**Lipidomic Profiling in HIV: Implications for Risk-Prediction Models**

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**Background:** HIV positive patients are at increased risk for coronary artery disease (CAD) with both HIV and antiretroviral associated dyslipidaemia contributing. Targeted analysis of over 400 plasma lipid species by mass spectrometry can sensitively identify changes in the plasma lipidome associated with the development of atherosclerosis.

**Methodology:** In a retrospective case-control study we profiled the plasma lipidome (268 lipid species included) of 113 subjects. Cases (n=23) were HIV positive individuals who had a blood sample available in the 12 months prior to the diagnosis of CAD. They were age and sex matched 1:2 with HIV positive individuals without a diagnosis of CAD (n=45, HIV+ controls) and with healthy HIV negative volunteers (n=45, Healthy controls). Risk prediction models incorporating the plasma lipidome were compared with established cardiovascular risk scores.

**Results:** 104 (92%) were male with a median age of 52.2 years (IQR 40.9-61.4). HIV patients (combined cases and HIV+ controls) were more likely to smoke (31 [45.5%] v's 3 [6.7%], p <0.001), had higher median hsCRP (2.78 [IQR 1.97 - 6.67] v's 0.64 [IQR 0.36 - 1.48], p<0.001) and triglyceride levels (1.77 [IQR 1.47-2.76] v's 1.00 [0.7-1.76], p <0.001) and lower high density lipoprotein cholesterol (0.95 [IQR 0.78 - 1.13] v's 1.50 [IQR 1.1 - 1.7], p <0.001) than healthy controls. 23 (100%) of cases and 40 (88.9%) of HIV+ controls were currently receiving antiretroviral therapy. 83 lipid species and 7 lipid classes were identified that were significantly associated with HIV infection. A further 74 species and 8 classes where significantly associated with future CAD event. 15 species (predominantly in the triacylglycerol and diacylglycerol classes) were elevated in HIV infection and further elevated in HIV subjects who went on to have a CAD event. Risk prediction models incorporating lipid species outperformed (AUC=0.78 (0.775,0.785)) all other tested risk scores (including the Framingham, Reynolds and the Data Collection on Adverse Events of Anti-HIV drugs [D:A:D] risk equations) in the identification of HIV positive subjects who went on to develop CAD.

**Conclusions:** Treatment-experienced HIV positive patients demonstrate significant differences in plasma lipidome when compared with healthy HIV negative controls. There is a potential application for improved cardiovascular risk screening of HIV positive patients in the clinical setting by including lipid species in risk prediction models.