**EE35901: Genomic Evolution: Problems and Approaches**

2017 Autumn

Title: Genomic Evolution: Problems and Approaches

Day/Time: Thur 10:00-11:45 am

Location: Erman (Conference room, Week 1) and Lillie Room (Week 2 ~ 11)

Instructors: Manyuan Long & Chung-I Wu

Although genomic evolution can be a diverse and vast field that almost every biologist has to rely on, we think it valuable to review its general problems and approaches and evaluate the strength and weakness of the field. We will discuss major and new scientific problems that have been examined, including sex-related genomic evolution, noncoding sequence evolution, adaptive significance of expression noise, plasticity in phenotypes and genomic structure, and detecting evolutionary forces on genomes. First, the sex-related genomic evolution continued to be a recent hot topic, elevated by genome sequencing in a number of organisms. The data created put previous theories and model into test and raised new scientific problems awaiting further investigations. Second, the cold spots of genomes in research – the evolution of non-coding regions and its potentials in regulation (gene regulation networks, GRNs) and gene functionality have made substantial progresses in recent years. Third, unexpected findings of adaptive significance of expression noise and non-perfection in the repairing system have brought new concepts into the research of genome research. Fourth, the evolution of adaptive plasticity and its impact on the complexity of genomes have connected phenotypic evolution and the environmental changes in the developmental time scale. Fifth, the role of epigenetics and chromatins in evolution has attracted serious consideration. Sixth, understanding of evolutionary forces acting on various genomes has attracted increase interests. With all evolutionary analyses on genomic sequences, the tools of computation to handle gigantic data is critical for an efficient genome comparison: e.g. testing selection and genome alighnment. Besides, there are numerous other new problems and corresponding approaches in active discussion. Correspondingly, the analysis means used in population genomics also evolved or are being developed and improved. The tools of computation to handle genome comparison become critical for an efficient genome comparison: e.g. sequence substitution computation and genome alighnment. The development of ideas related to these problems has been accompanied by vigorous and productive intellectual debate, and we hope to bring the same spirit to this class, and hence we encourage participants to present new ideas for comment and discussion. Relevant criticisms and new ideas to the genomic evolution are encouraged to present and discussed. Format of class will be a combination of lectures, discussion, literation search and computational calculation.

**Major topics:**

**Evolution of sex chromosomes**

D. W. Bellott et al., Convergent evolution of chicken Z and human X

chromosomes by expansion and gene acquisition. Nature 466, 612-616 (2010).

Bachtrog D, Mank J, Peichel C, Otto S, Kirkpatrick M, Ashman TL, Hahn M, Kitano J, Mayrose I, Ming R, Perrin N, Ross L, Valenzuela N, Vamosi J. (2014) Sex determination: Why so many ways of doing it? PLoS Biology, 2(7): e1001899.

Zhou Q, Ellison CE, Kaiser VB, Alekseyenko AA, Gorchakov AA, Bachtrog D (2013). The epigenome of evolving Drosophila neo-sex chromosomes: dosage compensation and heterochromatin formation, PLoS Biology, 11:e1000711.

B. Charlesworth, D. Charlesworth, The degeneration of Y chromosomes. Philos. Trans. R. Soc. Lond. B Biol. Sci. 355, 1563-1572 (2000).

Ref: J. J. Bull, Evolution of sex determining mechanisms. The Benjamin/Cummings

Publishing Company, Inc., 1983.

**Sexual-related selection and sexual antagonisms**

Gallach M & Betrán E. 2011. Intralocus sexual conflict resolved through gene duplication. Trends Ecol. Evol. 26, 222–228.

Innocenti P, Morrow EH. 2010. The sexually antagonistic genes of Drosophila melanogaster. PLoS Biol 8: e1000335

Cox RM and Calsbeek R. 2009. Sexually antagonistic selection, sexual dimorphism, and the resolution of intralocus sexual conflict. *Am Nat* **173**(2): 176-187. PMID: 19138156.

Charlesworth, B., Coyne, J.A., and Barton, N.H. 1987. The relative rates of evolution of sex chromosomes and autosomes. Am. Nat. 130: 113–146.

