CENTER FOR BIOMEDICAL RESEARCH AND TRANSLATIONAL SURGERY
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Open Lab Day 2024
Research Group: HOHENSINNER – Innate Immunity

Innate Immunity in the Cardiovascular System

We are interested in the influence of the innate immune system on the cardiovascular system. A key focus of our work is to identify the interplay between inflammation and proinflammatory stimuli on cells of the innate immune system. The goal of our research is to identify drug targets and to use a repurposing strategy for drug targeting to demonstrate new options in patients with cardiovascular disease. At the moment we are following two possible repurposing strategies towards clinical application.

Methods

- In vitro cell culture systems to study and manipulate innate immune cells (monocytes, macrophages, neutrophils) and vascular cells (endothelial cells and smooth muscle cells).
- Established mouse models include models of atherosclerosis (LDL-R knockout or ApoE knockout), pulmonary virus infection (coronavirus, respiratory syncytial virus) and vena cava ligation from studying deep vein thrombosis.
- In vivo mouse plethysmograph to study lung function in non anesthetized mice.
- AI assisted analysis of whole tissue section histological samples.
- Multicolor flow cytometry for cellular phenotyping and intracellular protein analysis (including phospho-flow).
- Protein detection using ELISA, western blot and dot plot techniques.

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Selected Publications:

- Reduced Monocyte and Neutrophil Infiltration and Activation by P-Selectin/CD62P Inhibition Enhances Thrombus Resolution in Mice. Kral-Pointner JB, Haider P, Szabo PL, Salzmann M, Brekalo M, Schneider KH, Schrottmaier WC, Kaun C, Bleichert S, Kiss A, Sickha R, Hengstenberg C, Huber K, Brostjan C, Bergmeister H, Assinger A, Podesser BK, Wojta J, **Hohensinner P**. Arterioscler Thromb Vasc Biol. 2024 Apr;44(4):954-968.
- Neutrophil extracellular traps induce persistent lung tissue damage via thromboinflammation without altering virus resolution in a mouse coronavirus model. Salzmann M, Gibler P, Haider P, Brekalo M, Plasenzotti R, Filip T, Nistelberger R, Hartmann B, Wojta J, Hengstenberg C, Podesser BK, Kral-Pointner JB, **Hohensinner PJ**. J Thromb Haemost. 2024 Jan;22(1):188-198.
- Pharmacologic modulation of intracellular Na+ concentration with ranolazine impacts inflammatory response in humans and mice. Lenz M, Salzmann M, Ciotu CI, Kaun C, Krychtiuk KA, Rehberger Likozar A, Sebestjen M, Goederle L, Rauscher S, Krivaja Z, Binder CJ, Huber K, Hengstenberg C, Podesser BK, Fischer MJM, Wojta J, **Hohensinner PJ (Corresp. Author)**, Speidl WS. Proc Natl Acad Sci U S A. 2022 Jul 19;119(29):e2207020119.
- Neutrophil Extracellular Trap Degradation by Differently Polarized Macrophage Subsets. Haider P, Kral-Pointner JB, Mayer J, Richter M, Kaun C, Brostjan C, Eilenberg W, Fischer MB, Speidl WS, Hengstenberg C, Huber K, Wojta J, **Hohensinner P**. Arterioscler Thromb Vasc Biol. 2020 Sep;40(9):2265-2278.

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Open Lab Day 2024

Research Group: PILAT - HTX Research Lab

Immunological tolerance - Transplantation Immunology

Our research combines basic science with clinical research to understand the basis of immunological tolerance and cellular/humoral immunity with special focus on transplantation immunology. The main research interest of my lab is the role and potency of regulatory T cells (Tregs) in the induction and maintenance of transplantation tolerance to improve patient and graft survival in (heart) transplant patients.

In particular we are investigating the potency of therapeutic Treg treatment in partially or fully mismatched murine models of skin and heart transplantation.

SCAN ME!

