

Molecular Genetics in the post-genomic era 2020/21

Mondays 12.15-14.00, Katzir room, Green building 010

Teacher: Martin Kupiec

Pre-requisite: Intro to Genetics 0455-2526

Course's aim: The course's aims are: a) To get to know the new technologies developed and the way questions can be asked once genomic sequences are available. b) To learn how to read scientific papers in a critical way. c) To learn how to present papers and how to discuss them. d) To enjoy Science. **Science is fun!**

Course format: Every week one or two students will each give (independently) a talk 30 min long (using Powerpoint). The talk will describe one paper from the provided list (in **YELLOW**). Each presenter is expected to read **a few additional papers** to become familiar with the subject presented. The papers are available in pdf format at the course site in Moodle. All students in the audience read the paper assigned for each week and are expected to participate in an active discussion following each presentation.

Grades will be based on 1) Active participation in discussions; 2) Quality of presentation.

Note: On each subject, **one paper** is to be read by all the class (1 or 2 per encounter usually). Additional papers on the subject may appear, and I recommend that you read as many as possible (the presenter HAS to read them).

- **19.10.20 Introduction, Orientation:** What is Systems Biology? How does this course work?
- **26.10.20 DNA Microarrays, the Revolution**

1) Giaever et al. Functional profiling of the *Saccharomyces cerevisiae* genome. Nature **418**:387-391. 2002

AND

2) Hughes TR, et al., Functional discovery via a compendium of expression profiles. Cell. 2000 Jul 7;102(1):109-26.

- **2.11.20 Stress and Drugs:** Things you can do if you have a collection of ALL the possible knockouts in an organism.

3) Gasch AP *et al.* 2000. Genomic expression programs in the response of yeast cells to environmental changes. *Mol Biol Cell*. **11**:4241-4257.

See also:

3b. Causton HC *et al.* 2001. Remodeling of yeast genome expression in response to environmental changes. *Mol Biol Cell*. 12 :323-337.

AND

4) Hillenmeyer ME *et al.* (2008) The chemical genomic portrait of yeast: uncovering a phenotype for all genes. *Science* 320(5874): 362-365.

See also:

4b. Perlstein *et al.* Genetic basis of individual differences in the response to small-molecule drugs in yeast. *Nature Genetics* 39, 496 - 502 (2007)

- **9.11.20 Large scale protein interaction studies** Trying to catch ALL the possible physical interactions among proteins

Yeast two hybrid:

5. Uetz P, *et al.* A comprehensive analysis of protein-protein interactions in *Saccharomyces cerevisiae*. *Nature*. 2000 Feb 10;403(6770):623-7.

See also

5b. Ito T *et al.* A comprehensive two-hybrid analysis to explore the yeast protein interactome. *Proc Natl Acad Sci U S A*. 2001 Apr 10;98(8):4569-74.

AND

Complex hunting:

6. Gavin AC, *et al.* Proteome survey reveals modularity of the yeast cell machinery. *Nature*. 2006 440:631-636.

See also

6b. Krogan NJ *et al.* Global landscape of protein complexes in the yeast *Saccharomyces cerevisiae*. *Nature*. 2006 Mar 30;440(7084):637-43.

- **16.11.20 Genetic circuits** What is the logic of life?

ChIP-exo and ChIP-chip (Location analysis).

7. Harbison *et al.* (2004) Transcriptional regulatory code of a eukaryotic genome. *Nature* 431, 99-104.

See also

7b. Rhee, HS and BF Pugh (2011) Comprehensive genome-wide protein-DNA interactions detected at single-nucleotide resolution. *Cell* 147, 1408–1419.

AND**Network motifs**

8. Milo R, Shen-Orr S, Itzkovitz S, Kashtan N, Chklovskii D, Alon U (2002). Network motifs: simple building blocks of complex networks. *Science* 298: 824-827.

[See also](#)

8b. Alon U (2007) Network motifs: theory and experimental approaches. *Nature Reviews Genetics* 8, 450-461

- **23.11.20 Genomics and Cancer** How to use new technologies in cancer detection and treatment

Diagnostics and Prognosis

9. Garber, ME (2001) Diversity of gene expression in adenocarcinoma of the lung. *Proc Natl Acad Sci U S A.* 98(24): 13784–13789.

[See also](#)

9b. Lu et al. (2006) A gene expression signature predicts survival of patients with stage I non-small cell lung cancer. *PLoS Med.* 3(12):e467

AND**Cancer signatures:**

10. Bild AH et al. (2006) Oncogenic pathway signatures in human cancers as a guide to targeted therapies. *Nature* 439(7074):353-357.

[See also:](#)

10b. Liu et al. (2006) A genome-wide screen reveals functional gene clusters in the cancer genome and identifies EphA2 as a mitogen in glioblastoma. *Cancer Res.* 66:10815-10823.

- **30.11.20 Large scale genetic interaction mapping** Trying to catch ALL the possible genetic interactions among genes

Synthetic lethality:

11. Tong AH et al. Global mapping of the yeast genetic interaction network. *Science* 303(5659):808-13 (2004).

[See also](#)

11b. Costanzo et al. A global genetic interaction network maps a wiring diagram of cellular function. (2016). *Science* 353:1381.

AND**Synthetic fitness analysis:**

12. St. Onge et al. Systematic pathway analysis using high-resolution fitness profiling of combinatorial gene deletions. *Nat Gen* 2007 39: 199-206.

