CHRD 2021: Abstract & Poster Submission Form

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Research Category:

○ Basic Science

◉ Clinical

○ Community Health / Policy

What was your role in the project?

☐ Design

☑ Perform Experiments

☑ Analyze Data

☑ Write Abstract

☐

Presenter Status:

◉ Undergraduate Students

○ Masters Student

○ PhD Student

○ Post-Doctoral Fellows

○ Residents

○ Non-Trainee

Title

Unfolded Protein Response (UPR) is a risk factor for Alveolar Rhabdomyosarcoma (RMS)?

Background

Rhabdomyosarcoma (RMS) is a muscle-derived tumor and is the most common pediatric soft tissue sarcoma, representing 5% of all childhood cancers. Recent assessments suggest that the incidence rate for RMS is higher than 250–350 cases per year in Canada. Subtypes of RMS include embryonal RMS (ERMS), Alveolar RMS (ARMS), spindle RMS (SRMS) and Pleomorphic RMS (PRMS). Alveolar RMS is an invasive subtype that is vastly suffered by adolescents and young adults. To this date, initial debulking surgery/ total removal, followed by adjuvant chemo/ RT (radiation therapy) is the only available treatment for ARMS.

The endoplasmic reticulum (ER) is the main organelle in the cell that is involved in the proper biosynthesis, maturation and folding of proteins. In case of stressful stimuli, the ER initiates a series of adaptive response mechanisms called the unfolded protein response (UPR). UPR has three arms namely PERK, IRE1α and ATF6. IRE1α has both RNAse and kinase activity after being activated in UPR pathway. RNAase activity of IRE1α induced splicing of (XBP1s) which is involved in regulation of cancer cell proliferation. XBP1s is a transcription factor regulating genes that are associated with the cellular stress response. UPR chaperone proteins also include BiP (GRP78), associated with ATF6, IRE1α, and PERK and keeping them inactive.

Objective

In this study, our team investigated if UPR is correlated with ARMS pathogenesis and is a risk factor for this deadly pediatric disease.

Methods

Human ARMS samples were assessed using tissue microarray (TMA) for BiP, IRE1α, and XBP1s. Proteins in question were stained using immunohistochemistry (IHC), enabling us to study their expression. Three blinded pathologist experts scored each protein expression using the following scales: None: no expression, 1 (weak expression), 2 (moderate expression), and 3 (high expression)

Results

Through this investigation, we were able to see the correlation between ARMS and the expression of BiP, IRE1α, cytosolic XBP and nuclear XBP ($P< 0.05$).

Our results revealed that the expression of BiP, sXBP1, and IRE1α, but not cytosolic XBP1, are significantly associated with ARMS compared to normal skeletal muscle tissues. The results also showed correlations of BiP with lymph node score in ARMS (p value = 0.05).

Conclusion

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