Methods

- Preclinical animal models in transplantation: heterotopic cardiac transplantation, hematopoietic stem cell transplantation, skin transplantation, tolerance approaches (mixed chimerism, adoptive Treg cellular therapy, IL-2 based immunomodulation)
- Multicolor flow cytometry for immune monitoring, leucocyte subset analysis and cytokine detection, flow crossmatch
- State- of-the-art molecular and cellular biology techniques, human and murine cell culture, magnetic cell sorting, intracellular cytokine detection
- Regulatory T cells (in vivo expansion via IL- 2 complexes, in vitro expansion culture, retroviral gene transfer, TGFß induction): cell therapy, in vitro suppression assays
- Mouse model of orthotopic renal cell carcinoma and heterotopic flank models, autologous tumor vaccines

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Selected Publications:

- Treg Therapy for the Induction of Immune Tolerance in Transplantation-Not Lost in Translation? Pilat N, Steiner R, Sprent J. **Int J Mol Sci**. 2023 Jan 16;24(2):1752.
- Impact of Graft-Resident Leucocytes on Treg Mediated Skin Graft Survival. Steiner R, Weijler AM, Wekerle T, Sprent J, Pilat N. **Front Immunol**. 2021 Nov 29;12:801595
- Treg-mediated prolonged survival of skin allografts without immunosuppression.
- Pilat N, Wiletel M, Weijler AM, Steiner R, Mahr B, Warren J, Corpuz TM, Wekerle T, Webster KE, Sprent J. **Proc Natl Acad Sci U S A**. 2019 Jul 2;116(27):13508-13516
- Blockade of adhesion molecule lymphocyte function-associated antigen-1 improves long-term heart allograft survival in mixed chimeras. Pilat N, Sabler P, Klaus C, Mahr B, Unger L, Hock K, Wiletel M, Schwarz C, Kristo I, Regele H, Wekerle T. **J Heart Lung Transplant**. 2018 Sep;37(9):1119-1130

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Open Lab Day 2024

Research Group: Podesser and Kiss Research Lab

Cardiac (reverse)remodeling, cardiovascular protection, cardiac phenotyping

Cardiovascular diseases (CVD) are emerging as major threats to modern societies. Our research aims to understand how **extracellular matrix (ECM) remodeling changes under stress (ischemia, pressure and volume overload) conditions.** Next to the role of ECM remodeling, our studies aim to characterize vascular endothelial cells and cardiomyocytes (dys)function as well as their interaction in the development of **heart failure with preserved/reduced ejection fraction**. Besides the chronic adaptation and changes of cardiac function due to pressure or volume overload, we investigate the mechanism and target pathways play role in **myocardial ischemia and reperfusion**. We also investigate the impact of cancers/cachexia; and cancer treatments induces cardiac(vascular) dysfunction.

Methods

- Preclinical small animal models of heart failure and myocardial ischemia reperfusion injury; pressure and volume overload induces heart failure, hypertrophy and diabetes, heart transplantation
- Large animal models of mitral valve regurgation and myocardial infarction
- Small animal models of Duchenne Muscular Dystrophy and cardiomyopathy: mice and rat models.
- Isolated working heart system, wire myogrpahy for the assessment of cardiac function as well as small or larger diameter vascular endothelial function ex vivo
- State- of-the-art cardiac imaging modelities; echocardiography, cardiac MRI, PET/CT
- Invasive hemodynamic assessment using pressure-volume loop analysis
- Primary cells and cell line (cardiomyocytes, caridac fibroblast, endothelial cells)
- Mouse model of various cancers and cachexia, to test the impact of active cancer on the development of cardiac dysfunction

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Ap.Prof.Dr. Attila Kiss

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Selected Publications:

- PM. Pilz, Al Jha, WT Chang, JE. Ward, A Kiss, JE Ward, S Fisch, BK Podesser, R Liao. **Large and Small Animal Models of Heart Failure with Reduced Ejection Fraction. Circulation Research; 130:1888–1905.**
- PL Szabó, J Ebner, X Koenig, O Hamza, S Watzinger, S Trojanek, D Abraham, H Todt, H Kubista, K Schicker, S Remy, I Anegon, A Kiss*, B K Podesser, K Hilber. Cardiovascular phenotype of the **Dmdmdx rat – a suitable animal model for Duchenne muscular dystrophy (2021). Disease Models & Mechanisms 14(2):dmm047704**
- O Hamza, A Kiss, A M Kramer, S Trojanek, D Abraham, E Acar, F Nagel, V E Tretter, M Kitzwögerer, B K. Podesser. **Tenascin C promotes valvular remodeling in two large animal models of ischemic mitral regurgitation. Basic Research in Cardiology 115(6):76**
- B Podesser, M Kreibeich, E Dzilic, D Santer, L Förster, S Ttrojanek, D Abraham, M Krssak, KU Klein, EV Tretter, C Kaun, , J Wojta, B Kapeller, , I F Gonsalves, K Treschert, A Kiss. **Tenascin-C Promotes Chronic Pressure Overload-induced Cardiac Dysfunction, Hypertrophy and Myocardial Fibrosis. J Hypertens. 2018 ;36(4):847-856**
- M Sárközy, S Watzinger, Zs Z. A. Kovács, E Acar, F Márványkövi, G Szűcs, A Siska, I Földesi, A Kriston, F Kovács, P Horváth, B Kővári, G Cserni, PL Szabó, G Szabó, K Zins, D Abraham, T Csont, P Pokreisz, BK Podesser, A Kiss. Neuregulin-1β improves uremic cardiomyopathy and renal dysfunction in rats. **JACC: Basic to Translational Science, 31;8(9):1160-1176.**

