Endothelial-Mesenchymal Transition


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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 effect of novel heart failure therapeutics on vascular function and remodeling processes is of pivotal interest. Furthermore, a non-necrotic mineralocorticoid receptor antagonist, 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 Mrg receptor agonists in vascular cells in vitro and the effect on vascular remodeling 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 as quantified 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.

**Conclusion:** Finerenone treatment significantly attenuates HCASMC prolifereation and simultaneously prevents 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 remodeling.

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**P702 | BENCH**

Endothelial-Mesenchymal Transition: mirR-101 as a new target to treat intimal hyperplasia

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**Introduction:** Endothelial-Mesenchymal Transition (EndMT) is a specific form of cellular 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.

**Methods and results:** We used in silico analysis to identify mirRNAs that could evoke posttranscriptional silencing of Ezh2. In Lucerase reporter assays, mir-101 efficiently inhibited expression of the luceralse reporter by interacting with the 3’UTR of Ezh2. Using a uniform laminar flow setup, we revealed that MAPK7 induced mirR101 expression, which was blocked by the selective MAPK7 inhibitor BIX02189 (p<0.05). Furthermore, ectopic expression of mir-101 in endothelial cells reduced the expression of Ezh2.

**Conclusion:** Ezh2 is the catalytic subunit of the Polycomb Repressive Complex 2 that methylates lysine 27 on histone 3 (H3K27me3). H3K27me3 is a repressive chromatin mark that inhibits gene expression. Currently, it is elusive how the crosstalk between MAPK7 and Ezh2 is regulated in the endothelium and if the balance between MAPK7 and Ezh2 is disturbed during 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 their age-matched healthy counterparts and an increased inflammatory burden that might be associated with their increased cardiovascular risk. While tumor 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-