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# HCN4 AND GATA5 PREVIOUSLY UNDESCRIBED VARIANTS IN A LARGE KINDRED WITH FAMILIAL ATRIAL FIBRILLATION

Poster Contributions
Poster Hall, Hall A/B
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Session Title: Newer Insights Into Atrial Fibrillation
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Authors: *Alfonso Fraile Sanz, Raquel Casado Alvarez, Ricardo Caballero, Eva Delpon, Jesus Perea Egido, Blanca Alcon Duran, Belen Gil-Fournier, Soraya Ramiro, Israel Thuissard, Juan Tamargo, Marisa Lefort, Joaquin Alonso Martin, Francisco Cosio, Hospital Universitario de Getafe, Getafe, Spain, Department of Pharmacology, Universidad Complutense de Madrid, Madrid, Spain*

**Background:** Genetic background can be difficult to relate to accepted mechanisms of atrial fibrillation (AF). Mutation of genes encoding cardiac structures can be associated to AF risk without clear definition of mechanisms.

**Long-Term ECG Monitoring:** Full-time, continuous monitoring of 1 ECG lead (average 12 days / 282±55 h / 22±1.5 h per day) was performed in subjects without clinical AF supported by a new type of textile electrodes mounted on a wearable band, with good tolerance.

**Genetic Study**: The 4 affected siblings were genotyped by a panel including coding regions and untranslated boundaries of 82 genes encoding cardiac channels, cardiac channelosomes, and other proteins that modulate ion channels. The variants found in the 4 index cases were searched in the rest of the family using the Sanger method.

**Results:** We studied a total of 42 subjects through genetic study of which 40 were studied through prolonged monitoring. All 4 subjects with clinical AF shared a heterozygous variant (NM_005477.2:c.3488C>A) at the HCN4 gene, leading to substitution of Pro1163 residue, located at the end of the C-terminus of the channel, to His (p.P1163H hcn4) and a heterozygous variant (chr20:61040536 G,A) at an intronic region of the GATA5 gene (NM_080473.4). The HCN4 variant was also indentified by Sanger in 10 subjects, of whom, 1 had frequent atrial extrasystoles (AE) and 2 had frequent atrial tachycardia (AT). Sinus node dysfunction was not evident in any of the subjects clinically or by Holter. The GATA variant was also identified by sanger in 18 subjects, of whom 2 had frequent AE and 3 had frequent AT. The only subject with AF not previously known also carries the GATA5 variant. Nevertheless no significant differences were found regarding the incidence of atrial arrhythmias or left atrial size between subjects carrying or not the two variants.

**Conclusion:** This large family with a new HCN4 and GATA5 variants and a somewhat high clinical incidence of AF shows a complex genotype/phenotype relationship. The relationship with AF and other clinically silent atrial arrhythmias was not clear in this large kindred. Follow-up of relatives without AF should help clarify the issue.