Systems Cell Biology Group

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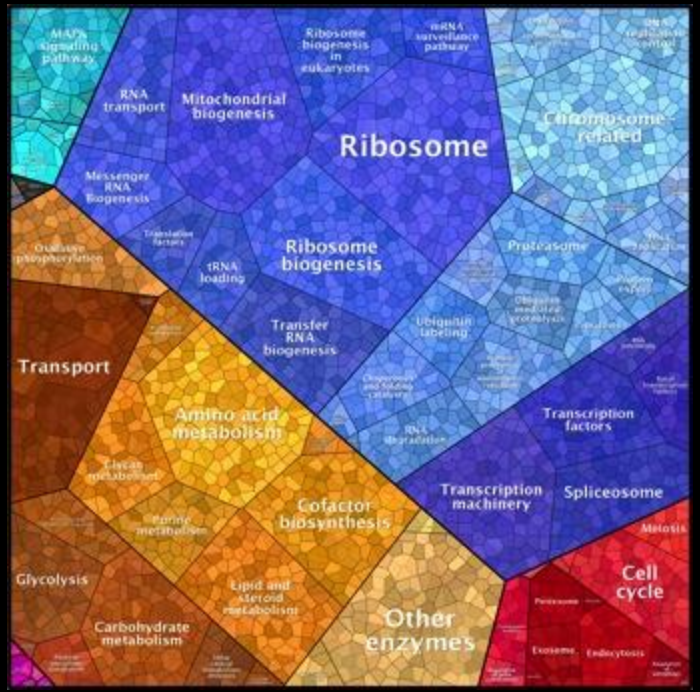
The research field performed in my lab is called “**Systems Cell Biology**” where cellular functions are analyzed using molecular biology and genomics with the help of computer sciences such as bioinformatics and mathematical modeling.

We have developed original method “**gTOW**” to analyze cellular **robustness** (how cellular systems cope with perturbations). We are focusing on how **overexpression** of certain proteins cause cellular growth defects, and how cells cope with the harmful effects.

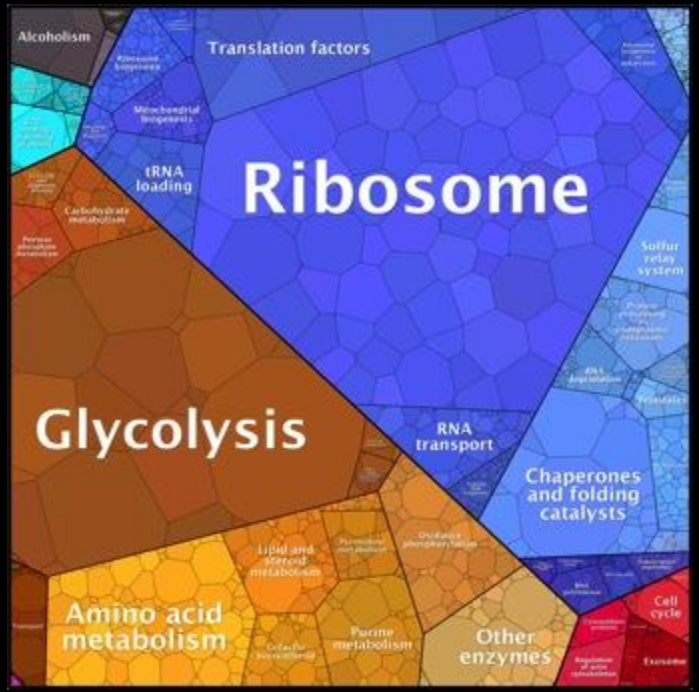
Our findings provide basic knowledge **how expression level of each protein is determined**, and may also help to understand the states of cancer cells where proteins are overexpressed due to the chromosomal number increase. The gTOW method is also used to produce large amount of proteins in yeast cells.

Main issue : How expression level of each protein is determined?

