

**Congratulations to IMCB's latest PhD graduate - Nathan Palmer**

Monday, 24 Jun 2019

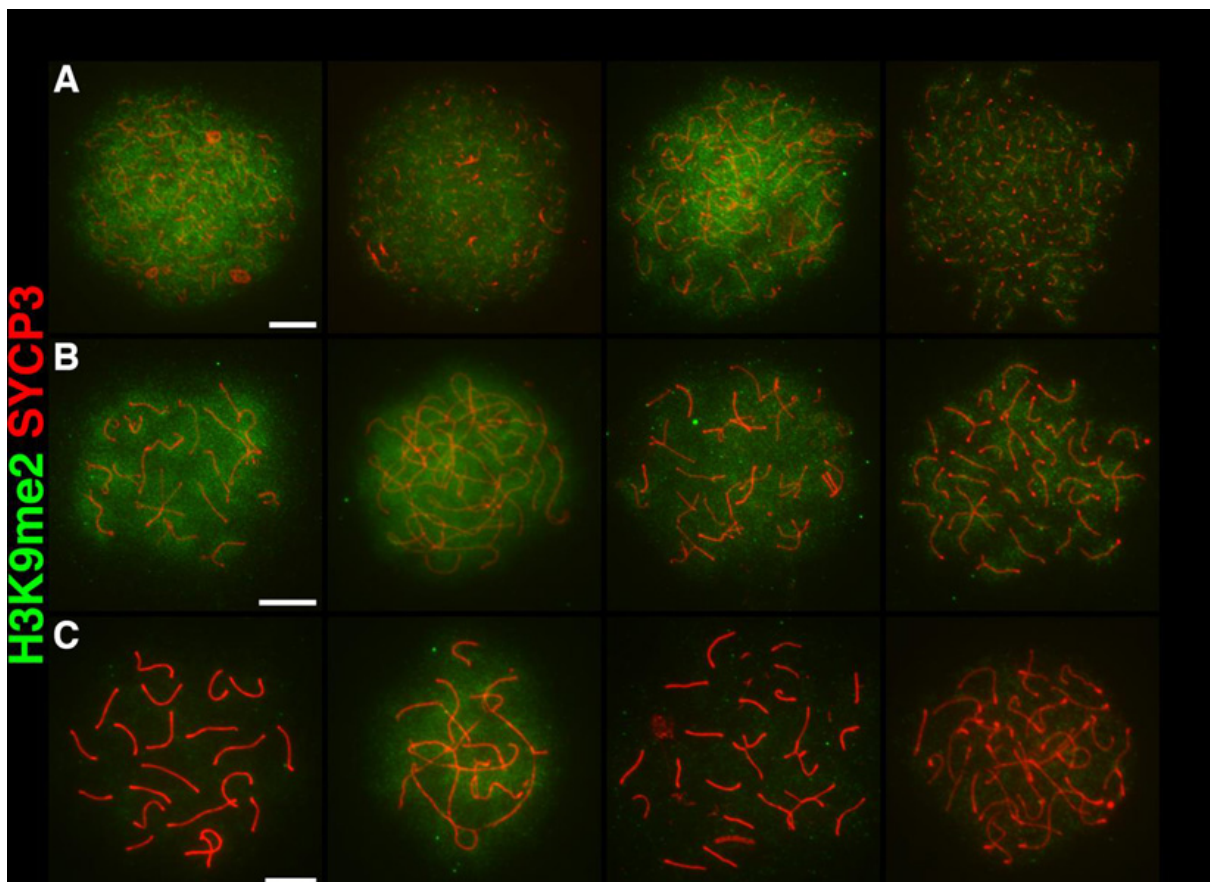


## Thesis Title: Analysis of CDK2 function during meiosis

Meiosis generates four genetically distinct haploid gametes over the course of two reductional cellular divisions. Meiotic divisions are characterized by the coordinated deposition and removal of various epigenetic marks. We propose that nuclear respiratory factor 1 (NRF1) regulates the transcription of euchromatic histone methyltransferase 1 (EHMT1) to ensure ensures normal patterns of H3K9 methylation during meiotic prophase I. We demonstrate that cyclin-dependent kinase (CDK2) can bind to the promoters of a number of genes in male germ cells including that of Ehmt1 though a novel interaction with the NRF1 transcription factor. Our data show that CDK2-mediated phosphorylation of NRF1 can occur at two distinct serine residues and negatively regulates NRF1 DNA binding activity in vitro. Furthermore, induced deletion of Cdk2 in spermatocytes results in increased expression of many NRF1 target genes including Ehmt1. We hypothesize that the regulation of NRF1 transcriptional activity by CDK2 may allow the modulation of Ehmt1 expression therefore controlling the dynamic methylation of H3K9 during meiotic prophase.

## Supervisor

Dr. Philipp Kaldis



## **H3K9me2 expression is abnormally retained in pachytene stage *Cdk2KO* spermatocytes**

Immunostaining of P18 meiotic chromosome spreads from wild type, *Cdk2KO*, *Prdm9KO* or *Sun1KO* mice. Representative images of leptotene (A), zygotene (B), and pachytene (C) sub-stages of prophase I of the first meiotic division are shown as indicated (top to bottom). Co-staining of SYCP3 (red) and H3K9me2 (green) indicates *Cdk2KO* mice show aberrant retention of H3K9me2 signal into pachytene stage. The scale bar represents 5µm in all panels.

### **Publications:**

#### **Book Chapters/Review articles**

**Palmer N** and P Kaldis. Regulation of the Embryonic Cell Cycle During Mammalian Preimplantation Development. Chapter 1: Mammalian Preimplantation Development, Volume 120 1st Edition. Also published in: Current Topics in Developmental Biology. 2016.

**Palmer N**, MK Shanmugam, G Sethi, P Kaldis. NF- κ B as a Potential Molecular Target for Therapy of Gastrointestinal Cancers: Novel Therapies for Digestive Diseases Chapter 9: Therapeutic Targets for Inflammation and Cancer. 2017

**Nathan Palmer**, S. Zakiah A. Talib\* and Philipp Kaldis. Cdk/cyclin complex functionality during meiotic prophase (In preparation, FEBS Letters (by Invitation)).

#### **Research Articles**

Saydam M, Cheng WP, **Palmer N**, Tierney R, Francis R, MacLellan-Gibson K, Khan A, Mawas F. Nano-sized Soluplus® polymeric micelles enhance the induction of tetanus toxin neutralising antibody response following transcutaneous immunisation with tetanus toxoid. Vaccine. 2016.

**N Palmer**, SZA Talib, KC Ratnacaram, D Low, X Bisteau, JHS Lee, E Pfeiffenberger, H Wollmann, JHL Tan, S Wee, RM SOBOTA, J Gunaratne, DM. Messerschmidt, E Guccione, and P Kaldis. The NRF1/CDK2 axis regulates Ehmt1 expression during meiotic prophase. (In review, Journal of Cell Biology).

P Singh, R Patel, **N Palmer**, J Grenier, D Paduch, P Kaldis, A Grimson and JC Schimenti. CDK2 kinase activity regulates male germ cell fate. (In review, Development).