WRIGHT STATE UNIVERSITY | BIOMEDICAL SCIENCES PhD PROGRAM

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DISSERTATION DEFENSE

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PhD Candidate

"DIFFERENTIAL MICRORNA EXPRESSION IN BARRETT'S ESOPHAGUS CORRELATES WITH REGULATION OF POSTERIOR HOMEOTIC GENES"

Monday, April 15th, 2019

9:00 a.m.

NEC Auditorium (Room 101)

Advisor: Scott Baird, PhD
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Barrett's Esophagus (BE) is characterized by the appearance of an intestinal-like epithelium in the distal esophagus. The molecular mechanisms behind BE development are unknown. BE is often preceded by Gastroesophageal Reflux Disease (GERD) and predisposes patients to esophageal adenocarcinoma (EAC). Due to the high mortality rate associated with EAC, BE patients are continuously monitored through upper endoscopy with biopsy for progression to low grade dysplasia (LGD), high grade dysplasia, and EAC. This monitoring technique poses numerous risks, so alternative surveillance and diagnostic techniques for BE pathogenesis are continually studied. microRNA biomarkers in BE pathogenesis may provide alternative means of diagnosis as well as a greater understanding of BE and its progression to EAC. Here, small RNA-sequencing of serum and tissue from GERD, BE, LGD, and EAC patients revealed three candidate tissue microRNAs differentially expressed in BE compared to GERD patients. Differential expression of the three candidate microRNAs was validated in a second cohort of BE and GERD patient tissues by quantitative PCR. Homeobox (HOX) genes are transcription factors which regulate gene expression along the anterior/posterior axis. BE resembles a homeotic transformation, which could be due to aberrant expression of posterior HOX genes in the esophagus, an anterior organ. Gene target analysis revealed two candidate microRNAs are HOX microRNAs, which directly target central and posterior HOX genes. The third candidate microRNA targets a component of Polycomb Repressive Complex 1, a transcriptional repressor of HOX genes. Thus, the three candidate microRNAs may modulate posterior HOX gene expression associated with BE development.