



## Course: Regulation of Gene Expression

**Date:** 29 Jan – 2 Feb 2018

**Location:** i3S, Room B

**Coordinator:** Alexandra Moreira

**Faculty:** Alexandra Moreira, Isabel Pereira-Castro, Jaime Freitas.

### Objectives:

Regulation of gene expression depends on a panoply of processes and factors, including chromatin remodelling, transcription, pre-mRNA processing, *cis*-regulatory elements, RNA binding proteins, miRNAs, mRNA localization and local translation. In this course international state-of-the-art research on the molecular basis of gene expression regulation and mRNA processing during the physiological events that occur in different types of cells and in different systems will be presented and discussed. Scientific challenges in the field and how they are experimentally addressed will be discussed with the students.

**Outline of the course:** Lectures, tutorials, J. Club/Lab meeting, paper discussions, research seminars, scientific questions/projects for the students to solve and present.

## Monday 29<sup>th</sup> Jan – Alexandra Moreira

### **Morning (10:00-12:30)**

1. Introduction.
2. *Lecture 1*: Overview of transcription and RNA processing. The mRNA factory model. Integration of co-transcriptional events. Mechanisms of mRNA 3' end formation in Eukaryotes.
3. *Research seminar and paper dissection*: 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.
4. *Students are presented with research questions to solve by the end of the week.*

#### Suggested reading:

- 1) Mayr C. (2016) Evolution and Biological Roles of Alternative 3'UTRs. *Trends Cell Biol.* 26(3):227-37.
- 2) Lutz CS, Moreira A (2011) Alternative mRNA polyadenylation in eukaryotes: and effective regulator of gene expression. *Wiley Interdisciplinary Reviews – RNA*, 2: 23-31.

## Tuesday 30<sup>th</sup> Jan – GR & Alexandra Moreira

### **Morning (10:00-12:00)**

*GR lab meeting – students will actively participate in our weekly lab meeting. One of the PhD students of the GR group will present their work.*

### **Afternoon (14:30-16:30)**

1. *Lecture* – The 3'UTR: a platform for gene expression regulation. The role of RNA binding proteins and alternative polyadenylation in mRNA localization and local translation.
2. *Paper dissection*: Braz SO, Cruz A, Lobo A, Bravo J, Moreira-Ribeiro J, Pereira-Castro I, Freitas J, Relvas JB, Summavielle T and Moreira A. (2017) Expression of Rac1 alternative 3' UTRs is a cell specific mechanism with a function in dendrite outgrowth in cortical neurons, *Biochimica et Biophysica Acta (BBA) - Gene Regulatory Mechanisms*, 1860: 685-694. doi: 10.1016/j.bbagr.2017.03.002.

#### Suggested reading:

- 1) Eliscovich C, Singer RH. (2017) RNP transport in cell biology: the long and winding road. *Curr Opin Cell Biol.* 45:38-46. doi: 10.1016/j.ceb.2017.02.008.
- 2) Gehring NH, Wahle E, Fischer U. (2017) Deciphering the mRNP Code: RNA-Bound Determinants of Post-Transcriptional Gene Regulation. *Trends Biochem Sci.* 42: 369-382. doi: 10.1016/j.tibs.2017.02.004.

## Wednesday 31<sup>st</sup> Jan – Jaime Freitas

### **Morning (10:00-12:30)**

1. Research seminar (discussion of ongoing projects):
  - a) RNA Polymerase II elongation rate and polyadenylation signal selection.  
Analysis of alternative polyadenylation by 3' Region Extraction and Deep Sequencing (3'READS).
  - b) Heph/PTB and Elav/HuR are recruited to *polo* upstream sequence element that modulates alternative polyadenylation  
Characterization of an RNA sequence element and protein factors involved in *polo* alternative polyadenylation.

#### Suggested reading:

- 1) Liu, X\*, Freitas, J\*, Hoque, M, Oliveira, MS, Martins, T, Henriques, T, Tian, B and Moreira A (2017) Transcription elongation has a tissue-specific impact in alternative cleavage and polyadenylation in *Drosophila melanogaster*, *RNA*, 23: 1807-1816. doi:10.1261/rna.062661.117
- 2) Danckwardt, S., Kaufmann, I., Gentzel, M., Foerstner, K. U., Gantzer, A.-S., Gehring, N. H., et al. (2007). Splicing factors stimulate polyadenylation via USEs at non-canonical 3' end formation signals. *EMBO J*, 26: 2658–2669.

## Thursday 1st Feb – Isabel Pereira-Castro

### **Morning (10:00-12:30)**

1. Research seminar - Dissecting the molecular mechanisms controlling alternative polyadenylation in human T cells.
2. Paper dissection:  
Domingues, RG, Lago-Baldaia, I, Pereira-Castro, I, Fachini, JM, Oliveira, L, Drpic, D, Lopes, N, Henriques, T, Neilson, J, Carmo, AM and Moreira A (2016) CD5 expression is regulated during human T-cell activation by alternative polyadenylation, PTBP1 and miR-204, *European Journal of Immunology*, 46: 1490–1503.

#### Suggested reading:

- 1) Sandberg R, Neilson JR, Sarma A, Sharp PA, Burge CB (2008) Proliferating cells express mRNAs with shortened 3' untranslated regions and fewer microRNA target sites. *Science*, 320(5883):1643-7.

## Friday 2<sup>nd</sup> Feb – Students presentations

*Students will present their scientific ideas/projects and the course will be evaluated.*