THE OHIO STATE UNIVERSITY
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Ph.D. Candidate

Molecular basis of the DExH-box RNA helicase
RHA/DHX9 in eukaryotic protein synthesis

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Biomedical Research Tower, Room 105
10:00 am

VITA


2010 . . . . . . . . . . B.S. Biochemistry & Molecular Biology
Gettysburg College

2015 . . . . . . . . . . Ph.D. Candidate in Biomedical Science:
The Ohio State University

COMMITTEE MEMBERS
Kathleen Boris-Lawrie, Ph.D. (Advisor)
Joanna Groden, Ph.D.
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ABSTRACT

RNA helicase A (RHA/DHX9) is a cellular protein and member of the DExH/D-box RNA helicase family that is necessary for the translation of pathogenic retroviral transcripts and the cellular proto-oncogene junD. The known characteristic of RHA-mediated protein synthesis is the select recognition and association of RHA with the distinguishing 5’ termini of retroviral and junD transcripts. These mRNAs harbor a distinct 5’ RNA motif known as the posttranscriptional control element (PCE). The PCE functions in cis to stimulate translation activity via the canonical cap-dependent scanning mechanism that defines eukaryotic protein synthesis. The main gap in knowledge is how RHA, as the host effector of the PCE, engages targeted translation activity.

In this study, the molecular basis of RHA in eukaryotic protein synthesis was defined. First, RHA was identified to selectively interact with the non-canonical CBP80/20 cap-binding protein. This distinct association conferred a novel role for RHA in maintained cap-dependent translation during cell stress. Second, novel significance was identified for RHA as a post-initiation effector of protein synthesis. This activity is unique for a DExH/D-box RNA helicase and was attributed to a role for its C-terminal arginine-glycine-rich domain in 80S ribosome stabilization. Third, RHA was recognized to engage in both homopolymeric and heteropolymeric RNP states that regulated its translation activity. Here RHA was identified to self-associate and selectively interact with related DExH-box RNA helicase DHX30 in a manner that impeded or facilitated its activity in protein synthesis, respectively.

Together the data obtained from this dissertation research provided novel and significant insight into the eukaryotic translation process. By elucidating the molecular basis of RHA in protein synthesis, new paradigms were identified for the eukaryotic translation process. These included: a molecular basis for maintained cap-dependent translation during cell stress, significance of DExH/D-box RNA helicases in post-initiation translation control, and a role for distinct homo- and hetero-polymeric binding events in the regulation of targeted translation. We posit that these findings afford molecular significance for the association of RHA with breast, prostate and lung cancer, its identification as the major auto-antigen in systemic lupus erythematosus patients, and the role for RHA as a major stimulator of pathogenic viruses that infect and cause disease within animal and human hosts. Future studies are aimed to connect the molecular findings of this dissertation research with the clinical significance of RHA. The objective is to provide a greater understanding of the relationship between RHA, eukaryotic protein synthesis, and cell biology that informs animal and human health and disease.
RECENT ABSTRACTS AND PRESENTATION

**Oral Presentations (National Meetings)**

"Molecular basis of RNA helicase A-dependent translation regulation of viral mRNA." 2013. Workshop on Posttranscriptional regulation of Virus Expression. Syria, VA.

**Oral Presentations (Invited Seminars)**


**Oral Presentations (Selected Presentations)**

"The DExH-box helicase RHA/DHX9 selectively regulates retroviral gene translation by a novel cap-dependent mechanism." 2014. OSU Biomedical Sciences Graduate Program Retreat. Columbus, OH.

"RHA/DHX9 regulates oncogenic retroviral and cellular gene expression through a distinct posttranscriptional mechanism." 2014. OSU College of Veterinary Medicine Research Day. Columbus, OH.

**Poster Presentations**

"The DExH-box helicase RHA/DHX9 selectively regulates pathogenic retroviral gene translation by a novel cap-dependent mechanism." 2015. 14th Annual OSU College of Medicine Trainee Research Day. Columbus, OH.

"RNA helicase A interacts with translational regulatory proteins to control the expression of viral and cellular mRNAs." 2012. OSU College of Veterinary Medicine Research Day. Columbus, OH.
**RECENT PUBLICATIONS**


**AWARDS AND HONORS**

2014 Procter & Gamble Award for Top Student Speaker at the OSU Biomedical Sciences Graduate Program Retreat

2014 OSU, College of Medicine, Scientific Travel Award for Top Student Speaker at the Biomedical Sciences Graduate Program Retreat

2014 OSU, College of Veterinary Medicine, Research Day Scientific Travel Award for Platform Presentation

2014 Kenyon Institute in Biomedical and Scientific Writing Scholar

2013 Preparing Future Faculty Fellow, Kenyon College

2013 OSU, College of Medicine, Research Day Scientific Travel Award for Top Poster Presentation

2011 OSU, College of Medicine, Systems and Integrated Biology Training Fellow

2010 OSU, University Fellow

**FUTURE PLANS**

Scientific research, teaching, and mentoring are equal passions of mine. I look forward to a career as an academic faculty member, inspiring the next generation of scientists like so many did for me.