Dimerization of cardiac sodium channel Nav1.5

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Not long ago, voltage-gated sodium channels were sought to function as monomers. However, this dogma was challenged by the recent studies that pointed to dimerization of neuronal Nav1.1. Nav1.2, Nav1.7 and cardiac Nav1.5 channels. Accordingly, functional cooperativity of the Nav dimers was emphasized for neuronal and cardiac diseases.

By using immunoblotting analysis, we have detected both dimers and monomers of Nav1.5 in HEK293 cells transiently or stably expressing human hH1 variant. Furthermore, we have shown that these α-α dimers are present at the plasma membrane and that reducing agents are disrupting them into monomers. In our hands, Nav1.5 dimers were not affected by 14-3-3 proteins as suggested in previous reports. Surprisingly, we were able to detect only monomers of Nav1.5 in healthy mice heart tissues. It is unclear at this point, whether our research method lacks sensitivity or whether endogenous α-α interaction of Nav1.5 is preconditioned by some pathological cardiac state.

Taken together, our results are bringing closer the understanding of the (patho)physiology of cardiac sodium channel on fundamental level.