See also:

12b. Collins et al. (2007) Functional dissection of protein complexes involved in yeast chromosome biology using a genetic interaction map. *Nature* 446, 806-810.

7.12.20 More about the meaning of Genetic interactions

13. van Leeuwen et al. (2016) Exploring genetic suppression interactions on a global scale. *Science* 354: 599.

See also:

13b. Ben-Shitrit, T., Yosef, N., Shemesh, K., Sharan, R., Ruppin, E., and M. Kupiec (2012) Systematic identification of gene annotation errors in the widely used yeast mutation collections. *Nature Methods* 9: 373-378.

AND

14. Michel, AH et al. Functional mapping of yeast genomes by saturated transposition (2017). *Elife*. 2017 May 8;6. pii: e23570. doi: 10.7554/eLife.23570.

See also:

14b. Liu, G. et al. Gene Essentiality Is a Quantitative Property Linked to Cellular Evolvability. *Cell*. 2015 Dec 3;163(6):1388-99.

- **14.12.20 Ribosome profiling:** A novel methodology to measure protein levels

15. Ingolia NT, Ghaemmaghami S, Newman JR, Weissman JS. (2009) Genome-Wide Analysis In Vivo of Translation with Nucleotide Resolution Using Ribosome Profiling. *Science* 324:218-223.

See also:

15b. Mills Ingolia (2016) Dynamic Regulation of a Ribosome Rescue Pathway in Erythroid Cells and Platelets. *Cell Reports* 17, 1–10.

AND

16. Cheng et al. (2018) Pervasive, Coordinated Protein-Level Changes Driven by Transcript Isoform Switching during Meiosis. *Cell* 172, 910–923.

See also:

16b. Wu et al. (2020) Ribosome Collisions Trigger General Stress Responses to Regulate Cell Fate. *Cell* 182, 404–416.

- **21.12.20 Hi-C: mapping the 3D configuration of the genome.**

17. Rao, S.S., Huntley M.H., Durand N.C., Stamenova E.K., Bochkov I.D., Robinson J.T., Sanborn A.L.5, Machol I., Omer A.D., Lander E.S., Aiden E.L (2015) A 3D Map of

the Human Genome at Kilobase Resolution Reveals Principles of Chromatin Looping. *Cell* **159**:1665-1680.

See also:

17b. Lieberman-Aiden E, et al. (2009). Comprehensive mapping of long-range interactions reveals folding principles of the human genome. *Science* 326:289-293.

AND

18. Lupian˜ez et al. (2015) Disruptions of Topological Chromatin Domains Cause Pathogenic Rewiring of Gene-Enhancer Interactions. *Cell* 161, 1012–1025.

See also:

18b. Umut Eser et al. (2017) Form and function of topologically associating genomic domains in budding yeast. *PNAS* 114 (15) E3061-E3070;

- **28.12.20** **Humanizing yeasts** Using yeast knowledge to study human disease

19. Outerio and Lindquist, 2003. Yeast Cells Provide Insight into Alpha-Synuclein Biology and Pathobiology (Parkinson). *Science* 302: 1772-1775

See also:

19b. Sun et al. (2016). An extended set of yeast-based functional assays accurately identifies human disease mutations. *Genome Res.* 26: 670-680.

AND

20. Srivas et al (2016) A Network of Conserved Synthetic Lethal Interactions for Exploration of Precision Cancer Therapy. *Molecular Cell* 63, 514–525.

See also:

20b. Kramer et al. (2017) Active Interaction Mapping Reveals the Hierarchical Organization of Autophagy. *Molecular Cell* 65, 1–14.

- **4.1.20** **New Genome wide screens** in mammalian cells

CRSPR/CAS screens

21. Olivieri et al. (2020) A Genetic Map of the Response to DNA Damage in Human Cells. *Cell* 182, 1–16.

See also:

21b. Dixit et al. 2016) Perturb-Seq: Dissecting Molecular Circuits with Scalable Single-Cell RNA Profiling of Pooled Genetic Screens. *Cell* 167, 1853–1866.

AND

22. Bassaganyas et al. (2019). New factors for protein transport identified by a genome-wide CRISPRi screen in mammalian cells. *JCB*, ahead of print

See also:

22b. Harel, I., Benayoun, B.A., Machado, B., Singh, P.P., Hu, C.K., Pech, C.F., Valenzano, D.R., Zhang, E., Sharp, S.C., Artandi, S.E., and Anne Brunet (2015) *Cell* 160, 1013–1026.

- **11.12.20 Combining heterogeneous data and analyzing epigenetic memory**

Compendium of heterogeneous data: How to get the most of it by using ALL available information.

23. Tanay, A. et al. (2005) Integrative analysis of genome-wide experiments in the context of a large high-throughput data compendium. *Mol. Sys. Biol.*
doi:10.1038/msb4100005

See also:

23b. Lamb, J. et al. The Connectivity Map: Using Gene-Expression Signatures to Connect Small Molecules, Genes, and Disease. *Science* 313, 1929 (2006)

AND

Epigenetic memory

24. Bheda et al. (2020) Single-Cell Tracing Dissects Regulation of Maintenance and Inheritance of Transcriptional Reinduction Memory. *Molecular Cell* 78, 1–11.

See also:

24b. Brickner et al. (2016) Subnuclear positioning and interchromosomal clustering of the GAL1-10 locus are controlled by separable, interdependent mechanisms. *Mol Biol Cell.* 27:2980-2993.