

Genética Molecular e Populacional

Course: Regulation of Gene Expression

Date: 23rd – 27th January 2012

Location:

23rd- 25th Jan- IBMC – Main auditorium, except Wednesday morning:
Auditorium C

26th-27th Jan – IMM, Lisbon – Portuguese RNA 2012 Meeting

<http://imm.fm.ul.pt/web/imm/rna2012>

Coordinator: Alexandra Moreira

Teaching Staff: Alexandra Moreira, Mafalda Araújo, Mafalda Pinto, Simon Lee, Telmo Henriques (IBMC); Francisco Enguita, Sérgio Almeida and M. Carmo-Fonseca (IMM).

Gene expression is often spoken of as if it were the same thing as initiation of transcription, whereas it actually involves all steps leading to production of an active gene product. A major challenge facing scientific research in the post-genomic era is, rather than collecting data on whether a given gene is expressed at a particular moment, to go further into the molecular mechanisms that regulate gene expression. Only then will we be able to assertively predict which protein products will be produced in different situations, and how they will influence cellular functions. Thus, the extended knowledge of the mechanisms involved in the formation of a mature messenger RNA (mRNA) is of crucial for understanding the life cycle of the cell. In this course we will discuss the molecular basis of controlling gene expression and mRNA processing during the physiological events that occur in different types of cells and in different systems. Challenges in the field and how they are experimentally addressed will be discussed.

Outline of the course: Lectures, tutorials, research seminars, students presentations, round table, Portuguese RNA2012 meeting.

Program:

Monday 23rd

Morning – Alexandra Moreira

1. Introduction
2. Lecture 1: Overview of transcription and RNA processing: capping, splicing and mRNA 3' processing – integration of events
3. Lecture 2: Alternative polyadenylation and regulation of mRNA 3' end formation
Paper dissection / research seminar: Pinto, PAB, Henriques, T, *et al.* (2011) EMBO J 30:2431-44.

Afternoon – Mafalda Araújo

1. Lecture 1: Pre-mRNA Splicing – mechanisms of gene expression regulation.
2. Lecture 2: Signal transduction pathways mediating activation-induced alternative splicing of CD6 ligand-binding domain in T lymphocytes.
3. Paper dissection: Lijima T *et al* (2011) "SAM68 Regulates Neuronal Activity-Dependent Alternative Splicing of Neurexin-1." Cell. 147: 1601-14.
4. Genetic therapies for RNA mis-splicing diseases.

Tuesday 24th

Morning – Telmo Henriques

1. Lecture: Principles of gene expression:
 - a) Interconnection between the transcription steps
 - b) Pol II CTD code – changes along the transcription cycle and the interaction with transcription factors
 - c) Models for transcriptional termination
2. Paper dissection: Henriques *et al* (2012) "Transcription termination between closely spaced genes", *in preparation* (pdf available).

Afternoon – Simon Lee

1. Lecture: Next generation sequencing and gene expression
 - a. Principles of next generation sequencing (NGS)
 - b. Brief overview of microarray techniques and comparison with NGS
 - c. Applications of NGS in gene expression studies
 - d. Approaches to NGS data analysis
2. Discussion and problem solving – *how you can do RNAseq without doing any sequencing yourself ...*



Wednesday 25th

Morning – Mafalda Pinto

1. Lecture: miRNA biogenesis and function; Regulation of gene expression by miRNAs
2. Paper dissection – Ponomarev ED, Veremeyko T, et al. (2011) "MicroRNA-124 promotes microglia quiescence and suppresses EAE by deactivating macrophages via C/EBP- α -PU.1 pathway" Nat Med 17: 64-70.

