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Atrial structural remodeling gene variants in patients with atrial fibrillation

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Statement of the Problem: Atrial fibrillation (AF) is a common arrhythmia with a well-recognized inherited component. Until now, AF genetic studies mainly focused on the genes involved in electrical remodeling, rather than left atrial muscle remodeling.

Methodology: A high-throughput next-generation sequencing (NGS) workflow was developed based on a custom AmpliSeq™ panel of 55 genes potentially involved in atrial myopathy. This workflow was applied to a cohort of 94 patients with AF, 66 with atrial dilatation and 28 without. Patients with variants in the selected genes underwent further screening for pathogenic mutations in prevalent arrhythmia-causing genes. Bioinformatics analyses used a pipeline based on NextGENe® software and in silico tools for variant interpretation.

Findings: Our AmpliSeq™ custom-made panel efficiently explored 96.58% of the targeted sequences. Based on *in silico* analysis, 11 potentially pathogenic missense variants were identified that were not previously associated with AF. These variants were located in genes involved in atrial tissue structural remodeling. Three patients were also carriers of potential variants in prevalent arrhythmia-causing genes, usually associated with AF. Most of the variants were found in patients with atrial dilatation (n=9, 82%).

Conclusion & Significance: This NGS approach was a sensitive and specific method that identified 11 potentially pathogenic variants, which are likely to play roles in the predisposition to left atrial myopathy. Functional studies are needed to confirm their pathogenicity.

Biography

Philippe Chevalier is the Head of the Rhythmology unit of HCL and the Coordinator of the National Reference Center for inherited arrhythmia. He is an internationally recognized clinical expert in the field of Cardiac Arrhythmias. He has been implicated in more than 10 clinical studies. He is the Principal Investigator and Coordinator of a European multicenter study on molecular markers of sudden death. He develops fundamental studies on the pathophysiology of atrial fibrillation. He organized every year the national congress of "les journées de rythmologie" in Lyon. He is also a member of several societies (French Society of Cardiology and American Heart Association). He has more than 200 publications in refereed journals.

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