

## SUR2A AS A CARDIOPROTECTOR?

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SUR2A is a protein serving as a regulatory subunit of sarcolemmal ATP-sensitive K<sup>+</sup> (KATP) channels. It has been shown that an increase in the myocardial level of this protein protects the heart against different types of metabolic stresses, including ischemia. An increase in SUR2A leads to an increase in the number of KATP channels, which is associated with earlier channel activation during ischemia as well as increased levels of subsarcolemmal ATP. Activation of KATP channels shortens action membrane potential to prevent Ca<sup>2+</sup> influx while increased subsarcolemmal ATP levels provide energy for vital processes in the environment surrounding the channel. How to increase SUR2A expression in an efficient and safe manner has been considered. Two possible approaches have been found to be promising. One is a gene therapy approach with virus-containing SUR2A and the other was nicotinamide, a form of vitamin B3 rarely used in clinical practice. In experimental animals, it has been shown that oral intake of relatively small doses of nicotinamide is cardioprotective due to SUR2A increase (1). Not only that increased SUR2A is devoid of adverse effects, it even prolongs the lifespan in healthy animals (2). Based on all these findings, we believe that SUR2A-based strategies against heart ischemia deserve to be seriously considered in clinical practice. The use of nicotinamide in this context is particularly interesting, as this compound is almost devoid of adverse effects, especially in doses used to upregulate SUR2A. Such therapy would be a good adjunct to current therapies for ischemic heart disease.

### References

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2. Mohammed Abdul KS, Jovanović S, Jovanović A. Exposure to 15% oxygen *in vivo* up-regulates cardioprotective SUR2A without affecting ERK1/2 and Akt: A crucial role for AMPK. J Cell Mol Med. 2017; 21: 1342-1350.

## **SUR2A: ZAŠTITNIK SRCA?**

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SUR2A je protein koji služi kao regulatorna podjedinica sarkolemalnih ATP-senzitivnih kalijumovih (KATP) kanala. Ovi kanali povezuju intraćelijski metabolizam sa membranskim potencijalom. Ustanovljeno je da porast nivoa ovog proteina u srčanom mišiću štiti srce od različitih vrsta metaboličkih stresova, uključujući i ishemiju. Povećanje SUR2A dovodi do porasta broja KATP kanala, što ima za posledicu njihovu raniju aktivaciju tokom ishemije i povećanje nivoa ATP-a. Aktivacija KATP kanala skraćuje akcioni potencijal i time sprečava ulazak Ca<sup>2+</sup>, dok povećani subsarkolemalni nivo ATP-a osigurava energiju za vitalne procese u okolini kanala. Razmatrano je kako povećati ekspresiju SUR2A u srcu na efikasan i siguran način. Dva moguća pristupa su se pokazala odgovarajućim. Jedan je pristup genske terapije virusom koji sadrži SUR2A, a drugi je nikotinamid, forma vitamina B3 koja se retko koristi u kliničkoj praksi. Na eksperimentalnim životinjama je pokazano da unos relativno malih doza ovog vitamina štiti srce od ishemije povećanjem nivoa SUR2A u srcu (1). Povećani nivo SUR2A ne samo da nema neželjena dejstva nego i produžava život čak i zdravih životinja (2). Na osnovu svih ovih istraživanja, verujemo da strategije zasnovane na SUR2A protiv srčane ishemije zaslužuju da se ozbiljno razmatraju u kliničkoj praksi. Korišćenje nikotinamida u ovom kontekstu je posebno zanimljivo, jer je ovaj vitamin poznat kao bezbedna supstanca koja ima malo neželjenih efekata, posebno u dozama u kojima povećava nivo SUR2A. Ovakva terapija bi bila koristan dodatak sadašnjim načinima lečenja ishemijske srčane bolesti i ostalih bolesti gde je povećana otpornost srca prema stresu poželjna.

### **Literatura**

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