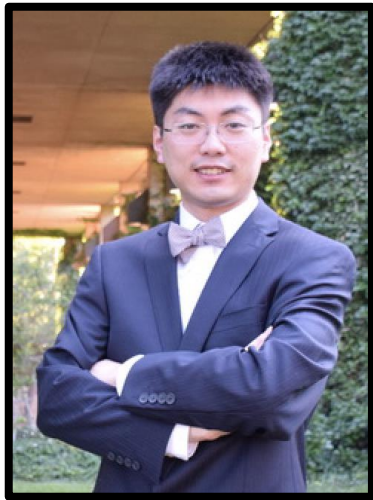


THE GRADUATE COLLEGE OF THE  
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER  
ANNOUNCES THE FINAL EXAMINATION OF

# Yifan Xu

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE



GRADUATE COLLEGE  
*Department of Pathology*

Monday, July 15, 2019, 9:00 am

Hensley Library | Biomedical Sciences Building, Room 433

**EXOSOMAL MICRORNAS IN PANCREATIC CANCER: MECHANISMS OF  
SELECTIVE ENRICHMENT AND THE POTENTIAL FOR BIOMARKER  
DEVELOPMENT**

COMMITTEE IN CHARGE: Wei-Qun Ding, PhD; Joe Z. Zhao, PhD;  
Priyabrata Mukherjee, PhD; Guangpu Li, PhD; Doris M. Benbrook, PhD

ABSTRACT: Pancreatic ductal adenocarcinoma (PDAC) is the third-leading cause of cancer death in the US. A better understanding of the biology of PDAC is essential for the development of novel therapeutic and diagnostic strategies against this malignant disease. Exosomes, the endosome-derived extracellular vesicles containing cellular lipids, proteins, and microRNAs (miRNAs), are secreted from most cell types and act as mediators of intercellular communication. While recent studies have shown that cancer exosomal miRNA signaling promotes tumor progression via interacting with the tumor microenvironment, the biology behind and its potential implications in PDAC remain less explored. Using human PDAC cell lines, xenograft nude mice, and plasmas from patients with localized PDAC, we demonstrate that: 1) SRSF1 mediates selective exosomal miRNA enrichment to initiate exosomal miRNA signaling in PDAC cells; 2) Exosomal miR-1246 is derived from RNU2-1 through a non-canonical biogenesis process; 3) The highly enriched exosomal miRNAs, such as miR-1246 and miR-196a, are potential non-invasive biomarkers for early detection of PDAC. These findings provide molecular insights into the cellular process that enriches exosomal miRNAs in PDAC cells and indicate novel strategies for the development of PDAC therapeutics and diagnostics.