key event in vascular proliferative diseases by releasing cytokines and growth factors. This activation is mediated by Shh and PDGF-BB induced activation of Smo-dependent signalling and the selective inhibitor GDC-0449 may serve as a novel and promising therapeutic strategy to prevent neointima formation.

P700 | BENCH
The novel mineralocorticoid receptor antagonist Finerenone attenuates neointima formation after vascular injury

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Background: Ischemic cardiomyopathy as a result of coronary artery disease is the leading cause for heart failure. In consequence, the novel mineralocorticoid receptor antagonist Finerenone, holds the promise to be safe and efficient in the treatment of patients with heart failure and/or chronic kidney disease. However, the effects on vascular function remain elusive.

Purpose: The aim of this study was to determine the functional effect of selective mineralocorticoid receptor antagonists in vascular cells in vitro and the effect on vascular remodelling following acute vascular injury in vivo.

Methods and results: Finerenone dose-dependently and significantly reduced aldosterone-induced human coronary artery smooth muscle cell (HCA-SMC) proliferation and migration, as assessed by BrdU incorporation. Furthermore, Finerenone dose-dependently and significantly prevented aldosterone-induced apoptosis in human umbilical vein endothelial cells (HUVEC) as measured with a flow cytometry based FLICA-assay. In vivo, oral application of Finerenone dose-dependently and significantly inhibited intimal and medial cell proliferation following femoral artery wire-induced injury in C57BL/6J mice as quantified by staining for Ki-67 10 days following injury (vehicle vs. 1 mg/kg/d vs. 10 mg/kg/d; each p < 0.01). Concomitantly, Finerenone attenuated neointimal lesion formation following femoral artery wire-induced injury 21 days following injury (luminal stenosis, vehicle vs. Finerenone 1 mg/kg/d vs. Finerenone 10 mg/kg/d: 90.2±11.1% vs. 60.1±17.3%; p<0.0061 to vehicle, n=8). Furthermore, there was a trend towards an accelerated re-endothelialization of the injured vessel segments in Finerenone-treated mice three days following electric injury of the murine carotid artery.

Conclusion: Finerenone treatment significantly attenuates HCA-SMC proliferation and migration, while simultaneously preventing apoptosis of endothelial cells in vitro. This is reflected by a significantly reduced neointima formation and reduction of luminal stenosis as well as a trend towards an accelerated endothelial healing of the injured vessels. Thus, apart from its beneficial effects in heart failure therapy, Finerenone might provide favorable vascular effects through restoring vascular integrity and preventing adverse vascular remodelling.

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P701 | BENCH
Endothelial protein tyrosine phosphatase-1B deletion enhances neointima formation in mice with diet-induced obesity

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Background: Obesity and metabolic dysfunction are associated with increased expression of protein tyrosine phosphatase (PTP)-1B, a negative regulator of receptor tyrosine kinase (Tie2) promoter. Cre recombinase activity and endothelial-restricted PTP1B gene excision (End.PTP1B-KO) was induced by systemic inhibition or genetic deletion of PTP1B protects endothelial receptor tyrosine kinase signalling, and PTP1B overexpression may be causally linked to the development of atherosclerosis. Thus, we investigated whether PTP1B deletion in endothelial cells attenuates neointima formation in mice with diet-induced obesity has not been studied.

Methods and results: Male mice carrying a floxed PTP1B gene were subjected to a high-fat diet (HFD) for 6 weeks later. Obesity was induced by feeding mice tamoxifen-containing rodent chow for 6 weeks. Furthermore, there was a trend towards an accelerated re-endothelialization of the injured vessel segments in Finerenone-treated mice three days following electric injury of the murine carotid artery.

Conclusion: Finerenone treatment significantly attenuates HCA-SMC proliferation and migration, while simultaneously preventing apoptosis of endothelial cells in vitro. This is reflected by a significantly reduced neointima formation and reduction of luminal stenosis as well as a trend towards an accelerated endothelial healing of the injured vessels. Thus, apart from its beneficial effects in heart failure therapy, Finerenone might provide favorable vascular effects through restoring vascular integrity and preventing adverse vascular remodelling.

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P702 | BENCH
Endothelial-Mesenchymal Transition: mir-101 as a new target to treat intimal hyperplasia

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Introduction: Endothelial-Mesenchymal Transition (EndMT) is a specific form of transformed dysfunction wherein endothelial cells acquire a mesenchymal phenotype and lose their endothelial functions. We, and others, recently described that EndMT contributes to intimal hyperplasia and atherosclerosis.

Purpose: We used in silico analysis to identify miRNAs that could evoke posttranscriptional silencing of Ezh2. In Luciferase reporter assays, miR-101 efficiently inhibited expression of the lucerlaser reporter by interacting with the 3'UTR of Ezh2. Using a uniform laminar flow setup, we revealed that MAPK7 expression is reduced. Moreover, miR-101 expression is decreased, whereas MAPK7 expression is increased, which may cause EndMT to type and lose their endothelial functions. We, and others, recently described that EndMT contributes to intimal hyperplasia and atherosclerosis.

Methods and results: We conducted a meta-analysis to assess the effect of TNF-antagonists on arterial stiffness, a predictor of cardiovascular events and mortality, in RA patients.

Conclusion: Targets of miR-101 include TNF-antagonists. In human coronary artery stenosis Ezh2 levels are increased, which associated with the increase of Ezh2 (R 2=0.23, p=0.051) and severity of the annotated (Intima/Media Thickness, R2=0.45, p<0.003).

Conclusion(s): Under uniform laminar flow MAPK7 inhibits Ezh2 expression via activation of miR-101. In coronary artery stenosis, endothelial cells are exposed to non-uniform shear stress which decreases MAPK7 activation, miR-101 expression and concurrently increases Ezh2 expression, which may cause EndMT and intimal hyperplasia. Therefore, the restoration of miR-101 expression or the silencing of Ezh2 in the endothelium might provide novel therapeutic approaches to treat intimal hyperplasia.

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P703 | BEDSIDE
TNF-antagonists improve arterial stiffness in patients with rheumatoid arthritis: a meta-analysis

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Background: Patients with rheumatoid arthritis (RA) have a higher arterial stiffness than those with age-matched healthy counterparts and an increased inflammatory burden that might be associated with their increased cardiovascular risk. Whether tumour necrosis factor alpha (TNF-)antagonists have been found to reduce inflammatory markers in RA, it is debatable if they have favorable effects on surrogate markers of cardiovascular outcomes.

Purpose: We conducted a meta-analysis to assess the effect of TNF-antagonists on arterial stiffness, a predictor of cardiovascular events and mortality, in RA patients.

Methods: A search of PUBMED was conducted to identify studies into the ef-