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IMPACT OF IN VITRO CULTIVATION ON POTENTIAL TARGETS FOR ANTIMUSCARINICS - EXPRESSION PROFILES FOR TRANSPORT PROTEINS AND MUSCARINIC RECEPTORS OF PRIMARY PORCINE UROTHELIAL CELLS IN CONTRAST TO PORCINE BLADDER UROTHELIUM

Hypothesis / aims of study
As the basic research on porcine bladder shows a high translational potential to the human bladder, we want to determine some of the uptake and release mechanisms of the antimuscarinic drug Trospium chloride (TrCl) in primary porcine urothelial cells. Here we present first data on the expression profile of native urothelium and urothelial cells (UCs) concerning proteins possibly relevant for the transport of TrCl.

Study design, materials and methods
Pieces of urothelium from whole pig bladders were frozen in liquid nitrogen and the remaining tissue was used for isolation of UCs. The cells were passaged until senescence whereas a part of each cell passage, too was frozen for analysis. All collected samples were processed and real-time PCR was performed.

Results
Transport proteins ABCB1 and OCT3 as well as the enzyme CarAT are highly expressed in the native porcine urothelium in comparison to OCT1, OCT2 and OATP1A2. The expression profile of the cultivated UCs shows a strong decline of all examined proteins except from CarAT and ABCB1. All muscarinic receptors M1-M5 could be detected in the native urothelium, but are down regulated, too in the derived UCs.

Interpretation of results
UCs derived from fresh porcine urothelium are not suitable for uptake assays as their expression profile differs strongly from the native tissue. Especially transporters for the uptake of TrCl like OCT1, OCT2 and OATP1A2 are down regulated in the cultivated cells. Contrary to that, the ABCB1 level, as a response to cellular stress, stays nearly equal and thus would lead to an imbalance in favor of the discharge of TrCl from the UCs.

Concluding message
Native porcine urothelium is a very good model for the human urothelium concerning transporter and muscarinic receptors. Therefore the use of the pig for short- and long-term experiments in vivo is reasonable. However, the use of derived primary porcine urothelial cells in vitro has to be seen critically.

Disclosures
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