extent of fibrosis in DN; (2) podocytes directly mediate macrophage migration; (3) macrophage-dependent soluble factors directly induce podocyte injury through the pro-inflammatory M1 but not the anti-inflammatory M2 subsets.

Disclosure of interest: None declared.

OC-112
HYDROGEN SULFIDE INHIBITS CARDIOMYOCYTIC AUTOPHAGY INDUCED BY ISCHEMIA/REPERFUSION INJURY

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Hydrogen sulfide (H2S) has been implicated in cardioprotection during ischemia/reperfusion (IR) injury. Autophagy is the primary pathway for degrading and recycling long-lived proteins, and its activation has recently been shown to mediate myocardial injury in response to IR injury. In this study we investigated the ability of H2S preventing autophagy as a potential mechanism underlying its cardioprotective effects against IR injury. Male rats were subjected to myocardial ischemia for 45 min followed by 2 h reperfusion. NaHS, a H2S donor, at doses of 10, 30, 100 μmol/kg was injected i.p. at 30 min before ischemia. The autophagous related genes beclin 1 and ATG5 mRNA were elevated in the area at risk (AAR) of hearts subjected to IR. NaHS reduced myocardial infarct size and attenuated the increase of beclin 1 and ATG5 expressions. In vitro, cultured neonatal rat cardiomyocytes were subjected to 24 h hypoxia followed by 2 h reoxygenation, and NaHS at doses of 10, 30, 50, 100 μmol/L, were added 30 min prior to hypoxia. Detection of microtubule-associated protein 1 light chain 3 (LC3) conversion, i.e., LC3-I to LC3-II, and monodansylcadaverine (MDC) staining were also used for the determination of autophagy activity in cardiomyocytes. Autophagy was induced in cardiomyocytes subjected to hypoxia/reoxygenation (H/R), as indicated by the increases of beclin 1 and ATG5 mRNA expression. LC3 conversion as well as MDC staining. NaHS pretreatment reduced cardiomyocyte death induced by H/R. At meantime, NaHS dose-dependently attenuated the H/R-induced autophagy activity. Our results indicate that inhibition of autophagy might be one of the mechanisms underlying H2S cardioprotective effects against ischemia reperfusion injury.

Keywords: Hydrogen sulfide, cardiomyocyte, autophagy, ischemia reperfusion.

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OC-113
ABSENCE OF MICRONORNA-155 PROTECTS AGAINST ADVERSE CARDIAC INFLAMMATION AND HYPERTENSION

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Cardiac hypertrophy, accompanied by progressive inflammation, and consequent heart failure continue to burden Western society. In the current study, we show that mir-155, an inflammatory cell-expressed microRNA, stimulates the sequestration of pro-hypertrophic and inflammatory factors by macrophages and thereby causes adverse inflammation and heart failure. We subjected mir-155 KO and WT mice to 1 and 4 weeks of angiotensin II (AngII) to induce cardiac hypertrophy, inflammation and failure. Whereas AngII significantly increased both cardiac mass and hypertrophic signalling in WT mice, the absence of mir-155 inhibited this hypertrophic response. Moreover, absence of mir-155 prevented inflammatory cell influx in the heart following AngII, more specifically the influx of macrophages. These data were independently confirmed using antagonists against miR-155 in AngII-treated mice. In situ hybridization predominantly identified cardiac miR-155 in macrophages and very little was detected in cardiac myocytes. Therefore, we hypothesized that macrophage miR-155 mediates pro-hypertrophic signalling towards cardiac myocytes. Indeed, bone marrow transplantation with miR-155 KO and WT mice and in vitro experiments independently confirmed that miR-155 in the macrophage modulates cardiac hypertrophy. We found that miR-155 represses its direct target Suppressors of Cytokine Signalling-1 in the macrophage, leading to increased IL-6 secretion and consequent STAT3 activity, implicated in cardiac inflammation and hypertrophy. These data reveal miR-155 expression in the macrophage to be mandatory to allow cardiac hypertrophy, inflammation and failure, by permitting cytokine signalling, identifying miR-155 as a crucial inflammatory regulator of cardiac hypertrophy.

