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for the Study of Diabetes

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**The sodium-dependent glucose transporters (SGLT) as a new promising**

**pharmacological target in human ischaemic hearts**

A. Di Franco, G. Cantini, L. Raimondi, E. Mannucci, M. Luconi;

University of Florence, Florence, Italy.

Background and aims: Recently, EMPAREG OUTCOME trial has

shown that empagliflozin reduces cardiovascular mortality and the rate

of hospitalization for heart failure, in patients with type 2 diabetes with

previous cardiovascular events. The mechanisms underlying the

cardioprotective effects of this sodium/glucose transporter 2 (SGT2) inhibitor

are still unknown, though a direct action of the drug on the

cardiomyocytes could be hypothesized.

Materials and methods: We evaluated the expression of SGLT1 and

SGLT2 by quantitative-real time-RT-PCR and western blot analyses, in

tissue biopsies of healthy, ischemic and hypertrophic human hearts.

Results: In this study, we evaluated the relative expression of SGLT2 and

SGLT1, the two most relevant members of the SGLT family being potentially

responsive to empagliflozin, in tissue biopsies of healthy (n=9),

ischemic (n=9) and hypertrophic (n=6) human hearts. We found no expression

of SGLT2 in either normal or pathological conditions, whereas

SGLT1 was expressed in normal myocardial tissue and was significantly

upregulated in ischemia and hypertrophy, in association with increased

phosphorylation in activating domains of the intracellular secondmessengers

AMP-activated protein kinase (AMPK), extracellular-signal regulated

kinase 1 and 2 (ERK-1/2) and mammalian target of rapamycin

(mTOR).

Conclusion: Our findings suggest that the hyper-expression of SGLT1 in

cardiomyocytes may represent a potential pharmacological target for

cardioprotection.

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