Abstract 113 Figure 1 One way ANOVA showed significant difference between the groups, F=5.26, p=0.002. Post hoc comparison with Bonferroni test showed that BT was significantly higher in T2DM with non-obstructive CAD compared to the other three groups p<0.05.

Abstract 113 Figure 2 Patients are grouped according to their diabetic status and coronary lesion characteristics. One way ANOVA for IL-6 F=5.608, p=0.03, TNF α F=3.153, p=0.03, P-selectin F=3.44, p=0.02, post hoc tests including Bonferroni showed t p<0.05 for multiple comparisons between T2DM + Non obstructive CAD group and the rest.

activation as measured by P selectin were highest in this group. (p=0.022, ANOVA F=3.422) (Abstract 115 figure 2). Interleukin 1, interferon γ and soluble CD40 ligand levels were similar between the groups.

Conclusion Patients with T2DM and non-obstructive CAD had highest BT and markers of platelet activation and inflammation. These findings suggest biochemical changes also play a significant role in evolution of NSTE-ACS in T2DM. A causal link, if confirmed by large-scale studies may offer us an opportunity to identify therapeutic targets like individualised anti thrombotic therapy and anti inflammatory therapy in this high risk population.

114 WHOLE GENOME SEQUENCING TO IDENTIFY GENETIC VARIANTS UNDERLYING CARDIOVASCULAR DISEASE AMONG INDIAN ASIANS

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Introduction Indian Asians have a twofold higher risk of cardiovascular disease compared to Europeans which is not explained by conventional cardiovascular risk factors or known genetic variants. The genetic architecture of Indian Asians has not previously been described. We hypothesised that whole genome sequencing of Indian Asians may identify both common and rare variants specific to this population that contribute to their increased cardiovascular disease risk.

Methods We carried out whole genome sequencing (mean depth 28.4×) in eight men of Indian Asian origin participating in the London Life Sciences Population (LOLLIPOP) study. Sequencing was carried out using paired end and mate pair libraries on an Illumina GA2 machine. Read alignment was done by BWA, and variants called using GATK and SAMtools. Sensitivity for single nucleotide polymorphism (SNP) detection was assessed by comparison to whole genome data.

Results We identified 6602840 autosomal variants, 436823 of which are novel SNPs. Of these, 50856 appear to be common (present at least twice, corresponding to minor allele frequency >10%). We found 21659 autosomal SNPs that were expected to affect protein coding, of which 21744 are novel. Among the coding SNPs identified, 145 are in genes linked to human diseases, such as obesity (FTO, UCP1), diabetes mellitus (CDKAL1, GCCR, HNF1B), lipid metabolism (APOB), hypertension (NO32), and renal disease (NPH4, PKD1). We also found 65613 novel autosomal indels of which 35097 are present at least twice, and 2301 novel deletions >100 bp. We show that >50% of the novel genetic variants are not in high LD (r2<0.8) with tag SNPs and hence not captured on available high-density microarrays.

Conclusions We identify more than 500000 genetic variants not previously reported in 1000 genomes or dbsNP, and likely to be Indian Asian specific. The novel variants identified here are strong candidates for genetic factors underlying the increased risk of diabetes and cardiovascular disease among Indian Asians.

115 UNIQUE CHARACTERISTICS OF CD14++CD16+ MONOCYTES IN PATIENTS WITH ACUTE HEART FAILURE AND IMPLICATIONS FOR CLINICAL OUTCOME

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Background Monocytes play important roles in inflammation, angiogenesis and tissue repair and may contribute to the
pathophysiology of heart failure (HF). We examined differences in monocyte subset numbers and expression of cell surface markers of activation (CD14) and chemotaxis (CCR2) in patients with acute HF (AHF), stable HF (SHF) and controls and evaluated their impact on clinical outcomes.

Methods: Three monocyte subsets [CD14++CD16−CCR2+ (Mon1), CD14++CD16+CCR2+ (Mon2) and CD14+CD16+ +CCR2− (Mon3)] were analysed by flow cytometry in 51 patients with AHF, 42 patients with SHF, 44 patients with stable coronary artery disease (CAD) and 40 healthy controls (HC). Surface marker expression of CD14 and CCR2 was also measured and expressed as median fluorescent intensity (MFI). The prognostic impact of monocyte subsets was examined in patients with AHF.

Results: Patients with AHF had significantly higher Mon1 counts compared to other groups (p<0.001 for all) (Abstract 115 table 1). Similarly, Mon2 counts were increased in AHF compared to SHF (p=0.011), CAD (p<0.001) and HC (p<0.001). Mon3 counts were also increased in SHF compared to both CAD and HC groups (p=0.023, p=0.085 respectively). In AHF, CD14 expression by Mon2 was significantly higher than in CAD patients (1481±473 vs 1228±408, p=0.039) and in SHF patients, CD14 expression by Mon2 was significantly higher than in CAD patients (1502±494 vs 1228±408, p=0.031). CCR2 expression by Mon2 in AHF was higher than in HC (128±43.9 vs 104±28.5, p=0.015) and CCR2 expression by Mon2 was higher in SHF compared to HC (126±56.2 vs 104±28.5, p=0.032). 20 patients (39.2%) with AHF reached the primary end point of death or re-hospitalisation, with a median time to event of 129 (IQR 70.0–209) days. In Cox regression analysis, after adjustment for age, left ventricular ejection fraction, serum creatinine and brain natriuretic peptide, Mon2 count remained an independent negative predictor of combined death and re-hospitalisation [HR (for an increase of 10 cells/μl) 0.829 (CI 0.713 to 0.964; p=0.015)]. In Kaplan–Meier analysis AHF patients with Mon2 above median (59.9 cells/μl) had significantly better outcomes compared to those below the median (Abstract 115 figure 1).

Conclusion: We have shown for the first time that CD14++CD16+ monocytes (Mon2) are an independent negative predictor of adverse prognosis in patients with AHF. This subset is phenotypically different from the other monocyte subsets, with increased expression of markers of activation (CD14+) and chemotaxis (CCR2). Consequently, the Mon2 subset merits further evaluation as a prognostic marker and potential therapeutic target in patients with HF.