

Genética Molecular e Populacional

Course: Regulation of Gene Expression

Date: 2nd- 4th May 2011

Location: IBMC - Auditorium C

Coordinator: Alexandra Moreira

Teaching Staff: Alexandra Moreira (IBMC/UP), Mafalda Araújo (IBMC), Natalia Gromak (Univ. Oxford), Kelly Perkins (Univ. Oxford).

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 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, journal clubs, papers dissection, students presentations: J. clubs, problems solving.

Program:

Monday 2nd

Morning – Alexandra Moreira + Mafalda Araújo

1. Introduction
2. Brief overview of transcription and RNA processing: capping, splicing and mRNA 3' processing – integration of events
3. Lecture: Alternative polyadenylation
Paper dissection / research seminar: RNA polymerase II kinetics in *polo* polyadenylation signal selection
5. Lecture: Alternative splicing - Mafalda Araújo

Afternoon – Natasha Gromak

1. Lecture (Part 1): Principles of gene expression - Pol II CTD code and histone code
 2. Lecture (Part 2): Inter-connection between gene expression steps: transcriptional termination and RNA splicing
 3. Discussion and problem solving
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Tuesday 3rd

Morning – Natasha Gromak

1. Lecture: miRNAs and their role in the regulation of gene expression
2. Paper dissection: TUT4 in concert with Lin28 suppresses microRNA biogenesis through pre-microRNA uridylation. Heo I, Joo C, Kim YK, Ha M, Yoon MJ, Cho J, Yeom KH, Han J, Kim VN. Cell. 2009 Aug 21;138(4):696-708

Afternoon – Kelly Perkins

Kelly Perkins

1. Lecture: Transcription dynamics; from the gene to the genome.
2. Paper dissection: An oestrogen-receptor-alpha-bound human chromatin interactome. Fullwood MJ et al., Nature. 2009 Nov 5;462(7269):58-64.

Wednesday 4th

Morning – Natasha + Kelly + Alex – problems solving

Afternoon – Students Presentations

Students 10-15 min presentations

Thursday 5th and Friday 6th

I3S Scientific Retreat

Suggested reading:

1. Daisuke Kaida, Michael G. Berg, Ihab Younis, Mumtaz Kasim, Larry N. Singh, Lili Wan, Gideon Dreyfuss (2010) U1 snRNP protects pre-mRNAs from premature cleavage and polyadenylation. *Nature*, 468: 664-668
2. Huili Guo, Nicholas T. Ingolia, Jonathan S. Weissman, David P. Bartel (2010) Mammalian microRNAs predominantly act to decrease target mRNA levels *Nature*, 466: 835-840
3. Heo I, Joo C, Kim YK, Ha M, Yoon MJ, Cho J, Yeom KH, Han J, Kim VN. (2009) TUT4 in concert with Lin28 suppresses microRNA biogenesis through pre-microRNA uridylation. *Cell*. 138(4):696-708.
(This paper will be dissected by Natasha Gromak).
4. West S, Proudfoot NJ. (2009) Transcriptional termination enhances protein expression in human cells. *Mol Cell*. 33:354-64.
5. Ulf Andersson Ørom, Thomas Derrien, Malte Beringer, Kiranmai Gumireddy, Alessandro Gardini, Giovanni Bussotti, Fan Lai, Matthias Zytnicki, Cedric Notredame, Qihong Huang, Roderic Guigo, and Ramin Shiekhattar (2011) Long Noncoding RNAs with Enhancer-like Function in Human Cells. *Cell*, 143: 46-58
6. A long noncoding RNA maintains active chromatin to coordinate homeotic gene expression. Kevin C. Wang^{1,2}, Yul W. Yang^{1*}, Bo Liu^{3*}, Amartya Sanyal⁴, Ryan Corces Zimmerman¹, Yong Chen⁵, Bryan R. Lajoie⁴, Angeline Protacio¹, Ryan A. Flynn¹, Rajnish A. Gupta¹, Joanna Wysocka⁶, Ming Lei⁵, Job Dekker⁴, Jill A. Helms³ & Howard Y. Chang¹. *Nature* 2011.
7. Pinto, PAB, Henriques, T, Freitas, MO, Martins, T, Domingues, R, Wyrzykowska, PS, Coelho, PA, Carmo, AM, Sunkel, CE, Proudfoot, NJ and Moreira A (2011), RNA polymerase II kinetics in

polo polyadenylation signal selection. EMBO J. (this paper will be dissected by Alexandra Moreira)

8. Fullwood MJ et al., (2009) An oestrogen-receptor-alpha-bound human chromatin interactome. Nature. 462:58-64 (this paper will be dissected by Kelly Perkins).

Contacts list

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