Rice WR.1984. Sex chromosomes and the evolution of sexual dimorphism. *Evolution* **38**(4): 735-742.

**Interaction between sex chromosomes and autosomes**

Jiang L et al. (2017). RPL10L is required for male meiotic division by compensating for RPL10 during meiotic sex chromosome inactivation in mice. Curr. Biol. 27, 1498–1505.e6.

Long M & Emerson JJ, 2017. Meiotic Sex Chromosome Inactivation: Compensation by Gene Traffic. Curr. Biol. 27, R642–R666.

Betrán, E., K. Thornton, and M. Long 2002. Retroposed new genes out of the *X* in

*Drosophila.* ***Genome Research.*** 12: 1854-1859.

Emerson J.J., H. Kaesmann, E. Betrán and M. Long 2004. Extensive gene traffic on the human X chromosome. ***Science*** 303: 537-540.

Wu, C.-I and E. Y. Xu, 2003 Sexual antagonism and X- inactivation - The SAXI hypothesis. Trends in Genetics 19: 243-247

Vibranovski MD, Zhang Y, Long M, 2009. General gene movement off the X chromosome in the *Drosophila* genus. ***Genome Research*** 19: 897-903.

**Evolutionary significance of expression noise and plasticity:**

Bratulic S, Toll-Riera M & Wagner A, 2017. Mistranslation can enhance fitness through purging of deleterious mutations. Nature Comm 8:15410.

McAdams H & Arkin A, 1997. Stochastic mechanisms in gene expression. Proc. Natl. Acad. Sci. USA 94: 814–819.

Skanata A & Kussel E, 2016. Evolutionary Phase Transitions in Random Environments. Phys Rev Lett 117: 038104.

Huh I, Zeng J, Park T and Yi SV, 2013. DNA methylation and transcriptional noise. *Epigenetics & Chromatin* 6:9.

**Evolution of Plasticity and its impact on the complexity in genome structure:**

Price TD, Qvarnstrom A & Irwin DE, 2003. The role of phenotypic plasticity in driving genetic evolution. Proc. R. Soc. Lond. B 270: 1433–1440.

Lauren W. Ancel, 2000. Undermining the Baldwin Expediting Effect: Does Phenotypic Plasticity Accelerate Evolution? Theor Pop Biol 58: 307-319.

Murat, F., Van de Peer, Y. & Salse, J. Decoding plant and animal genome plasticity from differential paleo-evolutionary patterns and processes. Genome Biol Evol 4, 917-28 (2012).

Huey, R.B. et al. Plants versus animals: do they deal with stress in different ways? Integr Comp Biol 42, 924 415-23 (2002).

Sultan SE. 2000. Phenotypic plasticity for plant development, function and life history. *Trends Plant Sci* **5**: 537-542.

**Evolution of Epigenetics, Chromatins and Regulation**

Keller TE and Yi SV, 2014. DNA methylation and evolution of duplicate genes. PNAS 111: 5932–5937.

Connelly CF, Wakefield J, Akey JM, 2014. Evolution and Genetic Architecture of Chromatin Accessibility and Function in Yeast. *PLoS Genet* 10: e1004427.

Zhou Q, Bachtrog D, 2015. Ancestral Chromatin Configuration Constrains Chromatin Evolution on Differentiating Sex Chromosomes in *Drosophila. PLoS Genet* 11(6): e1005331.

**Stability issues for microRNAs and other non-coding RNAs:**

Requirement – Each student should adopt at least one paper from each lecture. The group of students sharing one paper should spend about 3 minutes to present the substance, followed by discussions.

**miRNAs and gene regulation**

I. The standard view of microRNAs (miRNAs as the junior version of regulators such as transcription factors)

Clop, A. C. et al. (2006) A mutation creating a potential illegitimate microRNA target site in the myostatin gene affects muscularity in sheep. Nature Genetics 38: 813 – 817.

Baek, D., Villen, J., Shin, C., Camargo, F. D., Gygi, S. P., & Bartel, D. P. (2008). The impact of microRNAs on protein output. *Nature, 455*(7209), 64-U38. *(weak effects of miRNA on gene expression and translation)*

Karres, J. S. et al. (2007) The Conserved microRNA MiR-8 Tunes Atrophin Levels to Prevent Neurodegeneration in Drosophila. Cell 131: 136-145.