Disclosure of interest: None declared.

Young Investigator Award Winner.
For mini paper see page 289

OC-114
ADIPONECTIN TISSUE-DERIVED STEM CELL TREATMENT PREVENTS RENAL DISEASE PROGRESSION
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Adipose tissue-derived stem cells (ASCs) are an attractive source of stem cells with regenerative properties that are similar to those of bone marrow stem cells. Here, we analyze the role of ASCs in reducing the progression of kidney fibrosis. Progressive renal fibrosis was achieved by unilateral clamping of the renal pedicle for 1 h, after that, the kidney was reperfused immediately. Four hours after the surgery, 2 × 10³ ASCs were intraperitoneally administered, and animals were followed for 24 h post-treatment and then at some other time interval for the next 6 weeks. Also, animals were treated with 2 × 10³ ASC at 6 weeks after reperfusion and sacrificed 4 weeks later to study their effect when interstitial fibrosis already is present. At 24 h after reperfusion, ASC-treated animals showed reduced renal dysfunction and enhanced regenerative tubular processes. Renal miRNA expression of IL-6 and TNF was decreased in ASC-treated animals, whereas IL-1, IL-10 and HO-1 expression increased despite a lack of ASC in the kidneys as determined by SRY analysis. As expected, untreated kidneys shrank at 6 weeks, whereas the kidneys of ASC-treated animals remained normal in size, showed less collagen deposition and decreased staining for FSP-1, type I collagen and hypoxyprobe. The renal protection seen in ASC-treated animals was followed by reduced serum levels of TNF-c, KC, RANTES and IL-1β. Surprisingly, treatment with ASC at 6 weeks, when animals already showed installed fibrosis, demonstrated amelioration of functional parameters, with less tissue fibrosis observed and reduced miRNA expression of type I collagen and vimentin. ASC therapy can improve functional parameters and reduce progression of renal fibrosis at early and later times after injury, mostly due to early modulation of the inflammatory response and to less hypoxia, thereby reducing the epithelial-mesenchymal transition.

Disclosure of interest: None declared.

Respiratory diseases (OC11)
OC-115
REPRESSION OF THE NUCLEOSIDE TRANSPORTERS I AND -2 REDUCES INFLAMMATORY ACUTE LUNG INJURY
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Acute lung injury (ALI), a devastating disorder characterized by hypoxemia and overwhelming pulmonary inflammation, remains a primary factor of morbidity and mortality in critically ill patients. Extracellular adenosine has been implicated as central signalling molecule during conditions of limited oxygen availability (hypoxia), important in attenuating tissue damage, acute inflammation and the preservation of pulmonary barrier function. During periods of acute inflammation extracellular levels of adenosine are increased in the affected tissues, yet the molecular mechanisms are presently unknown. The Equilibrative Nucleoside Transporters (ENT) have significant impact on regulation of the levels of extracellular adenosine. During periods of hypoxia, the expression levels of ENT1 and -2 are significantly reduced, leading to the attenuation of adenosine uptake and resulting in an increased extracellular adenosine concentration. Cellular hypoxia is part of the pathobiological correlate of an acute inflammatory process, yet in addition a variety of cytokines are released upon the stimulation of the immune system. Given this, we investigated consequences of pulmonary acute inflammation on the expression of ENTs. Our initial studies with endothelia and pulmonary epithelia demonstrate attenuation of adenosine uptake as result of diminished expression of ENTs during acute inflammation in vitro. Studies with siRNA confirmed the major contribution of ENT2 as main adenosine transporter in lung. Furthermore, examination of the ENT2 promoter suggests nuclear factor-kappa B in ENT2 repression. Additional in vivo studies using a