CHRD 2022: Abstract & Poster Submission Form

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Presenter Status
- ○ Undergraduate Students
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- ◉ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
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Research Category
- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

Role in the project
- ☐ Design
- ☑ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☐

Title
Replicative senescence in pancreatic beta cells alters extracellular vesicle characteristics

Background

With an increasing aging population, there is a concomitant increase in age-associated co-morbidities like type 2 diabetes (T2D), wherein a sustained elevated demand for insulin likely drives the accumulation of senescent pancreatic β-cells. Senescent cells secrete higher amounts of pro-inflammatory cytokines as well as extracellular vesicles (EVs). EVs are membrane-bound nanoparticles that are critical in cellular communication and can exert autocrine, paracrine and endocrine effects. EVs vary in size: small-EVs (sEVs) vs. medium/large-EVs (m/lEVs) and enclosed cargo.

Objective

Little is known about EVs released from pancreatic β-cells during replicative senescence.

Methods

Low-passage (LP) and high-passage (HP) murine pancreatic β-cells (MIN6) were grown in EV-depleted media for 48hrs. EVs were isolated from LP (P22-30) and HP (P50-60) conditioned media using differential ultracentrifugation and ultrafiltration, and characterized using tunable resistive pulse sensing (N=6). Cell viability was determined (trypan blue exclusion), cells harvested, and lysates frozen at -80°C for future analysis of senescence markers.

Results

sEV concentration was ~23-fold higher in LP-cells (1.18E+09 particles/ml; p=0.0002) and ~16-fold higher in HP-cells (1.35E+0.9 particles/ml; p<0.0001) vs. m/lEVs in each group, illustrating a preponderance of sEV release from cells irrespective of passage. Comparing between passages, secretion of m/lEVs was 1.77-fold higher in HP-EVs vs. LP-EVs (p=0.02, N=6). No significant increase was observed in sEV secretion from HP vs. LP cells. Average EV size was 9% lower in HP-EVs (113nm) vs. LP-EVs (125nm; p=0.04, N=5). EV protein yield, cell count and viability remained unchanged across groups.

Conclusion

Our data show: 1) a preferential release of small-EVs from MIN6 cells irrespective of passage, 2) HP-EVs are smaller in average size, and 3) a 1.77-fold increase in m/lEVs secretion in HP-MIN6 cells. Overall, there is increased EV release with replicative senescence in MIN6 cells. The upstream pathways regulating EV biogenesis, and the functional effects of senescent cell-derived EVs have yet to be elucidated.

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