**motifs in Gene Regulation Networks (GRNs)**

II. A intermediate step toward understanding the systems of transcription network (Motifs in GRNs and phenotypic canalization)

Tsang, J., Zhu, J., & van Oudenaarden, A. (2007). MicroRNA-mediated feedback and feedforward loops are recurrent network motifs in mammals. *Molecular Cell, 26*(5), 753-767.*(the enrichment of miRNA motif in different tissue and potential function in transcriptional homeostasis. )*

Hornstein, E. and Shomron, N. 2006. Canalization of development by microRNAs. Nat. Genet. 38: S20–S24.

Wu, C. I., Shen, Y., & Tang, T. (2009). Evolution under canalization and the dual roles of microRNAs--A hypothesis. *Genome Res, 19*(5), 734-743.

**Stability of GRNs**

III. Transcriptome as a full network (in relation to the foodweb network)

III-1 Background of the theory (the matrix as the expression of all interactions)

7) May, R. M. (1972). Will a Large Complex System be Stable? *Nature, 238*(5364), 413-414.

8) Allesina, S., & Tang, S. (2012). Stability criteria for complex ecosystems. *Nature, 483*(7388), 205-208.

III-2 Synthesis and degradation of mRNAs (the diagonal elements of the matrix)

9) Schwanhausser, B., Busse, D., Li, N., Dittmar, G., Schuchhardt, J., Wolf, J., . . . Selbach, M. (2011). Global quantification of mammalian gene expression control. *Nature, 473*(7347), 337-342.

10) Dori-Bachash, M., Shema, E., & Tirosh, I. (2011). Coupled evolution of transcription and mRNA degradation. *PLoS Biol, 9*(7), e1001106.

III-3 A short lecture of summary by Chung-I Wu.

**Genome Comparison and Computational Techniques:**

1.Genome Alignment: why and how?

UCSC [Whole genome alignment howto - Genomewiki](http://genomewiki.ucsc.edu/index.php/Whole_genome_alignment_howto) ( <http://genomewiki.ucsc.edu/index.php/Whole_genome_alignment_howto>)

BlastZ: a nucleotide local alignment program developed by Webb Miller's group at PSU

Harris, R.S. (2007) Improved pairwise alignment of genomic DNA. Ph.D. Thesis, The Pennsylvania State University.

2.Substitution analyses of DNA coding regions: Calculate tools.

PAML: its procedures, values and shortcomings: gKaKs & DPOM

Yang, Z. PAML 4: phylogenetic analysis by maximum likelihood. *Mol Biol Evol* **24**, 1586-91 (2007).

Yang, Z. Likelihood ratio tests for detecting positive selection and application to primate lysozyme evolution. *Mol Biol Evol* **15**, 568-73 (1998).

Zhang CJ, Wang J, Long M and Fan C, 2013. gKaKs: the pipeline for genome level Ka/Ks calculation. Bioinformatics Published online January 12, 2013.

Zhang CJ, Wang J, Xie WB, Zhou G, Long M, Zhang QF, 2011. A dynamic programming procedure for searching optimal models estimate substitution rates based on the maximum-likelihood method. Proc Natl Acad Sci USA 108:7860-7865.

**Schedule:**

**Week 1: September 28: Long: Introduction and Interaction between sex chromosomes and autosomes**

Betrán, E., K. Thornton, and M. Long 2002. Retroposed new genes out of the *X* in

*Drosophila.* ***Genome Research.*** 12: 1854-1859.

Wu, C.-I and E. Y. Xu, 2003 Sexual antagonism and X-inactivation - The SAXI hypothesis. ***Trends in Genetics***19:243-247.

Emerson J.J., H. Kaesmann, E. Betrán and M. Long 2004. Extensive gene traffic on the human X chromosome. ***Science*** 303: 537-540.

Jiang L et al. (2017). RPL10L is required for male meiotic division by compensating for RPL10 during meiotic sex chromosome inactivation in mice. Curr. Biol. 27, 1498–1505.e6.

Long M & Emerson JJ, 2017. Meiotic Sex Chromosome Inactivation: Compensation by Gene Traffic***. Curr. Biol***. 27, R642–R666.