Thursday 26th and Friday 27th

Portuguese RNA2012 meeting, IMM, Lisbon:

<http://imm.fm.ul.pt/web/imm/rna2012>

Suggested reading and bibliography:

1. Moreira, A (2011) Integrating transcription kinetics with alternative polyadenylation and cell cycle control. Nucleus, Nov 1;2(6)
2. Pinto*, PAB, Henriques*, H, Freitas, MO, Martins, T, Domingues, RG, Wyrzykowska, PS, Coelho, PA, Carmo, AM, Sunkel, CE, Proudfoot, NJ and Moreira, A (2011) RNA polymerase II kinetics in polo polyadenylation signal selection, The EMBO Journal, 30: 2431–2444 (this paper will be dissected by Alexandra Moreira)
3. Lutz CS, Moreira A (2011) Alternative mRNA polyadenylation in eukaryotes: and effective regulator of gene expression. Wiley Interdisciplinary Reviews – RNA, 2 (1): 23-31
4. Castelo-Branco, P, Furger, A, Wollerton, M, Smith, C, Moreira, A and Proudfoot, NJ (2004) Polypyrimidine tract binding protein modulates efficiency of polyadenylation. Mol. Cell. Biol. 24 (10): 4174-4183.
5. Moreira A, Pinto P, Sunkel C, Carmo A (2005) "Upstream sequence elements are required for mRNA 3'-end formation of the Drosophila melanogaster cell cycle POLO kinase", FASEB J. 19: A876
6. Castro, MAA, Oliveira, MI, Nunes RJ, Fabre, S, Barbosa, R, Peixoto, A, Brown, MH, Parnes, JR, Bismuth, G, Moreira A, Rocha, B and Carmo, A (2007) Extracellular isoforms of CD6 generated by alternative splicing regulate targeting of CD6 to the immunological synapse. J. Immunol., 178: 4351-4361.

7. Lijima T *et al* (2011) "SAM68 Regulates Neuronal Activity-Dependent Alternative Splicing of Neurexin-1." *Cell*. 147: 1601-14. (this paper will be dissected by Mafalda Araújo)
8. Han J, Xiong J, Wang D, Fu XD. Pre-mRNA splicing: where and when in the nucleus. *Trends Cell Biol*. 2011 Jun;21(6):336-43.
9. Will CL and Luhrmann R. (2011) Spliceosome structure and function. *Cold Spring Harb Perspect Biol*. Jul 1;3(7).
10. Barash Y, Calarco JA, Gao W, Pan Q, Wang X, Shai O, Blencowe BJ, Frey BJ. Barash Y *et al*. (2010) Deciphering the splicing code. *Nature*. 2010 May 6;465(7294):53-9.
11. Heyd F and Lynch KW. (2011) Degrad, move, regroup: signaling control of splicing proteins. *Trends Biochem Sci*. 36(8):397-404.
12. Salz HK. (2011) Sex determination in insects: a binary decision based on alternative splicing. *Curr Opin Genet Dev*, 21(4):395-400.
13. [Oesterreich FC](#), [Bieberstein N](#), [Neugebauer KM](#). (2011) Pause locally, splice globally. *Trends Cell Biol*. 21(6):328-335.
14. Lynch KW. (2007) Regulation of alternative splicing by signal transduction pathways. *Adv Exp Med Biol*. 623:161-174.
15. West S, Proudfoot NJ. (2009) Transcriptional termination enhances protein expression in human cells. *Mol Cell*. 33:354-64.
16. Kuehner JN, Pearson EL, Moore C. (2011) Unravelling the means to an end: RNA polymerase II transcription termination. *Nat Rev Mol Cell Biol*. 12:283-94
17. Richard P, Manley JL. (2009) Transcription termination by nuclear RNA polymerases. *Genes Dev*. 23:1247-69.
18. Buratowski S. (2009) Progression through the RNA polymerase II CTD cycle. *Mol Cell*. 36:541-6
19. Bartel, DP. (2004) MicroRNAs: Genomics, mechanism, and function. *Cell*. 116:281-297.
20. Ponomarev ED, Veremeyko T, *et al*. (2011) MicroRNA-124 promotes microglia quiescence and suppresses EAE by deactivating macrophages via C/EBP- α -PU.1 pathway. *Nat Med*. 17:64-70 (this paper will be dissected by Mafalda Pinto)

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