Michaelmas Term 2025 **Dr. Marisa Segal**
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Module 1: The Eukaryotic Cell Cycle (Lecture 1-8)

AIMS: a) To derive principles of human cell cycle control from studies in **model systems**. b) To explore the impact of cell cycle controls on **cell and chromosome integrity** and their relevance to **cancer.** c) To dissect **decision-making switches** across cell cycle transitions.

M1 Lecture 1: THE LANGUAGE OF GENETICS
Learning outcomes: understanding the evolving Genetics Viewpoint underpinning experimental design
. Basic genetic and molecular concepts
. Relevance of model organisms
. Forward genetics as a "starting point"
. Genetics in the whole genome sequencing era

The yeast cAMP pathway, *a case study*. Concept of essential gene, allele, conditional mutant, complementation, genetic interaction (synthetic lethality, redundancy, second site suppressor, dosage suppressor, epistasis). The *relevance* of models: yeast vs human *RAS* genes. Outlook with whole genomes and related tools.

M1 LECTURES 2-8: THE EUKARYOTIC CELL CYCLE.
Learning outcomes:
. Competent interpretation of source experimental data and problem solving
. Confidence in experimental design exploiting tools introduced in the lectures and recommended readings
. With emphasis on evaluation of experimental evidence, develop a broad understanding of cell cycle controls and their significance
. Gaining molecular insight into human cell cycle control

M1 LECTURE 2: THE EUKARYOTIC CELL CYCLE. PRINCIPLES AND MASTER REGULATORS
Biological importance of cell cycle control. Cell growth and cell division. Embryonic vs. somatic cell cycle. *A universal Master Regulator of the eukaryotic cell cycle*: CDK. Multiple CDK complexes: G1, S-phase and M-phase cyclins. Stage specific Cdk catalytic subunits in higher eukaryotes.

M1 LECTURE 3: THE EUKARYOTIC CELL CYCLE. THE G1/S TRANSITION
Feedback loops sharpen the G1/S transition in yeast. Transcriptional control of G1 cyclins. SBF/MBF and the repressor Whi5. Ubiquitin-dependent proteolysis of the CDK inhibitor (CKI) Sic1. Lessons from yeast: SCF control of cyclin E and CKIs in humans. Control of D-cyclins by $CRL4^{AMBRA1}$. E2F and Rb. Common circuitry themes.

M1 LECTURE 4: THE EUKARYOTIC CELL CYCLE. IN AND OUT OF MITOSIS AND THE PERFECT OSCILLATOR
More post-translational modifications switching CDK on & off. *S. pombe*: *wee1*$^{+}$ and *cdc25*$^{+}$. Ubiquitin-dependent proteolysis in M phase. *APC/C targets: mitotic cyclins, mitotic kinases and securin.* Control of sister chromatid cohesion: The players - securin and separase. APC/C and the control of mitotic exit. *Downstream events responding to the oscillator*: cell cycle control of DNA replication. FUCCI.

M1 LECTURE 5: THE EUKARYOTIC CELL CYCLE. CHECKPOINTS
In the beginning - the DNA damage paradigm in yeast. Screening for checkpoint mutants. Brief overview of checkpoints monitoring replication, spindle integrity and orientation. Lessons from yeast: checkpoints in humans.

M1 LECTURE 6: THE EUKARYOTIC CELL CYCLE. TEMPORAL AND SPATIAL CONTROL OF MITOTIC EXIT
Cdc14 and the reversal of CDK phosphorylation. The Fourteen early anaphase release (FEAR) network, the Mitotic Exit Network (MEN) and the Spindle Position Checkpoint (SPOC). Principles for a spatial biosensor at the spindle pole. Conserved core components in higher eukaryotic cells.

M1 LECTURES 7: THE EUKARYOTIC CELL CYCLE. HOW DO CDKS IMPART ORDER —SPECIFICITY OR ACTIVITY THRESHOLDS?
Qualitative (specificity) vs. quantitative (threshold) models, evidence from yeast versus humans. Measuring CDK activity *in vitro* and apparent specificity dictated by cyclins. Studies using analog-sensitive CDK and biosensors. Tug of war between CDK and phosphatases. Time-resolved analysis for in vivo interactors of CDKs in human cells.

M1 LECTURES 8: SINGLE CELL ANALYSIS AND THE ELUSIVE RESTRICTION POINT (R)
Cdk2 biosensor , single cell analysis and R. Multiplex analysis and the structure of the human cell cycle. Revisiting R with START in mind. R biological relevance -- indications from genomic cancer projects.

GENERAL REFERENCES

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Tools for cell cycle analysis

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Core Cell Cycle

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FEAR, MEN & SPOC

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Order in the cell cycle, switches, feedback, thresholds and more...

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