CHRD 2024: Abstract Submission Form

Presenter Name
Rushie Tyagi

Presenter Status
PhD Student

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Islet-Derived Extracellular Vesicles – A Potential Biomarker for Amyloid Formation in Type 2 Diabetes and Human Islet Transplants in Type 1 Diabetes

Background
Amyloid formation in pancreatic islets contributes to progressive beta-cell dysfunction/death in Type 2 diabetes (T2D). Amyloid also forms in human islets during pre-transplant culture and post-transplantation in patients with Type 1 diabetes (T1D) which contributes to islet graft failure. Islet amyloid mainly forms by aggregation of human islet amyloid polypeptide (hIAPP; amylin), a peptide hormone normally produced by beta cells. Therapeutic strategies to prevent amyloid-mediated beta-cell death are currently limited by lack of diagnostic tools to assess amyloid formation in patients before irreversible beta-cell damage occurs.

Objective
We examined the role of islet derived extracellular vesicles as a potential biomarker for detection of islet amyloid formation in patients with T2D and transplanted islets in T1D.

Methods
Isolated human islets from cadaveric donors (n=3) were cultured in normal (5.5 mM) glucose (no amyloid) or elevated (11.1 mM) glucose (to form amyloid) for 7 days. EVs were isolated from culture medium, characterized, and their purity was assessed by EV specific markers. (Pro)hIAPP and its aggregates (oligomers) were detected in purified EVs by Western blot and quantified by densitometric analysis. The proportion of beta cells containing oligomer-positive small EVs was assessed by quantitative CD63 (exosome marker) and A11 (oligomer) immunolabelling.

Results
(Pro-hIAPP) forms were detectable in human islets before and after culture in both normal and elevated glucose. Mature hIAPP was the major form detected in EVs from islets cultured in normal glucose while culture with elevated glucose promoted amyloid formation and increased EV content of immature hIAPP forms. Moreover, hIAPP aggregates (oligomers) were detectable in EVs derived from amyloid-forming islets but not amyloid-negative islets.

Conclusion
In summary, these data suggest that EVs released from amyloid-forming human islets contain immature and aggregated forms of hIAPP. Islet-derived EVs may therefore provide a novel biomarker for assessment of amyloid formation in patients with diabetes.

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No

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