Yeast Genome (SGD)



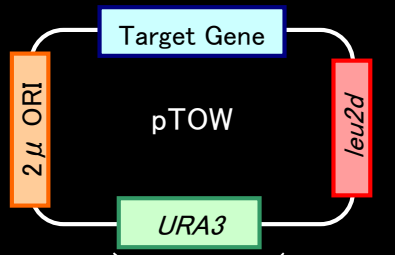
Yeast Proteome (Kulak 2014)

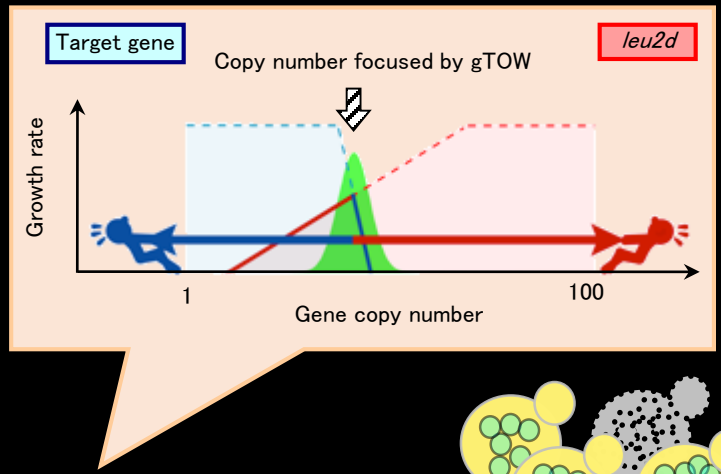


Main technology: gTOW method

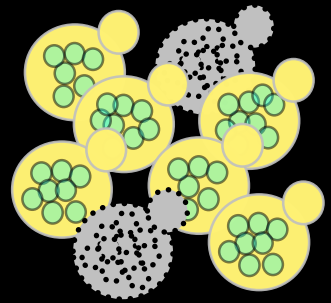
Measure the over-expression limit of each target protein

① Introduce a gTOW plasmid with a target gene into cells





② Leu− conditions: Increase plasmid copy number (>100)

