CHRD 2024: Abstract Submission Form

Presenter Name
Bhavya Bhushan

Presenter Status
Undergraduate Students

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Targeting Autophagy in Juvenile Zebrafish to Enhance Alveolar Rhabdomyosarcoma Treatment Strategies

Background
Alveolar rhabdomyosarcoma (ARMS) is an aggressive childhood cancer with poor differentiation and resistance to therapies. Autophagy, a key stress response, regulates differentiation and proliferation. Our team is exploring therapeutic strategies targeting autophagy pathways to improve ARMS outcomes. Preliminary investigations suggest autophagy influences tumour differentiation in ARMS. In this pilot study, we aimed to establish a method to control autophagy in juvenile zebrafish and investigate its impact on proliferation.

Objective
This pilot study aimed to establish a method to control autophagy in juvenile zebrafish and assess its impact on muscle cell proliferation, with implications for ARMS treatment.

Methods
Juvenile zebrafish (2.5 months old) were treated with 2.5 and 10 nM Bafilomycin A1 (Baf-A1), an autophagy flux inhibitor, for 14 days with dosing every 72 hours. Behaviour (velocity and distance travelled) was assessed at each time point. EdU, an S-phase marker, was added 24 hours before euthanasia to assess muscle cell proliferation. Sectioned tissues were collected for immunohistochemistry of autophagy markers (LC3 and SQSTM1), cell proliferation analysis, and eye diameter in whole juvenile fish.

Results
Baf-A1 at 10 nM significantly inhibited autophagy flux in zebrafish skeletal muscle, as demonstrated by a marked increase in LC3 and SQSTM1 puncta, indicating autophagosome accumulation. This inhibition led to a significant rise in muscle cell proliferation, shown through increased EdU staining. Notably, Baf-A1 had no significant impact on zebrafish behavior, as both velocity and distance travelled remained unchanged across all time points. Furthermore, no alterations in eye size were observed, suggesting that autophagy inhibition did not result in any adverse developmental effects or impact general fish health.

Conclusion
Inhibition of autophagy via Baf-A1 enhances muscle cell proliferation without affecting behaviour or development in juvenile zebrafish. These findings support further investigation of autophagy inhibition as a co-treatment with chemotherapy drugs targeting ARMS tumour differentiation.

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No

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