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# Arrhythmias and Clinical EP

## PHENOTYPING OF ANGIOTENSIN-CONVERTING ENZYME IN THE HUMAN HEART

Poster Contributions
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**Background:** Angiotensin-converting enzyme (ACE) metabolizes biologically active peptides (AI, BK, Ac-SDKP) and plays a key role in many cardiovascular pathologies, including arrhythmia. Patients with atrial fibrillation (AF) are known to have increased level of ACE in atria. The increased ACE expression in the heart might be a causative factor for AF and sudden cardiac death.

**Methods:** We performed ACE phenotyping of postmortem human heart tissues. Parameters assessed included: 1) ACE activity/level; 2) ratio of the rates of ACE hydrolysis of two substrates, ZPHL/HHL, which allows to detect the presence of endogenous and exogenous ACE inhibitors; 3) conformational fingerprint of ACE using monoclonal antibodies (mAbs) to 17 epitopes on the human ACE.

**Results:** ACE activity in human heart tissues (~80 mU/g of tissue) was just 3-fold higher than the ACE level in the blood and 15-fold lower than that in lung. Apparent ACE activity in atria, together with different binding of some mAbs with ACE in atria and ventricles, indicates towards significant difference in the levels of endogenous ACE inhibitors/ACE effectors between human atria and ventricles. Conformational fingerprint of human heart ACE revealed several mAbs (BB9, 1B3, 1B8) which binding to atrial ACE differ from that to ventricle ACE. It allows us to suggest different glycosylation of ACE molecule in atria compared to ACE in ventricle. The conformational fingerprint of ACE from lung and heart also revealed dramatic difference in the conformations of ACE from these organs.

**Conclusion:** We developed and validated on the human postmortem heart tissues a novel method of ACE quantification and characterization - ACE phenotyping. Different human tissues contained high (and different) levels of endogeneous ACE inhibitors/ACE effectors. Local conformational changes of ACE in different human tissues allow us to expect the possibility of the generation of mAbs specific to ACE from specified tissue. The generation of the mAbs specific for heart ACE and discrimination of heart and lung ACE could be the base for the development of new blood test which will have diagnostic significance for the revelation of the risk group for atrial fibrillation.