superoxide release in atrial samples of patients with post-operative AF but had no effect in patients with permanent AF. Similarly, atorvastatin did not induce a mevalonate-reversible changes in the atrial BH4 concentration and NOS uncoupling in neither group.

**Conclusions** Together, these findings indicate that upregulation of NOX2-NADPH oxidases is an early but transient event in the natural history of AF, as mitochondrial oxidases and uncoupled NOS account for the statin-resistant increase in atrial superoxide production in permanent AF. Variation in atrial sources of reactive oxygen species with the duration and substrate of AF may explain the reported variability in the effectiveness of statins in the prevention and management of AF.

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**Abstract 143**

**Figure 1**

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**Abstract 143**

**Figure 2**

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**Abstract 144**

**Figure 1**

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**Abstract 144**

**Figure 2**

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Cardiac hypertrophy is a prerequisite for the development of heart failure. It currently affects almost one million people in the UK. Few effective anti-hypertrophic agents with druggable properties have been identified. Recently, our group showed that plasma membrane calcium ATPase isoform 4 (PMCA4) knockout mice showed a reduced response to hypertrophic stress prompting us to hypothesise that a novel PMCA4 specific inhibitor would modify the development of cardiac hypertrophy. A library of 1230 medically optimised compounds was screened using a novel in vitro assay which measures the Ca2+ dependent ATPase activity of PMCA4. The compound AP2 was identified, which inhibited PMCA4 activity with high affinity (IC50=300 nM) but not other PMCAisoforms (PMCA1, PMCA2 and PMCA3) or related ATPases which are expressed in the heart including the Ca2+ dependent ATPase activity of PMCA4. The compound AP2 inhibited endothelial cell tube formation on Matrigel and migration using an injury migration model. Human TFPIct (hTFPIct) inhibited tube formation and migration through inhibition of Vascular Endothelial Growth Factor Receptor-2 (VEGFR2) tyrosine-951 phosphorylation, a key event in migration. hTFPIct did not inhibit VEGF121-induced migration, which lacks the heparin-binding domain of VEGF165. Utilising the chimeric receptor, EGDR, which contains the extracellular domain of epidermal growth factor (EGF) and the intracellular domain of VEGFR2/KDR, a direct effect of TFPIct on the intracellular domain of VEGFR2 was excluded (Abstract 143 figure 2). TFPIct did not block phosphorylation of EGDR when stimulated with EGF.