Wahlfachtitel	Novel approachs in cardiac disease - Regeneration & new drugs
Lehrperson(en)	Prof. Dr. Jaya Krishnan
Empfohlen ab klinischem Semester	ab 1. Klin. Semester
Kursort	Cardio-Pulmonary Institute (CPI), Haus 25B, Theodor-Stern-Kai 7, 60590 FFM und online
Gruppengröße	4 Teilnehmer
Eingangsvoraussetzungen	This elective course is aimed at students who wish to pursue an experimental doctoral thesis.
Lernziele	This course will provide the experimental background to study cardiac regeneration ex vivo, in a state-of-the-art self-organised human cardiac organoid system that we have established.
Veranstaltungsinhalte	Myocardial infarction causes cardiac cell death and contractile dysfunction leading to adverse patient outcomes – yet effective therapies remain lacking. Patients with heart failure suffer from major impairments in quality of life and poor long-term prognosis. Loss of cardiomyocytes is a major hallmark of heart failure and is linked to an approximate 25% decrease in cardiomyocytes due to cell death. However, unlike other tissues that can compensate cell death through proliferative induction, cardiomyocytes are post-mitotic and have very limited capacity for proliferation, regeneration or repair to restore damaged tissue to overcome remodeling and fibrotic processes leading to heart failure and death. Thus, there remains a high unmet need for novel therapeutics to reduce heart failure morbidity and mortality. This course will provide the experimental background to study cardiac regeneration ex vivo, in a state-of-the-art self-organised human cardiac organoid system that we have established. iPSC-derived human cardiac organoids have been shown to recapitulate heart tissue function and pathophysiologic responses – providing a powerful in vitro system to study cardiogenesis, genetic cardiomyopathies, stress-induced disease, and as a platform to identify and validate novel drugs. Our lab has established the generation of adult self-organizing cardiac organoids (SCOs), which spontaneously organize into epicardial, myocardial and endocardial layers, and contain all cell types of the native human myocardium including cardiomyocytes, endothelial cells, cardiac fibroblasts, pericytes, smooth muscle cells, macrophages and neurons. Further, the SCOs reveal a distinct cardiac lumen, contain mature 3D vascular networks, and mimicked mature human myocardial responses to stress and benchmark compound stimulation.

Veranstaltungsinhalte	In this setting, we will study the differential effects of drugs on proliferative responses in cardiomyocytes, endothelial cells and pericytes/smooth muscle cells. This Elective will run over 2 consecutive days, comprising of a Teaching/Seminar component (2-3hrs) and a Practical component (8-12hrs). The Practical component will involve observation, handling and staining of 3D cardiac cultures with proliferation and cell lineage markers, followed by confocal microscopic imaging and quantitative analysis of lineage-specific cell proliferation. Depending on student interest, there would be the opportunity to tailor the course towards a greater focus and emphasis on metabolic or contractile/functional adaptations of drugs on proliferative responses.
Studienleistungen	At the end of the elective course, each student will write an experimental protocol (max 3 pages) and will present (max 10 min/ student) at an online event. Grades will be cumulatively based on protocol and presentation. No missing hours are allowed.
Art der Prüfung	Assessment will be based on a Scientific paper-format (Abstract, Introduction, Materials and Methods and Discussion) report - where the student is expected to qualitatively and quantitatively detail their observations, findings and conclusions. No missing hours are allowed.
Literaturhinweise	J. U. G. Wagner, M. D. Pham, L. Nicin, M. Hammer, K. Bottermann, T. Yuan, R. Sharma, D. John, M. Muhly-Reinholz, L. Tombor, M. Hardt, J. Madl, S. Dimmeler, J. Krishnan, Dissection of heterocellular cross-talk in vascularized cardiac tissue mimetics. J Mol Cell Cardiol 138, 269-282 (2019). N. Guimarães-Camboa, J. Stowe, I. Aneas, N. Sakabe, P. Cattaneo, L. Henderson, Michael S. Kilberg, Randall S. Johnson, J. Chen, Andrew D. McCulloch, Marcelo A. Nobrega, Sylvia M. Evans, Alexander C. Zambon, HIF1α Represses Cell Stress Pathways to Allow Proliferation of Hypoxic Fetal Cardiomyocytes. Developmental Cell 33, 507-521 (2015). N. Guimarães-Camboa, P. Cattaneo, Y. Sun, T. Moore-Morris, Y. Gu, N. D. Dalton, E. Rockenstein, E. Masliah, K. L. Peterson, W. B. Stallcup, J. Chen, S. M. Evans, Pericytes of Multiple Organs Do Not Behave as Mesenchymal Stem Cells In Vivo. Cell Stem Cell 20, 345-359.e345 (2017). T. Moore-Morris, N. Guimarães-Camboa, I. Banerjee, A. C. Zambon, T. Kisseleva, A. Velayoudon, W. B. Stallcup, Y. Gu, N. D. Dalton, M. Cedenilla, R. Gomez-Amaro, B. Zhou, D. A. Brenner, K. L. Peterson, J. Chen, S. M. Evans, Resident fibroblast lineages mediate pressure overload–induced cardiac fibrosis. Journal of Clinical Investigation 124, 2921-2934 (2014). 12. P. Hofbauer, S. M. Jahnel, N. Papai, M. Giesshammer, A. Deyett, C. Schmidt, M. Penc, K. Tavernini, N. Grdseloff, C. Meledeth, L. C. Ginistrelli, C. Ctortecka, Š. Šalic, M. Novatchkova, S. Mendjan, Cardioids reveal self-organizing principles of human cardiogenesis. Cell 184, 3299-3317.e3222 (2021). 13. M. Alexanian. P. F. Przvtvcki. R. Micheletti. A. Padmanabhan. L. Ye. J. G.