Further Reading:

Vibranovski MD, Zhang Y, Long M, 2009. General gene movement off the X chromosome in the *Drosophila* genus. ***Genome Research*** 19: 897-903.

**Week 2: October 5: Long: The theories of sex-related evolution**

**Student presentation: 1 ~ 2.**

B. Charlesworth, D. Charlesworth, The degeneration of Y chromosomes. Philos. Trans. R. Soc. Lond. B Biol. Sci. 355, 1563-1572 (2000).

D. W. Bellott et al., Convergent evolution of chicken Z and human X

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Bachtrog D, Mank J, Peichel C, Otto S, Kirkpatrick M, Ashman TL, Hahn M, Kitano J, Mayrose I, Ming R, Perrin N, Ross L, Valenzuela N, Vamosi J. (2014) Sex determination: Why so many ways of doing it? PLoS Biology, 2(7): e1001899.

Zhou Q, Ellison CE, Kaiser VB, Alekseyenko AA, Gorchakov AA, Bachtrog D (2013). The epigenome of evolving Drosophila neo-sex chromosomes: dosage compensation and heterochromatin formation, PLoS Biology, 11:e1000711.

**Week 3: October 12: Long: Evolution of Epigenetics, Chromatins and Gene Regulation**

**Student presentation: 1 ~ 2.**

Keller TE and Yi SV, 2014. DNA methylation and evolution of duplicate genes. PNAS 111: 5932–5937.

Connelly CF, Wakefield J, Akey JM, 2014. Evolution and Genetic Architecture of Chromatin Accessibility and Function in Yeast. *PLoS Genet* 10: e1004427.

Zhou Q, Bachtrog D, 2015. Ancestral Chromatin Configuration Constrains Chromatin Evolution on Differentiating Sex Chromosomes in *Drosophila. PLoS Genet* 11(6): e1005331.

**Week 4: October 19: UnJin Lee: Expression noise and plasticity analysis**

**Student presentation: 1 ~ 2.**

Bratulic S, Toll-Riera M & Wagner A, 2017. Mistranslation can enhance fitness through purging of deleterious mutations. Nature Comm 8:15410.

McAdams H & Arkin A, 1997. Stochastic mechanisms in gene expression. Proc. Natl. Acad. Sci. USA 94: 814–819.

Skanata A & Kussel E, 2016. Evolutionary Phase Transitions in Random Environments. Phys Rev Lett 117: 038104.

Huh I, Zeng J, Park T and Yi SV, 2013. DNA methylation and transcriptional noise. *Epigenetics & Chromatin* 6:9.

**Week 5: October 26: Long: Sexual antagonism in evolution**

**Student presentation: 1 ~ 2.**

Gallach M & Betrán E. 2011. Intralocus sexual conflict resolved through gene duplication. Trends Ecol. Evol. 26, 222–228.

Innocenti P, Morrow EH. 2010. The sexually antagonistic genes of Drosophila melanogaster. PLoS Biol 8: e1000335

Cox RM and Calsbeek R. 2009. Sexually antagonistic selection, sexual dimorphism, and the resolution of intralocus sexual conflict. *Am Nat* **173**(2): 176-187. PMID: 19138156.

Charlesworth, B., Coyne, J.A., and Barton, N.H. 1987. The relative rates of evolution of sex chromosomes and autosomes. Am. Nat. 130: 113–146.

Rice WR.1984. Sex chromosomes and the evolution of sexual dimorphism. *Evolution* **38**(4): 735-742.

**Week 6: November 2: Jianhai Chen and Manyuan Long: Detect selection: Methods and Computation**

**Student presentation: 1 ~ 2**

PAML: its procedures, values and shortcomings: gKaKs & DPOM

Yang, Z. PAML 4: phylogenetic analysis by maximum likelihood. *Mol Biol Evol* **24**, 1586-91 (2007).

Yang, Z. Likelihood ratio tests for detecting positive selection and application to primate lysozyme evolution. *Mol Biol Evol* **15**, 568-73 (1998).

