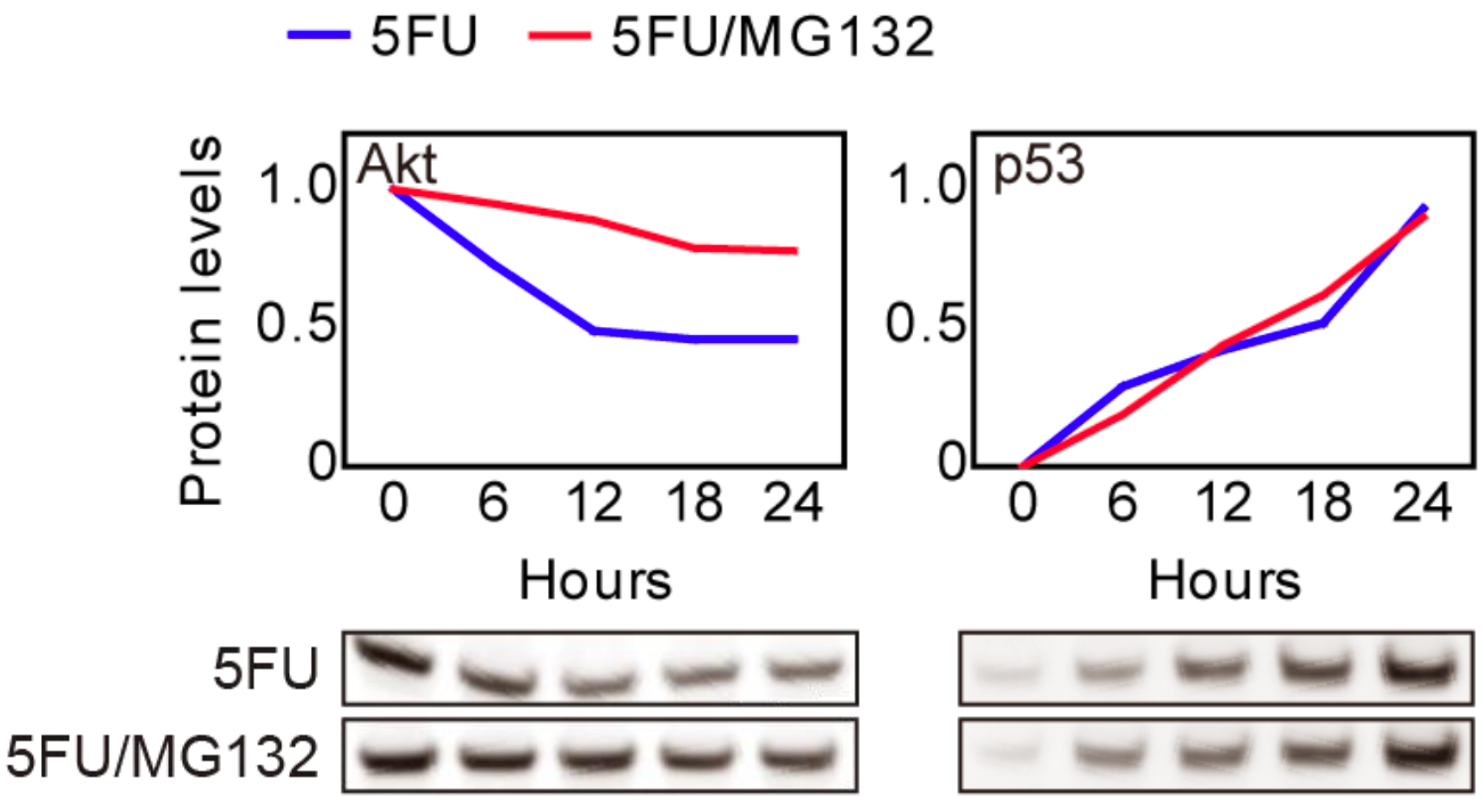
Wilcoxon test, p=0.86

Functionally distinct proteins may be regulated by common degradation machinery.