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Research Group: BERGMEISTER– Vascular Grafts

Small-diameter vascular grafts- Material development and testing

Over the past decades, various materials and surface modifications have been investigated to improve the patency rates of synthetic vascular graft implants. Despite intensive efforts, autologous, patient-derived vascular grafts remain superior to artificial materials. Our research goal is to develop new implants with good long-term function for the replacement of small caliber vessels. Besides conventional biocompatibility testing of materials, we aim to develop new assessment methods to better characterize the interactions between recipient and biomaterial and the healing process.

Methods

- Established preclinical small and large animal models for cardiovascular implant testing
- Complex 2D and 3D cell culture models for the *in vitro* evaluation of cell/material interactions
- Perfusion bioreactor systems to evaluate cardiovascular implants under physiological pressure and flow conditions
- Biocompatibility and hemocompatibility testing according to ISO 10993-5 and ISO 10993-4
- Primary cell isolation and expansion from human and animal tissue
- State-of-the-art molecular biology techniques

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Selected Publications:

- Rohringer, S., Grasl, C., Ehrmann, K., Hager, P., Hahn, C., Specht, S. J., ... & Bergmeister, H. (2023). **Biodegradable, Self-Reinforcing Vascular Grafts for In Situ Tissue Engineering Approaches.** *Advanced Healthcare Materials*, *12*(23), 2300520.
- Enayati, M., Schneider, K. H., Almeria, C., Grasl, C., Kaun, C., Messner, B., ... & Bergmeister, H. (2021). **S-nitroso human serum albumin as a nitric oxide donor in drug-eluting vascular grafts: Biofunctionality and preclinical evaluation**. *Acta Biomaterialia*, *134*, 276-288.
- Schneider, K. H., Enayati, M., Grasl, C., Walter, I., Budinsky, L., Zebic, G., ... & Bergmeister, H. (2018). **Acellular vascular matrix grafts from human placenta chorion: Impact of ECM preservation on graft characteristics, protein composition and in vivo performance.** *Biomaterials*, *177*, 14-26.
- Enayati, M., Eilenberg, M., Grasl, C., Riedl, P., Kaun, C., Messner, B., ... & Bergmeister, H. (2016). **Biocompatibility assessment of a new biodegradable vascular graft via in vitro co-culture approaches and in vivo model**. *Annals of biomedical engineering*, *44*, 3319-3334.
- Bergmeister, H., Seyidova, N., Schreiber, C., Strobl, M., Grasl, C., Walter, I., ... & Schima, H. (2015). **Biodegradable, thermoplastic polyurethane grafts for small diameter vascular replacements.** *Acta biomaterialia*, *11*, 104-113.

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Open Lab Day 2024

Research Group: Hallström – Kapeller

HPLC-Lab

High-performance liquid chromatography (HPLC) is a technique in analytical chemistry used to separate, identify and quantify specific compounds in mixtures (e.g., tissue and liquid samples like plasma, liquor).
We utilize this tool for instance to investigate the energy status of heart tissue in ischemia/reperfusion injury.

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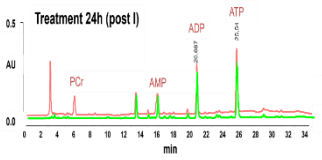


Methods

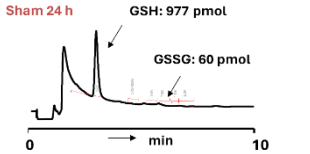
The following methods are available in our new HPLC -Lab

Determination of:

High-energy phosphates in tissue and cells
(HX, X, PCr, AMP, ADP, ATP etc.)

