lipid-lowering treatments. Coronary artery bypass grafting (CABG) is commonly used to bypass coronary arteries diseased by atherosclerosis, routinely using the saphenous vein (SV) as a conduit. Early after grafting the SV adapts to the arterial environment through remodelling, and increased motility of smooth muscle cells (SMC). A clinical association between Lp(a) and coronary artery disease is evident; however, its role in vein graft failure is less clear.

Conclusions Our previous studies have developed an efﬁcient method for producing a large number of smooth muscle cells (SMCs) from embryonic stem (ES) cells. However, little is known about the underlying mechanism.

Methodology and results Nuclear proteins were harvested and isolated from undifferentiated and differentiating ES cells at different time points, and subjected to proteomics analysis. Notably, the majority of upregulated nuclear proteins during SMC differentiation were involved in chromatin remodelling, cellular morphogenesis, cell proliferation, DNA replication, protein synthesis, mRNA transport and RNA processing processes. We further focused on chromobox protein homologue 3 (Cbx3) owing to its involvement in the regulation of gene-specific expression. Knockdown of Cbx3 in the differentiating ES cells resulted in downregulation of smooth muscle differentiation markers, while enforced expression of this gene enhanced SMC differentiation in a dose-dependent manner. Our data also suggested that Cbx3 mediates SMC differentiation from ES cells through regulation of smooth muscle-specific transcription factor, serum response factor (SRF) and its coactivator myocardin. Furthermore, we also demonstrated that another smooth muscle transcription factor, Dia1, functions as bridge protein between Cbx3 and SRF, through which Cbx3 modulates SRF activation, and mediates ultimately SMC differentiation from stem cells. Importantly, in vivo perivascular knockdown of Cbx3 signiﬁcantly increased wire-injury-induced neointima formation in mice.

Conclusions We examined the effects of a novel NAADP inhibitor, Ned-19, on ischaemia-reperfusion injury in isolated adult rat ventricular cardiomyocytes (ARVC). The sensitivity of mitochondrial permeability transition pore (mPTP) was measured in ARVC using a laser-induced protective function in vessel injury-induced neointima formation, indicating that Cbx3 could be a potential new therapeutic target for intervention in SMC proliferative-related vascular diseases.

Rationale We have recently established a transgenic mouse model for conditional induction of long-term hibernation via myocardium-speciﬁc induction of a VEGF-sequestering soluble receptor.

Objective Using a combined ‘omics’ approach, we aim to resolve the cardioprotective response that preserves myocardial viability under chronic hypoxia by integrating mRNA, protein and metabolite changes in unsupervised network analysis.

Methods and results A genome array, difference in gel electrophoresis and proton nuclear magnetic resonance spectroscopy were employed to dissect the hibernation process into an initiation and a maintenance phase. The initiation phase was characterised by peak levels of K( ATP) channel and glucose transporter 1 (GLUT1) expression. Glibenclamide, an inhibitor of K( ATP) channels, blocked GLUT1 induction. In the maintenance phase, tissue hypoxia and GLUT1 expression were reduced and metabolite concentrations were kept relatively constant. Unguided bioinformatics analysis on the combined datasets conﬁrmed that anaerobic glycolysis was affected and that the observed enzymatic changes in cardiac metabolism were directly linked to hypoxia-inducible factor (HIF)-1 activation. Notably, the combination of the proteomic and transcriptomic datasets improved the statistical conﬁdence of the pathway analysis by two orders of magnitude, with HIF—hypoxia—Akt signalling and glycolysis being the most signiﬁcant.

Conclusions We demonstrate how combining different ‘omics’ datasets aids in the identiﬁcation of key biological pathways: chronic hypoxia resulted in a pronounced adaptive response at the transcript and the protein level to keep metabolite levels steady. This preservation of metabolic homeostasis is likely to contribute to the long-term survival of the hibernating myocardium.

Conclusions Our ﬁndings demonstrated for the ﬁrst time that Cbx3 has a crucial role in SMC differentiation and possesses an important