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Zhang CJ, Wang J, Xie WB, Zhou G, Long M, Zhang QF, 2011. A dynamic programming procedure for searching optimal models estimate substitution rates based on the maximum-likelihood method. Proc Natl Acad Sci USA 108:7860-7865.

**Week 7: November 9: Wu: miRNAs and gene regulation**

**Student presentation.**

I. The standard view of microRNAs (miRNAs as the junior version of regulators such as transcription factors)

Clop, A. C. et al. (2006) A mutation creating a potential illegitimate microRNA target site in the myostatin gene affects muscularity in sheep. Nature Genetics 38: 813 – 817.

Baek, D., Villen, J., Shin, C., Camargo, F. D., Gygi, S. P., & Bartel, D. P. (2008). The impact of microRNAs on protein output. *Nature, 455*(7209), 64-U38. *(weak effects of miRNA on gene expression and translation)*

Karres, J. S. et al. (2007) The Conserved microRNA MiR-8 Tunes Atrophin Levels to Prevent Neurodegeneration in Drosophila. Cell 131: 136-145.

**Week 8: November 16: Wu: motifs in GRNs**

**Student presentation.**

II. A intermediate step toward understanding the systems of transcription network (Motifs in GRNs and phenotypic canalization)

Tsang, J., Zhu, J., & van Oudenaarden, A. (2007). MicroRNA-mediated feedback and feedforward loops are recurrent network motifs in mammals. *Molecular Cell, 26*(5), 753-767.*(the enrichment of miRNA motif in different tissue and potential function in transcriptional homeostasis. )*

Hornstein, E. and Shomron, N. 2006. Canalization of development by microRNAs. Nat. Genet. 38: S20–S24.

Wu, C. I., Shen, Y., & Tang, T. (2009). Evolution under canalization and the dual roles of microRNAs--A hypothesis. *Genome Res, 19*(5), 734-743.

Week 9: November 23: Thanksgiving.

**Week 10: November 30: Wu: Stability of GRNs**

**Student presentation.**

III. Transcriptome as a full network (in relation to the foodweb network)

III-1 Background of the theory (the matrix as the expression of all interactions)

7) May, R. M. (1972). Will a Large Complex System be Stable? *Nature, 238*(5364), 413-414.

8) Allesina, S., & Tang, S. (2012). Stability criteria for complex ecosystems. *Nature, 483*(7388), 205-208.

III-2 Synthesis and degradation of mRNAs (the diagonal elements of the matrix)

9) Schwanhausser, B., Busse, D., Li, N., Dittmar, G., Schuchhardt, J., Wolf, J., . . . Selbach, M. (2011). Global quantification of mammalian gene expression control. *Nature, 473*(7347), 337-342.

10) Dori-Bachash, M., Shema, E., & Tirosh, I. (2011). Coupled evolution of transcription and mRNA degradation. *PLoS Biol, 9*(7), e1001106.

III-3 A short lecture of summary by Chung-I Wu.

**Week 11: December 7:**

**Li Zhang: Computation of Genome Alignments:** why and how?

UCSC [Whole genome alignment howto - Genomewiki](http://genomewiki.ucsc.edu/index.php/Whole_genome_alignment_howto) ( <http://genomewiki.ucsc.edu/index.php/Whole_genome_alignment_howto>)

BlastZ: a nucleotide local alignment program developed by Webb Miller's group at PSU

Harris, R.S. (2007) Improved pairwise alignment of genomic DNA. Ph.D. Thesis, The Pennsylvania State University.

**Manyuan Long: lecture: Evolution of Plasticity and its impact on the complexity in genome structure:**

Price TD, Qvarnstrom A & Irwin DE, 2003. The role of phenotypic plasticity in driving genetic evolution. Proc. R. Soc. Lond. B 270: 1433–1440.

Murat, F., Van de Peer, Y. & Salse, J. Decoding plant and animal genome plasticity from differential paleo-evolutionary patterns and processes. Genome Biol Evol 4, 917-28 (2012).

Huey, R.B. et al. Plants versus animals: do they deal with stress in different ways? Integr Comp Biol 42, 924 415-23 (2002).

Sultan SE. 2000. Phenotypic plasticity for plant development, function and life history. *Trends Plant Sci* **5**: 537-542.