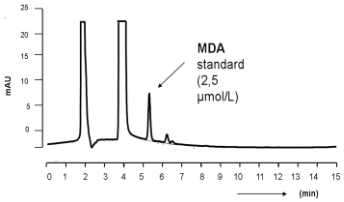
Glutathione status – oxidative stress

- GSH/GSSG-ratio in tissue and cells



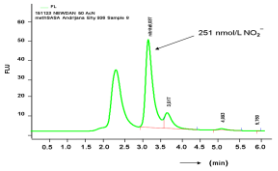
Lipidperoxydation

- Malondialdehyde in plasma



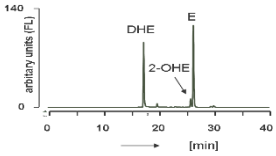
Indicators of nitric oxide and superoxide anion generation

- Nitrite (and nitrate) – cell supernatants
- Superoxide (2-Hydroxyethidium) – in cells and tissue



Other examples

Amino acids (including arginine, citrulline, ornithine, nitrotyrosine); Catecholamines; Pharmacokinetic analysis etc.



Selected Publications:

- The Antiplatelet Action of S-Nitroso Human Serum Albumin in Whole Blood. Tsiountsioura M, Cvirn G, Schlagenhauf A, Haidl H, Zischmeier K, Janschitz N, Koestenberger M, Wonisch W, Paar M, Wagner T, Weiss EC, **Hallström S.** Biomedicines. Mar 11;10(3):649 2022
- Single Donor Infusion of S-Nitroso-Human-Serum-Albumin Attenuates Cardiac Isograft Fibrosis and Preserves Myocardial Micro-RNA-126-3p in a Murine Heterotopic Heart Transplant Model. Schaefer AK, Kiss A, Oszwald A, Nagel F, Acar E, Aliabadi-Zuckermann A, Hackl M, Zuckermann A, Kain R, Jakubowski A, Ferdinandy P, **Hallström S**, Podesser BK.Transpl Int. Apr 13;35:10057 2022
- S-nitroso human serum albumin as a nitric oxide donor in drug-eluting vascular grafts: Biofunctionality and preclinical evaluation.Enayati M, Schneider KH, Almeria C, Grasl C, Kaun C, Messner B, Rohringer S, Walter I, Wojta J, Budinsky L, Walpoth BH, Schima H, Kager G, **Hallström S**, Podesser BK, Bergmeister H. Acta Biomater. Oct 15;134:276-288 2021
- The anticoagulant effects of ethyl pyruvate in whole blood samples.Haidl H, Schlagenhauf A, Krebs A, Plank H, Wonisch W, Fengler V, Fiegl A, Hörl G, Koestenberger M, Wagner T, Tafeit E, Cvirn G, **Hallström S**. PLoS One. 2020 Oct 9;15(10):e0240541.

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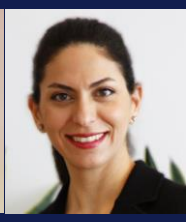

Open Lab Day 2024

Research Group: Schneider and Enayati

3D (Bio)printing

3D bioprinting is a cutting-edge technology that combines principles from 3D printing and biological sciences to create complex structures that can mimic the natural tissue structure of living tissues. Our group aims to provide a 3D printing platform to create biomaterials/bioinks to develop scaffolds for engineering both hard and soft tissues. Both synthetic and natural based materials have been utilized so far**. Dr Schneider** is working on the development and printing of new bioinks of biological origin, such as the **extracellular matrix (ECM)** of the human placenta, using novel freeform printing techniques **to produce tissue constructs such as heart valves, muscles or tendons. Dr. Enayati,** Focuses on creation and printing **high resolution smart constructs** with high fidelity to the native tissue such as **cardiac/aortic patches with anisotropic mechanical and electroconductive properties immunomodulatory** behaviors. Together they form a team that combines their expertise and strengths to conduct internationally competitive research in tissue engineering.

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Methods

Biomaterials:

Development and characterization of **human placenta extracellular matrix (hpECM) hydrogels** and **hpECM based composite bioinks** with high cellular affinity and biomechanical strength

Advanced biofabrication:

FRESH printing technology to create biomimetic tissues.

