

**EDITORIAL COMMENTARY**



# Atrial fibrillation as an autoimmune disease?

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“Might autoantibody generation also promote vulnerability to cardiac arrhythmias or be a primary cause for a common arrhythmia such as atrial fibrillation (AF)?”

“These observations are compelling and suggest that autoantibodies may have a functional role with agonist-like properties and promote electrophysiological changes consistent with an arrhythmia substrate.”

“Their data add to the cumulative evidence that autoimmunity may be contributory or even causal to primary arrhythmogenesis.”

“Such efforts may lead to a promising alternative in AF treatment involving the detection and removal of pathogenic autoantibodies as a therapeutic strategy.”



## High prevalence of antibodies against beta 1- and beta 2-adrenoceptors in patients with primary electrical cardiac abnormalities.

Chiale PA<sup>1</sup>, Rosenbaum MB, Elizari MV, Hjalmarson A, Magnusson Y, Wallukat G, Hoebcke J.

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#### Abstract

**OBJECTIVES:** This study sought to determine the prevalence of autoantibodies directed against the beta-adrenoceptors in patients with primary electrical cardiac abnormalities, including atrial arrhythmias, ventricular arrhythmias and conduction disturbances, in the absence of any other cardiac abnormality.

**BACKGROUND:** Using synthetic peptides corresponding to the predicted sequences for the second extracellular loop of the human beta 1- and beta 2-adrenoceptors as antigenic targets, autoantibodies directed against the beta-adrenoceptors were recently shown to occur in patients with idiopathic dilated cardiomyopathy and Chagas' heart disease.

**METHODS:** Eighty-six patients (57 with primary electrical abnormalities, 29 with idiopathic dilated cardiomyopathy) and 101 healthy and cardiopathic control subjects were studied. Antibodies against the beta 1- and beta 2-peptides were detected with an enzyme immunoassay performed in blinded manner. In nine selected (seropositive) cases, the immunoglobulin G (IgG) fraction was tested for functional effects on the rate of beating of cultured neonatal rat cardiomyocytes.

**RESULTS:** Antibodies recognizing the beta 1- and beta 2-peptides were found in 11 (52.3%) of 21 patients with ventricular arrhythmias ( $p < 0.01$ ), 5 (35.7%) of 14 patients with conduction disturbances ( $p < 0.05$ ), 3 (13.6%) of 22 patients with atrial arrhythmias ( $p > 0.05$ ) and 11 (37.9%) of 29 patients with dilated cardiomyopathy ( $p < 0.05$ ) compared with 15 (14.8%) of 101 control subjects. A rapid increase in the rate of beating of the cultured cardiomyocytes was induced by IgG from a selected group of patients, suggesting an agonist-like interaction with a functional epitope. This response was mediated by stimulation of both the beta 1- and beta 2-adrenoceptors in the patients with primary

**CONCLUSIONS:** Primary ventricular arrhythmias and conduction disturbances, like idiopathic cardiomyopathy, show a high prevalence of antibodies interacting with functional epitopes of the beta-adrenoceptors, suggesting a common or similar abnormal immunoregulatory process.

