TECHNISCHE HOCHSCHULE DEGGENDORF THD

ADPKD

SCHLAGEN EINER BRÜCKE ZWISCHEN DEN EXPERIMENTEN AN TIER UND MENSCHEN MIT HILFE DES 3D-IN-VIVO MODELLS IN DER FORSCHUNG DER AUTOSOMAL DOMINANTEN POLYZYSTISCHEN NIERENERKRANKUNG (ADPKD).

Weitere Infos

Title:

Human polycystic renal tissue perfusion visualized by high frequency ultrasound in a 3D-in-vivo model

Background

Autosomal dominant polycystic kidney disease (ADPKD) is a monogenetic kidney disease characterized by the presence of cysts in both kidneys. With an incidence of 1:1000 it is the most common hereditary kidney disease in the world. We have recently shown that human polycystic kidney tissue can be cultivated on the chorioallantoic membrane (CAM) for the first time. One central aspect of this innovative model is the vitality of the tissue which strongly depends on adequate blood perfusion. Ultra high frequency ultrasound enables the visualization of smallest structures that cannot be detected by conventional ultrasound. Here we propose UHF imaging as a new imaging technique in a 3D-in-vivo model to acquire new insights into tissue perfusion and survival. In addition to this method, we also established mass spectrometry imaging (MSI) as a powerful new technique to visualize the location of, for example, new potential drugs (e.g., benzbromarone) within the tissue when it is treated with them.

Methods

Human renal cystic tissue was incubated on the CAM and examined using UHF ultrasound imaging. Due to the unprecedented resolution of UHF, we have managed to visualize microvessels, their development, and the formation of anastomoses. This allowed us to observe the connection of human and chicken vessels only 12 hours after transplantation. The new method and the observations described with it were validated by 3D reconstructions from a light sheet microscopy image stack, indocyanine green angiography, and histological analysis. After one week of treatment with benzbromarone, the tissue is removed and snap-frozen in liquid nitrogen. The frozen tissue is cryopreserved and cut into 10 µm slices. MSI was then performed on these slices.

Results

Histological results showed numerous chicken erythrocytes within the human cystic tissue at the end of the incubation period of 7 days. Based on the distribution of active blood vessels detected by UHF ultrasound, corresponding functional anastomoses between chicken vessels and human vessels were detected as early as 12 hours after grafting the human renal cystic tissue onto the CAM. These results could be confirmed by 3D reconstructions.
The MSI images clearly show the cystic tissue and the presence of benzbromarone. Benzbromarone not only penetrates the tissue but also clearly accumulates around the cyst in the epithelium. No tissue is visible between the benzbromarone and the cyst lumen.

Conclusion

Contrary to the assumption that the nutrient supply of the human cystic tissue and the gas exchange happens through diffusion from CAM vessels, this study shows that the vasculature of the human cystic tissue is directly connected to the CAM network, and blood flow is established within a short period.
Moreover, MSI imaging enables the tracking of applied therapeutics within the tissue, as well as their metabolites.

Thus, this in vivo model, combined with UHF imaging and MSI, is ideal for studying the impact of intravenously or topically applied therapeutics on renal cyst growth.

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