were used. Washed RBCs from WT or db/db mice treated with vehicle or nitrate were adminis-
tered to WT hearts at the onset of ischemia. In both protocols post-ischemic recovery of cardiac
function was evaluated by determination of left ventricular developed pressure (LVEDP).
Results: Post-ischemic recovery of LVEDP was impaired in hearts from db/db mice in comparison
with hearts from WT mice in Protocol 1 (Fig. A). Dietary nitrate restored the ischemic tolerance
of hearts from db/db mice but did not affect post-ischemic recovery of hearts from WT mice (Fig. A).
In Protocol 2, administration of RBCs collected from vehicle-treated db/db mice significantly
impaired post-ischemic recovery of hearts from WT mice (Fig. B). Notably, administration of
RBCs from nitrate-treated db/db mice completely reversed the impairment of post-ischemic car-
diac function induced by diabetic RBCs (Fig. B). Interestingly, post-ischemic cardiac function did
not differ between hearts given RBCs from nitrate-treated db/db and WT mice (Fig. B).
Conclusion: Dietary nitrate restores cardiac ischemic tolerance in db/db mice and protects the
heart against ischemia–reperfusion injury via an effect mediated through RBCs.

P102
Effects of intravenous administration of HBOC-201 in two distinct open-chest pig
models of myocardial infarction
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Background: Hemoglobin oxygen carrier HBOC-201 can act as a direct oxygen donor and facili-
tate diffusive oxygen delivery between red blood cells and tissues to improve tissue oxygenation.
Previously we reported that pre-oxygenated HBOC-201 infused distal to a coronary occlusion,
fully restored myocardial aerobic metabolism and contractile function.

Purpose: To study the effects of systemic administration of HBOC-201 on left ventricular (LV)
function and myocardial infarct size in two distinct open-chest swine models: (i) total coronary
artery occlusion (CAO) of the left anterior descending (LAD) coronary artery for 45-min and (ii)
coronary artery stenosis (CAS) by placing a stenosis catheter with an inner diameter of 0.35 mm
for 120-min in the LAD reducing flow by 70±2%.

Methods: Five minutes after the onset of CAO, 8 swine received HBOC-201 (0.5 g/kg i.v.), while
8 swine received an equivalent volume of the plasma expander Voluven during 25-min. Fifteen
minutes after the onset of CAO, 14 swine received HBOC-201 (1 g/kg i.v.) alone, 12 swine received
HBOC-201 (1 g/kg i.v.) combined with nitroglycerine (NTG), while 16 swine received an equiva-
lent volume of the plasma expander Voluven during 30-min. Following restoration of LAD perfu-
sion, hearts were reperfused for 120-min and the area-at-risk (AR) and area of infarction (IA)
determined from which infarct size was calculated as IA/AR.

Results: HBOC-201 did not ameliorate ischemia-induced loss of regional systolic segment short-
ening (from 16±2% to -4±1% in CAO-model and from 20±3% to -3±1% in CAS-model) in the
anterior LV wall and had no effect on IS in either model compared to the corresponding controls
(CAO-model: 55±9% vs 55±9% and CAS-model: 33±5% vs 39±5%). To compensate for scav-
enging of nitric oxide by HBOC-201, we co-infused NTG during HBOC-201 infusion in a dose
that prevented HBOC-201-induced systemic and coronary vasoconstriction. However, even in
the presence of NTG, HBOC-201 unaffected regional dysfunction or limit IS (CAS-model: 40±6%).

Conclusion: Despite the established oxygen transport capacity of HBOC-201, intravenous
administration of HBOC-201 did not afford cardioprotection in the setting of irreversible ische-
ia-reperfusion damage in pigs.

P103
Short-term repeated remote ischemic conditioning effect on post-infarct myocardial
function: the importance of neuregulin-1
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Introduction: Adverse left ventricle (LV) remodelling following myocardial infarction plays a sig-
nificant role in the progression of heart failure (HF). Long-term repeated remote ischemic condi-
tioning (RIC) following MI improved post-infarct cardiac function. However the underlying mecha-
nisms are not completely understood. Clinical trials have shown that neuregulin-1 (NRG-1)
administration improves cardiac function in HF patients.

Aims: The present study’s aims were to (1) clarify the effect of short period of RIC on cardiac
hemodynamic function post MI and to (2) assess the effect of RIC’s correlation to NRG-1 plasma
levels

Methods: Male OFA rats were subjected to left coronary artery (LCA) occlusion and allocated
to two groups: (1) Myocardial infarction (MI) permanent ligation of LCA (n = 7) and (2) MI + RIC (n = 5). RIC treatment was performed by 3 cycles of 5 min of bilateral hindlimb ischemia and 5 min of
reperfusion once a day for 3 days starting on day 3 post-MI. Functional parameters were
assessed by echocardiography and were evaluated on an isolated erythrocyte-perfused working
heart model. The expression of plasma levels of NRG-1 was measured by ELISA.

