**APTAMERS BIND AND NEUTRALIZE BETA1-RECEPTOR AUTOANTIBODIES: BASICS FOR A NEW TREATMENT OPTION IN CARDIOMYOPATHY**

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Background: Autoantibodies directed against the beta1-adrenoceptor (beta1-AABs) have been proposed to drive the pathogenesis of idiopathic dilated cardiomyopathy, Chagas’ cardiomyopathy and peripartum cardiomyopathy. For patient treatment, beta1-AAB blood clearance by immunoapheresis or in vivo autoantibody neutralization using corresponding peptides are currently under study with - for immunoapheresis - with clearly demonstrated patient benefit. Aptamers (single short DNA or RNA strands) were recently discovered as new molecule class which binds high-specifically target molecules. Aptamers vs. proteins/peptides possess low immunogenicity, are more stable and - since synthetically produced - can easily be modified to optimize their pharmacokinetics. These properties would qualify an aptamer which specifically target beta1-AABs as binder in the beta1-AAB apheresis technique and in vivo neutralizer of beta1-AABs.

Methods and Results: We selected and identified an aptamer that high-specifically binds beta1-AABs such as present in a distinct number of cardiomyopathy patients. To demonstrate the aptamer’s neutralizing effect on beta1-AABs, we used cultured spontaneously beating neonatal rat cardiomyocytes, in which the aptamer reduced the beta1-AAB associated cell toxicity and neutralized the chonotropic effect of beta1-AABs. In the presence of aptamer neutralized beta1-AABs, cells remained fully responsive to beta1-receptor agonists and antagonists. To forwarding the concept of “aptamers for treatment of beta1-AAB positive cardiomyopathies”, we designed a beta1-AAB apheresis column containing the aptamer as binder which was able to clear animal and human sera from beta1-AABs.

Conclusions: Aptamers, if evidenced in future also their potency for in vivo neutralization of beta1-AABs, could establish a new hopeful treatment option for cardiomyopathy patients.