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Dietary saturated fatty acids reduce Interferon-Lambda response of airway epithelial cells to Influenza A Virus

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Obesity affects > 30% of Australian adults and is a rapidly growing health concern, on both national and global scales[1]. Obesity is associated with an excess of nutrients in the circulation, particularly saturated fatty acids which are thought to contribute to chronic low grade systemic inflammation[2]. People with obesity are also known to have an increased risk of severe respiratory viral disease, highlighted by both the recent SARs-CoV-2 pandemic and the 2009 Influenza A H1N1 pandemic[3,4]. Previously, our group has shown that consuming a meal high in saturated fatty acids can increase activation of the NLRP3 inflammasome in the airways of adults with asthma[5], while others have shown increased NLRP3 activation is implicated in the pathogenesis of severe inflammation observed during the peak of IAV-induced lung disease[6]. We sought to determine the impact of dietary saturated fatty acids on the immune response of airway epithelial cells to Influenza A Virus, and to examine if this is a factor for severe respiratory viral disease outcomes. We pre-treated BCI-NS1 cells, an airway epithelial cell line, with either media or physiologically relevant concentrations of the saturated fatty acids, palmitic acid (250 μM), stearic acid (1000 μM) or pentadecanoic acid (50 μM) for 3 hours at 37°C (5% CO_2). Cells were then washed with phosphate buffered saline and infected with Influenza A (H1N1pdm09) (Multiplicity of Infection 0.5) and incubated for 48 hours at 37°C (5% CO_2). Cell culture supernatants were collected and assayed by Enzyme-Linked Immunosorbent assay for Interleukin (IL)-6 and Interferon (IFN)-λ. Pre-treatment with saturated fatty acids reduced IFN-λ production of virus infected cells (following palmitic acid pre-treatment IFN-λ was 7.9 pg/mL ± 4.5 (SD); $n = 6$, $p < 0.01$, following stearic acid pre-treatment IFN-λ was 10.3 pg/mL ± 7.7 (SD); $n = 6$, $p < 0.01$, and following pentadecanoic acid pre-treatment IFN-λ was 11.3 pg/mL ± 8.1 (SD); $n = 6$, $p < 0.01$, compared to cells pre-treated with media alone (42.7 pg/mL ± 14.0 (SD); $n = 6$). IL-6 production was unchanged by pre-treatment with saturated fatty acids prior to H1N1pdm9 infection. As previously mentioned, the excess saturated fatty acids are correlated with chronic low-grade systemic inflammation[2]. This is thought to be of contribution to the worsened infection-induced outcomes in response to Influenza A. We conclude that dietary saturated fatty acids circulating in people with obesity may impair the anti-viral response of airway epithelial cells and further contribute to severe outcomes in respiratory viral disease experienced by those with obesity.

References

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