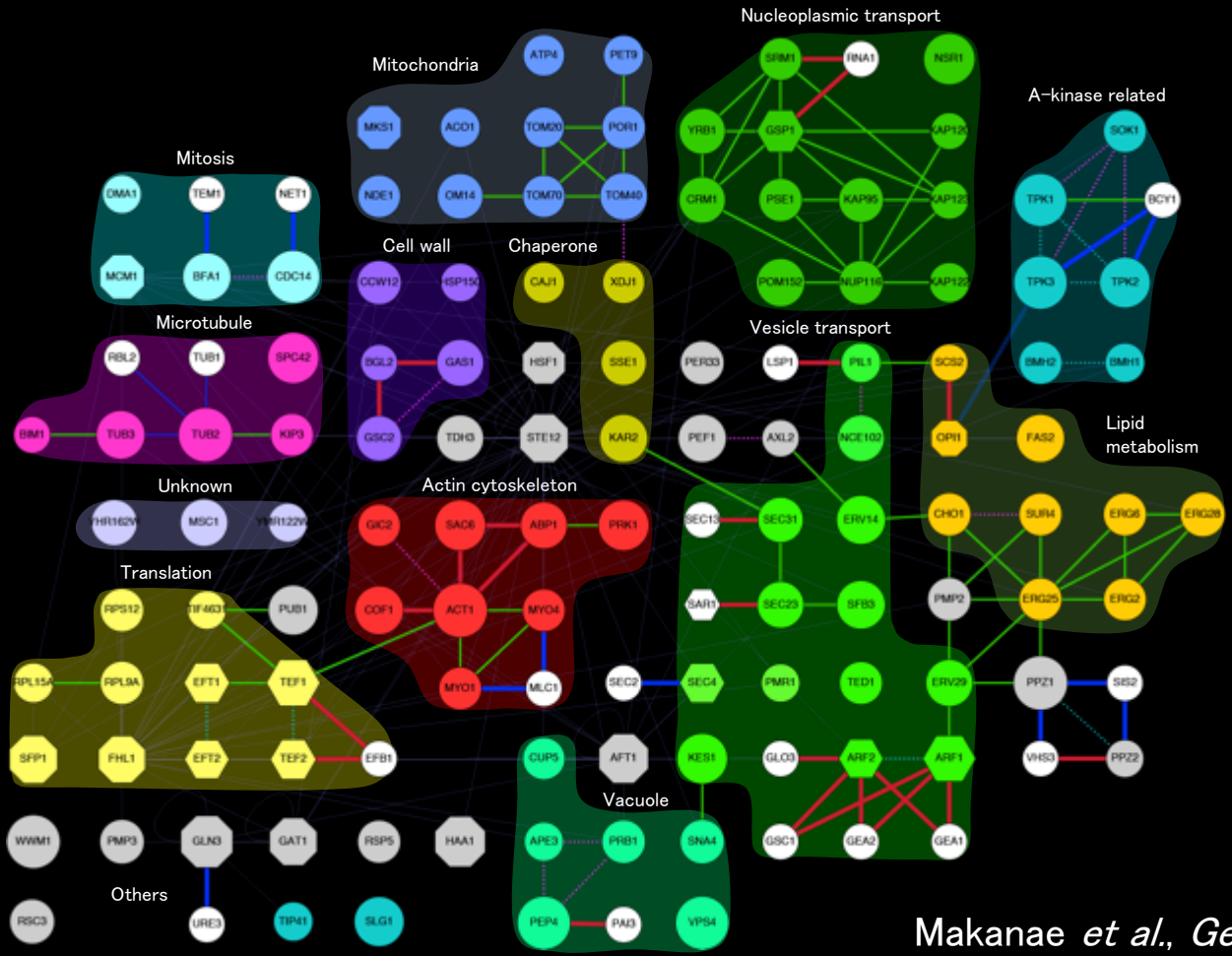


- Plasmid becomes multicopy
- Copy numbers are diverse

③ Measure plasmid copy number, growth rate, GFP fluorescence

Moriya *et al.*, *PLoS genet.* 2006

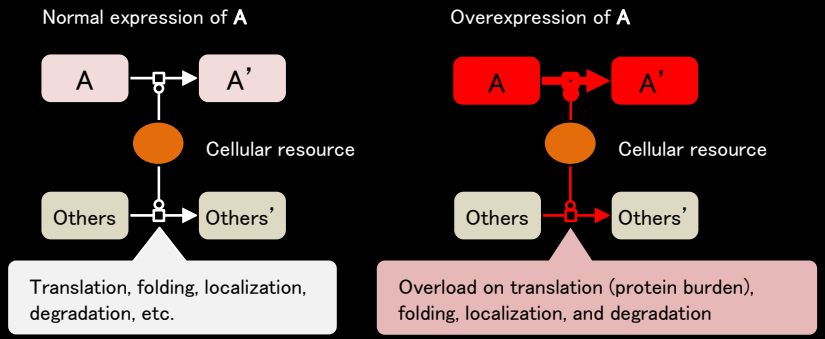
Proteins whose minor overexperssion causes growth defects



