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Topic Category: 4054-ASIP IMMUNOHISTOCHEMISTRY, MICROSCOPY, AND IMAGING

First Author: Kate Price
Brigham Young University 3054 LSB Provo, UT 84602
United States
Phone:
paul_reynolds@byu.edu

First Author is a: Undergraduate
First Author is a member of: Not a Member of a Host EB Society
First Author Degree:

Presentation Preference: Indifferent

Sponsor: Paul Reynolds
Sponsor Phone: 8014221933
paul_reynolds@byu.edu
Sponsor's Society: Pathology - American Society for Investigative Pathology (ASIP) - Host Society
Keywords: 1. placenta 2. mTOR

Differential Expression of mTOR Related Molecules in the Placenta of Gestational Diabetes Mellitus (GDM), Intrauterine Growth Restriction (IUGR) and Preeclampsia patients

Kate Price, Brent Kimbler, Nekel Knowlton, Levi Franson, Kelsey M Hirschi, Paul R Reynolds, Juan A Arroyo. Brigham Young University, Provo, UT

The mechanistic target of rapamycin (mTOR) pathway is involved in placental growth and function during pregnancy. The mTOR pathway responds to nutrient availability and growth factors that regulate protein expression and cell growth. mTOR disruptions are associated with the development of obstetric complications which often result in adverse health outcomes for the mother and/or fetus. The purpose of this study was to identify the differential placental expression of various mTOR-associated proteins during normal gestation (Control), gestational diabetes mellitus (GDM), intrauterine growth restriction (IUGR) and preeclampsia (PE). Immunohistochemistry was used to stain human placenta for activated proteins (phospho; (p)AKT, (p)ERK, (p)mTOR, (p)p70 and (p)4EBP1. Real-time PCR array was completed to show differing placental expression of additional mTOR-associated genes during these conditions. We observed: 1) increased (p)AKT during GDM, 2) increased (p)ERK during IUGR, 3) increased (p)mTOR during GDM and decreased (p)mTOR during IUGR and PE, 4) increased (p)p70 during IUGR and decreased (p)p70 during GDM and PE, 5) increased (p)4EBP1 during GDM, IUGR, and PE, and 6) differential placental expression of mTOR pathway associated genes. We conclude that regulation of the mTOR pathway is uniquely involved in the development of these obstetric complications. These results may provide insight into the physiological relevance of these pathways, and if so, their modification during gestation may help alleviate these diseases.

Support or Funding Information
This work was supported by a grant from the Flight Attendant's Medical Research Institute (FAMRI, PRR and JAA) and a BYU Mentoring Environment Grant (JAA and PRR).