CHARACTERIZATION AND REGULATION OF THE EXPRESSION OF SOLUTE CARRIER TRANSPORTERS IN HUMAN SKIN

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BACKGROUND

Most identified drug transporters belong to ATP-binding Cassette (ABC) and Solute Carrier (SLC). Recent research indicates that these transporters play an important role in the absorption, distribution and excretion of drugs, and are involved in clinically relevant drug-drug interactions.

Transporter-based interactions have been well documented in liver and kidney for systemic drugs. However very little is known about the role of SLC transporters in human skin in the disposition of topically applied drugs and their involvement in drug-drug interactions.

The aim of this work has been to characterize the expression of SLC transporters in human skin, to compare it to liver's and kidney's and to study regulation of SLC transporters by Rifampicin.

METHODS

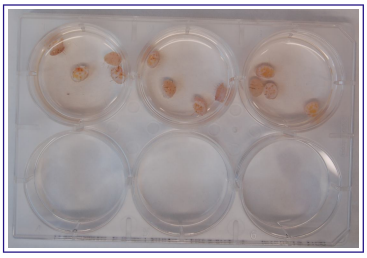
Measurement of gene expression

Gene expression of eleven SLC transporters in human skin, kidney and hepatocytes was measured by TaqMan Real-time RT-PCR.

Skin organoculture

Fresh human skin samples from 3 different donors were used and maintained in 6-well plates (Figure 1). Skin samples were treated with 20 µM Rifampicin during 72 hours. Untreated skin samples were used as control. The culture plates were kept in a cell culture incubator set at 37 °C, 5% CO_2 and saturated hygrometry. At the end of treatment period gene expression of SLC transporters was measured as described above.

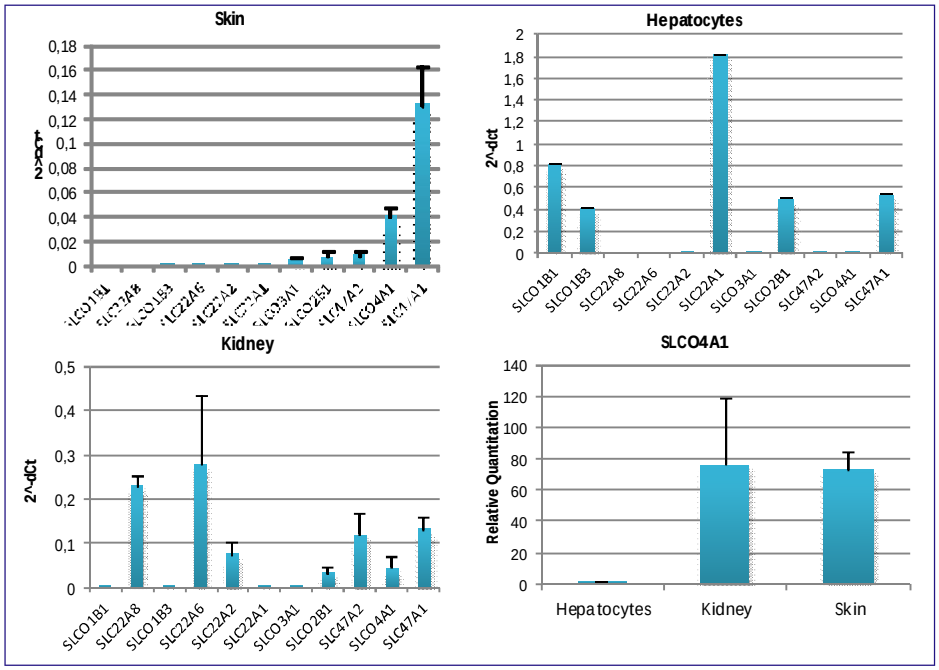
Figure 1 **SKIN ORGANOCULTURE**



RESULTS

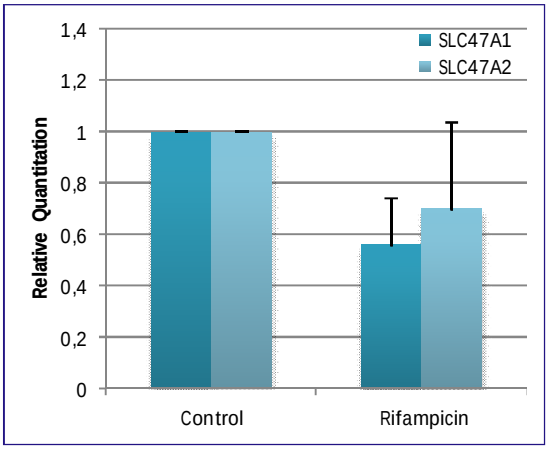
1. GENE EXPRESSION OF SLC TRANSPORTERS

Figure 2 **GENE EXPRESSION OF SLC TRANSPORTERS IN HUMAN SKIN, LIVER AND KIDNEY**



2. REGULATION OF SLC TRANSPORTERS IN HUMAN SKIN

Figure 3 **REGULATION OF SLC TRANSPORTERS BY RIFAMPICIN IN EX VIVO HUMAN SKIN**



DISCUSSION

The results show that SLC transporters have a very specific expression profile in human skin (Figure 2). At least five over the eleven SLC genes studied have been detected in skin, with SLCO4A1 (OATPE) and SLC47A1 (MATE1) being the most expressed (Figure 2). Expression of SLC transporters in skin is very different compared to hepatocytes and kidney. Indeed, expression of SLCO4A1 is about 60 times higher in human skin than in human hepatocytes but similar in human kidney (Figure 2). Moreover, the results showed that rifampicin down-regulated the expression of MATE1 and MATE2 in human skin (Figure 3).

CONCLUSION

Some SLC transporters are expressed in human skin and they may play an important role in drug exposure and in drug-drug interactions in dermatology.

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