High res. 3D printing of polymers for both hard and soft tissue engineering such as cardiac/aortic patch for myocardial repair

Inducing mechanically anisotropic behavior to 3D printing construct to mimic biological anisotropic behavior of target tissues such as heart, lung and skin

Functionalization of the printing construct to increase tissue regeneration

Selected Publications:

- **Schneider, K.H.**, et al.Silk fibroin, gelatin, and human placenta extracellular matrix-based composite hydrogels for 3D bioprinting and soft tissue engineering. *Biomater Res* **27**, 117 (2023). https://doi.org/10.1186/s40824-023-00431-5 **(IF:11.3), (Top 10 journal worldwide)**
- **M. Enayati, K.H. Schneider,** et al., S-nitroso human serum albumin as a nitric oxide donor in drug-eluting vascular grafts: Biofunctionality and preclinical evaluation, Acta Biomaterialia **(2021), (IF:9.7), (Top 10 journal worldwide)**
- M.Eilenberg, **M. Enayati**, et al. , Bioabsorbable Polycarbonate Urethane Grafts for Small Diameter Vessel Replacement in Rodents, **Eur J. Vas. Endovasc. Surg.** (**2020**), 59(4), 643-652, (**IF:5.7). (Top 10 journal worldwide**)
- S. A. Ferreira, **M. Enayati,** et al. , Bi-directional cell-pericellular matrix interactions direct stem cell fate, **NATURE COMMUNICATIONS (2018),** DOI: 10.1038/s41467-018-06183-4 **(IF:16.6**), (**Top 2 journal worldwide**)
- **K.H Schneider, M. Enayati,** et al. Acellular vascular matrix grafts from human placenta chorion: Impact of ECM preservation on graft characteristics, protein composition and in vivo performance **(2018)**, **Biomaterials**. **(IF:14.0)** (**Top 5 journal worldwide**)

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Open Lab Day 2024

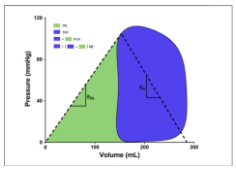
Research Group: Podesser and Kiss Research Lab

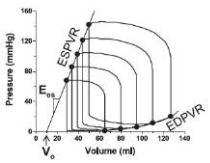
Invasive Hemodynamic Measurements in Cardiovascular Research – Dr. Peter Pokreisz

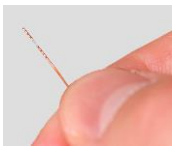
- **Invasive hemodynamic measurements are based on simultaneous recording of pressure and volume in the vascular and cardiac compartments and can be accompanied by flow measurements.**
- The method is applicable in broad spectrum of disease models from rodents to large, clinically relevant animals, including pigs and sheep.
- The technique is relevant during phenotyping of genetically modified animals, mechanically or pharmacologically induced disease models.

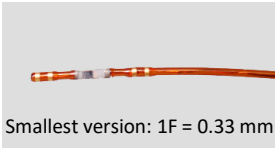
The Method of Pressure-Volume Analyses

- Pressure recording is performed using high fidelity piezoelectric sensors.
- Volume recording is based on conductometry.
- Following steady state baseline recordings, mechanical change of loading conditions is introduced to obtain load-independent indices.
- Parallel conductance of connective tissues is deducted.
- Drug-induced chronotropic or inotropic challenges are possible.

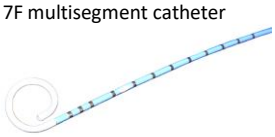








7F multisegment catheter



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Dr. Peter Pokreisz

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Relevant Publications:

- **Pokreisz P,** Vandenwijngaert S, Bito V, Van den Bergh A, Lenaerts I, Busch C, Marsboom G, Gheysens O, Vermeersch P, Biesmans L, Liu X, Gillijns H, Pellens M, Van Lommel A, Buys E, Schoonjans L, Vanhaecke J, Verbeken E, Sipido K, Herijgers P, Bloch KD, Janssens S: Ventricular phosphodiesterase 5 expression is increased in patients with advanced heart failure and contributes to adverse ventricular remodeling after myocardial infarction in mice. **Circulation 2009; 119:408-416.**
- Wu M, Claus P, Vanden Driessche N, Reyns G, **Pokreisz P,** Gillijns H, Caluwe E, Bogaert J, Collen D, Janssens S: Placental growth factor 2 - A potential therapeutic strategy for chronic myocardial ischemia. **International Journal of Cardiology. 2016; 203:534-542.**
- Wu M, **Pokreisz P,** Swinnen M, Caluwé E, Gillijns H, Vanden Driessche N, Casazza A, Verbeken E, Collen D, Janssens S: Sustained placental growth factor-2 treatment does not aggravate advanced atherosclerosis in ischemic cardiomyopathy. **Journal of Cardiovascular Translational Research. 2017; 10:348-358.**