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| **Saturated Fatty Acids Reduce Interferon-Lambda Response of Airway Epithelial Cells to Influenza A Virus** |
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| **Introduction/Aim:** Obesity affects >30% of Australian adults and is a major risk factor for severe viral respiratory disease. This was highlighted by both the SARs-CoV2 and 2009 H1N1 pandemics. Obesity is associated with increased levels of circulating saturated fatty acids (SFA), contributing to the chronic low-grade systemic inflammation observed in obesity. Previously, our group has shown that consuming a meal high in SFA can increase activation of the NLRP3 inflammasome in the airways of patients with asthma. While others have shown increased NLRP3 activation is implicated in the pathogenesis of severe inflammation observed during influenza A virus-induced lung disease. The aim of this study was to determine the impact of SFAs on the immune response of airway epithelial cells to IAV.  **Methods:** BCI-NS1 cells, an airway epithelial cell line, in submerged culture were pre-treated with media or SFAs palmitic acid (250µM), stearic acid (1000µM) or pentadecanoic acid (50µM) at physiologically relevant concentrations for 3 hours. Cells were then washed with phosphate buffered saline and infected with H1N1pdm09 (Multiplicity of Infection 0.5) for 48 hours. Cell culture supernatants were collected and assayed by Enzyme-Linked Immunosorbent assay for Interleukin (IL)-6 and Interferon (IFN)-λ. Data was analysed using Kruskal-Wallis Test, with Dunn’s multiple comparisons where appropriate.  **Results:** Pre-treatmentwith SFAs palmitic acid (7.9pg/mL±4.5 (SD); n=6, p<0.01), stearic acid (10.3pg/mL±7.7 (SD); n=6, p<0.01) and pentadecanoic acid (11.3pg/mL±8.1 (SD); n=6, p<0.01) reduced IFN-λ production of BCI-NS1 cells infected with H1N1pdm09 compared to cells pre-treated with media alone before H1N1pdm09 infection (42.7pg/mL±14.0 (SD); n=6). Production of IL-6 by BCI-NS1 cells was unchanged by pre-treatment with SFAs prior to H1N1pdm9 infection.  **Conclusion:** Saturated fatty acids may impair the anti-viral response of airway epithelial cells. Therefore, excess circulating SFAs observed in obesity may contribute to severe outcomes in respiratory viral disease.  **Grant Support:** John Hunter Hospital Charitable Trust |