Results: Despite comparable reduction in left ventricle ejection fraction (LVEF; 61±2% vs
62±1%+) and the elevation of left ventricle with an increase in end-diastolic (LVESD; 9.8±0.2
mm vs 8.8±0.07 mm) and end-systolic (LVESP; 6.2±0.2 mm vs 6.1±0.1 mm) diameters on the
3rd day following MI short-term RIC has slightly improved LVEF (63±1% vs 58±2%; p = 0.074).
Furthermore RIC had the tendency to prevent LV enlargement compared to the MI group
(LVESD: 5.9±0.06 mm and 6.4±0.2 mm, p = 0.064). In addition, both coronary flow (CF) and
LVESP was markedly enhanced in rats with RIC in comparison with MI (CF: 4.3±0.2 vs 3.1±2.0
ml/kg/h, LVSP: 109±2.2 mm Hg vs 119±6.1; p<0.01 and p=0.067, respectively). Of importance, the expression of NRG-1 in plasma was significantly elevated in RIC group (10.6±1.7 ng/ml vs 19.4±3.3
ng/ml; p<0.005).

Conclusion: Short-term RIC improved cardiac function, preserved systolic LV function and coro-
nary flow post-MI. This was associated with a marked increase of NRG-1 plasma levels. Our
results indicate that short-term RIC might be a novel, cost-effective approach to improve car-
diomyocyte function and minimize adverse LV remodelling following myocardial infarction.

P104
Long-term results of percutaneous coronary interventions in comparison with drug
therapy in patients with stable angina pectoris
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Background: Percutaneous coronary intervention (PCI) is a priority strategy in patients with
acute myocardial infarction, but the data on the prognostic benefits of PCI in patients with stable
coronary artery disease (CAD) is controversial.

Purpose: To evaluate the results of PCI and medical therapy (MT) in patients with CAD in the
long-term follow-up.

Methods: 300 patients selected from the “Register of coronary angiography” formed two groups:
i) 150 patients with CAD after PCI; ii) 150 patients with CAD treated with MT only. The groups
were matched by sex, age and angiographically proven CAD. Mean duration of follow-up was
97.08±42.8 months.

Results: In the late period in PCI group there was found the decrease in overall mortality (8.7% vs
17.3%; p=0.026) and cardiovascular mortality (7.3% vs 16.7%; p=0.013). Coronary artery bypass
grafting was performed less frequently in group I (21.3% vs 26.7%; p= 0.008). According
to the incidence of myocardial infarction significant differences were not found between the
groups.

Conclusion: PCI combined with MT has proven efficacy in the treatment of stable CAD com-
pared to isolated MT in the late period of observation.

P105
An iPSC-derived drug screening platform to identify therapeutic compounds for
marfan syndrome
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We have designed and validated a phenotypic assay for high-throughput drug screening using
human induced pluripotent stem cells (iPSCs) generated from patients with Marfan syndrome
(MFS). iPSCs is a connective tissue disorder with pleiotropic manifestations including severe cardio-
vascular complications, such as aortic aneurysms and aortic dissection. The aortic problems are
caused by mutations in FBN1, which codes for the extracellular matrix structural component,
fibrillin-1. Currently, MFS treatments focus on minimising aortic wall stress by controlling blood
pressure and haemodynamics. Although TGF-β signalling blockade has successfully prevented
aortic dilatation in a MFS mouse model (Halashi 2006), similar attempts have been unsuccessful in
clinical trials (Laaro 2014). Our recent work shows that p38 and JNK4 are novel disease drivers in
our human iPSC model (Granata 2017). However, the signalling pathways are complex and varied
hence our decision to focus on the downstream pathogenic phenotypes. One of these features
includes excessive matrix degradation coupled with increased expression of proteolytic enzymes.
Here, we show that MFS smooth muscle cells cultured in a 24-well format and treated with a
proteolytic compound library (AstraZeneca) provide a robust assay for high-throughput screening
conditions to identify drug activity reducing compounds. Putative hits will also be assayed for cell-
death and proliferation for further validation. These techniques will enable the identification
of novel drugs to treat MFS.

P106
Chronic hyperoncologization-activated inward current blockade increases both
sympathetic and parasympathetic activation
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Introduction: The effects of the hyperoncologization-activated inward current blocker ibradine
on sympathetic-vagal balance remain controversial. Previous studies have suggested either sympa-
thetic or parasympathetic dominance in iradine-treated individuals, or even no change.

Purpose: We aimed to assess the effects of chronic iradine treatment on heart rate variability
indexes.