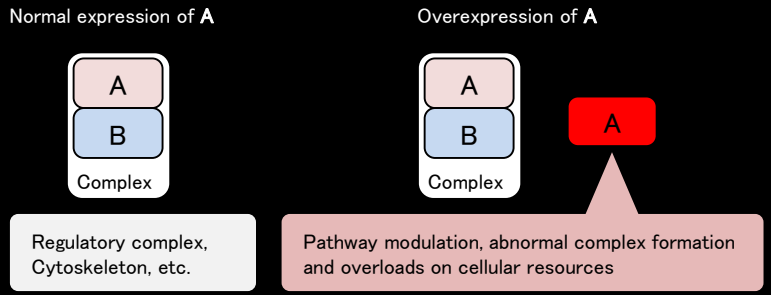
Makanae *et al.*, *Genome Res* 2013

Consequences of overexpression

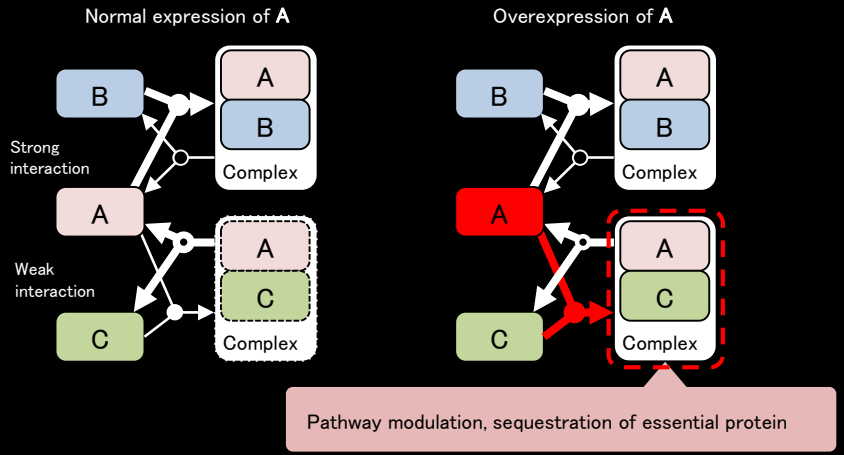
A. Resource overload



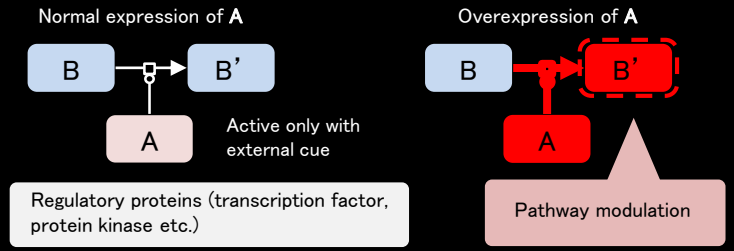
B. Stoichiometric imbalance



C. Promiscuous interactions



D. Pathway modulation



Moriya, *Mol. Biol. Cell* 2015

Selected publications

- Ishikawa K, Makanae K, Iwasaki S, Ingolia NT, Moriya H., Post-Translational Dosage Compensation Buffers Genetic Perturbations to Stoichiometry of Protein Complexes., PLoS Genet. 2017 Jan 25;13(1):e1006554.
- Kintaka R, Makanae K, Moriya H., Cellular growth defects triggered by an overload of protein localization processes., Sci Rep. 2016;6:31774.
- Moriya H., Quantitative nature of overexpression experiments., Mol Biol Cell. 2015 Nov 5;26(22):3932-9.
- Makanae K, Kintaka R, Makino T, Kitano H, Moriya H., Identification of dosage-sensitive genes in Saccharomyces cerevisiae using the genetic tug-of-war method., Genome Res. 2013 Feb;23(2):300-11.
- Moriya H, Makanae K, Watanabe K, Chino A, Shimizu-Yoshida Y., Robustness analysis of cellular systems using the genetic tug-of-war method., Mol Biosyst. 2012 Aug 28;8(10):2513-22.
- Moriya H, Chino A, Kapuy O, Csikász-Nagy A, Novák B., Overexpression limits of fission yeast cell-cycle regulators in vivo and in silico., Mol Syst Biol. 2011;7:556.
- Kaizu K, Moriya H, Kitano H., Fragilities caused by dosage imbalance in regulation of the budding yeast cell cycle., PLoS Genet. 2010;6(4):e1000919.
- Moriya H, Shimizu-Yoshida Y, Kitano H., In vivo robustness analysis of cell division cycle genes in Saccharomyces cerevisiae., PLoS Genet. 2006 Jul;2(7):e111.

Related webpages explaining our projects

- HM‘s personal website http://tenure5.vbl.okayama-u.ac.jp/~hisaom/HMwiki/index.php?TopEnglish
- Okayama University Medical Research Updates (OU-MRU) Vol.37 https://www.okayama-u.ac.jp/eng/research_highlights/index_id48.html
- Okayama University Medical Research Updates (OU-MRU) Vol.36 https://www.okayama-u.ac.jp/eng/research_highlights/index_id47.html
- Okayama University e-Bulletin Vol.3 http://www.okayama-u.ac.jp/user/kouhou/ebulletin/research_highlights/vol3/highlights_003.html

HM lab member y-2017

2 post-docs, 3 technicians, 2 PhD students, 1 MD student