THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

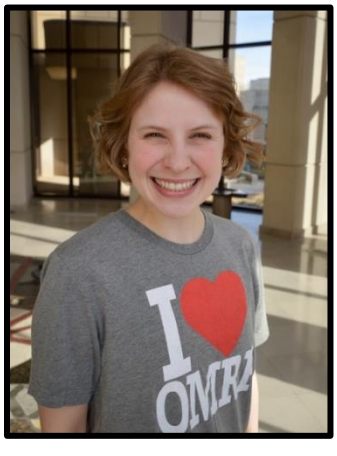
ANNOUNCES THE FINAL EXAMINATION OF

Emily Clowdus

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE

GRADUATE COLLEGE
Department of Cell Biology

Thursday, April 18, 2019, 10:00 am
Biomedical Research Center, Room 109



Separable Roles for Rif1 in Replication Timing and Transcription Control During Early Embryonic Development

COMMITTEE IN CHARGE: Christopher L. Sansam, PhD, Chair
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Scott M. Plafker, PhD; Courtney T. Griffin, PhD
David A. Jones, PhD

ABSTRACT: Eukaryotic replication origins follow a specific pattern of initiation termed the replication-timing program. Clusters of origins within large genomic domains activate together and each domain follows a temporal order of initiation throughout S-phase. Deregulated DNA replication contributes to human developmental disorders and cancer progression, but we know little about how DNA replication is coordinated with changes in transcription and chromatin structure. We have developed the zebrafish into a model system to study how modifications in replication timing coincide with the extensive alterations in the cell cycle, transcription and chromatin organization that occur in the developing embryo. Rif1 has previously been shown to mediate DNA replication timing by suppressing activation of late-replicating origins; in addition, Rif1 has also been linked to heterochromatin organization and gene silencing. The broader role of Rif1 in establishing the replication timing program, gene expression and chromatin structure during early vertebrate development remains unknown. We have performed RNA sequencing and whole-genome replication timing analyses on Rif1 mutant and wild-type zebrafish embryos isolated at multiple developmental stages. These analyses show that Rif1 loss causes general effects on replication timing in the developing zebrafish embryo as well as additional roles for Rif1 in zygotic genome activation and sex determination.