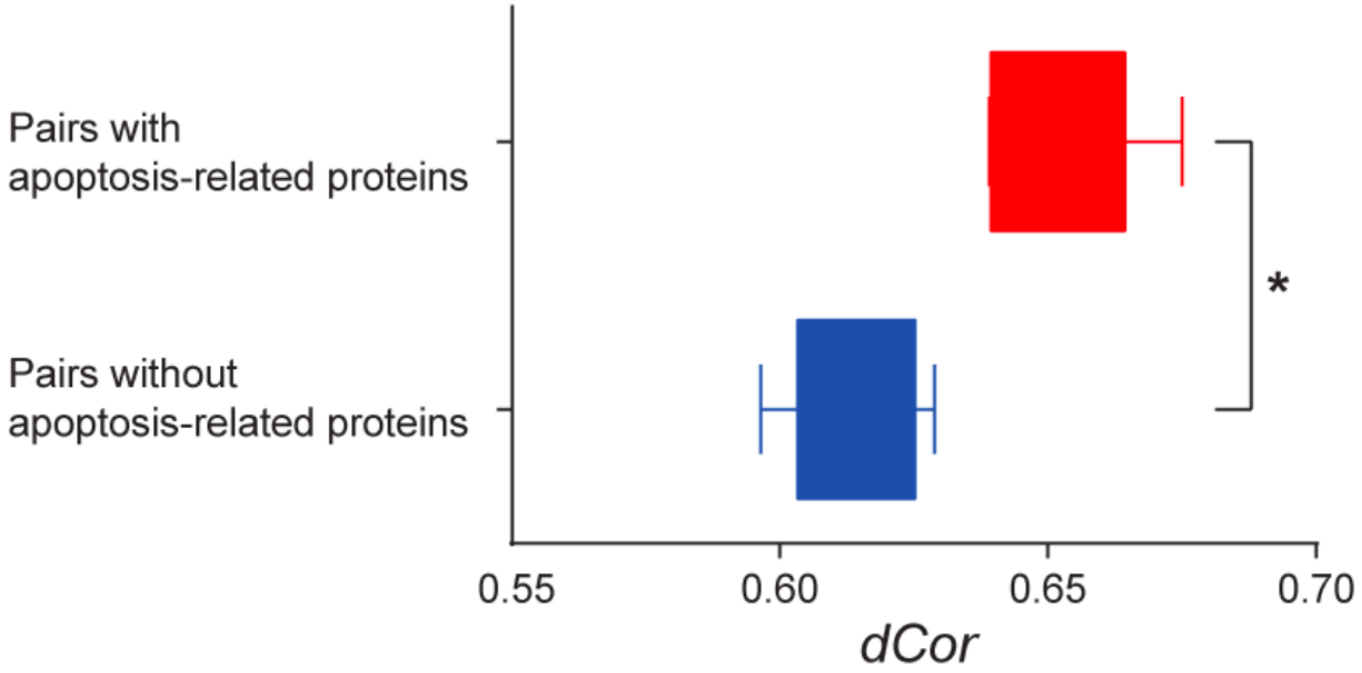
# Proteasome activity was increased in response to genotoxic drugs



# Protein dynamics altered by a proteasome inhibitor



# *dCor* in protein pairs with or without apoptosis-related proteins




The average dCor of pairs that had at least one apoptosis-related protein was significantly higher than those without the apoptosis-related proteins.

# Summary

- Protein levels could be changed immediately after drug administration.
- Functionally distinct proteins may be regulated by common degradation machinery.
- Apoptosis-related degradation machinery may play a key role in systematic protein level regulation.

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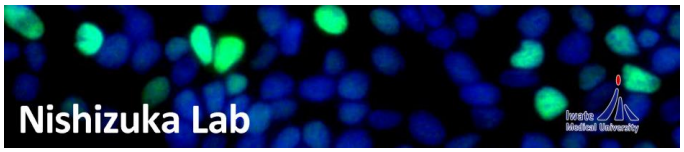
システム癌 新次元

科研費 KAKENHI

JAPAN PRIZE

Nishizuka Lab

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