Supplementary Figure Legend

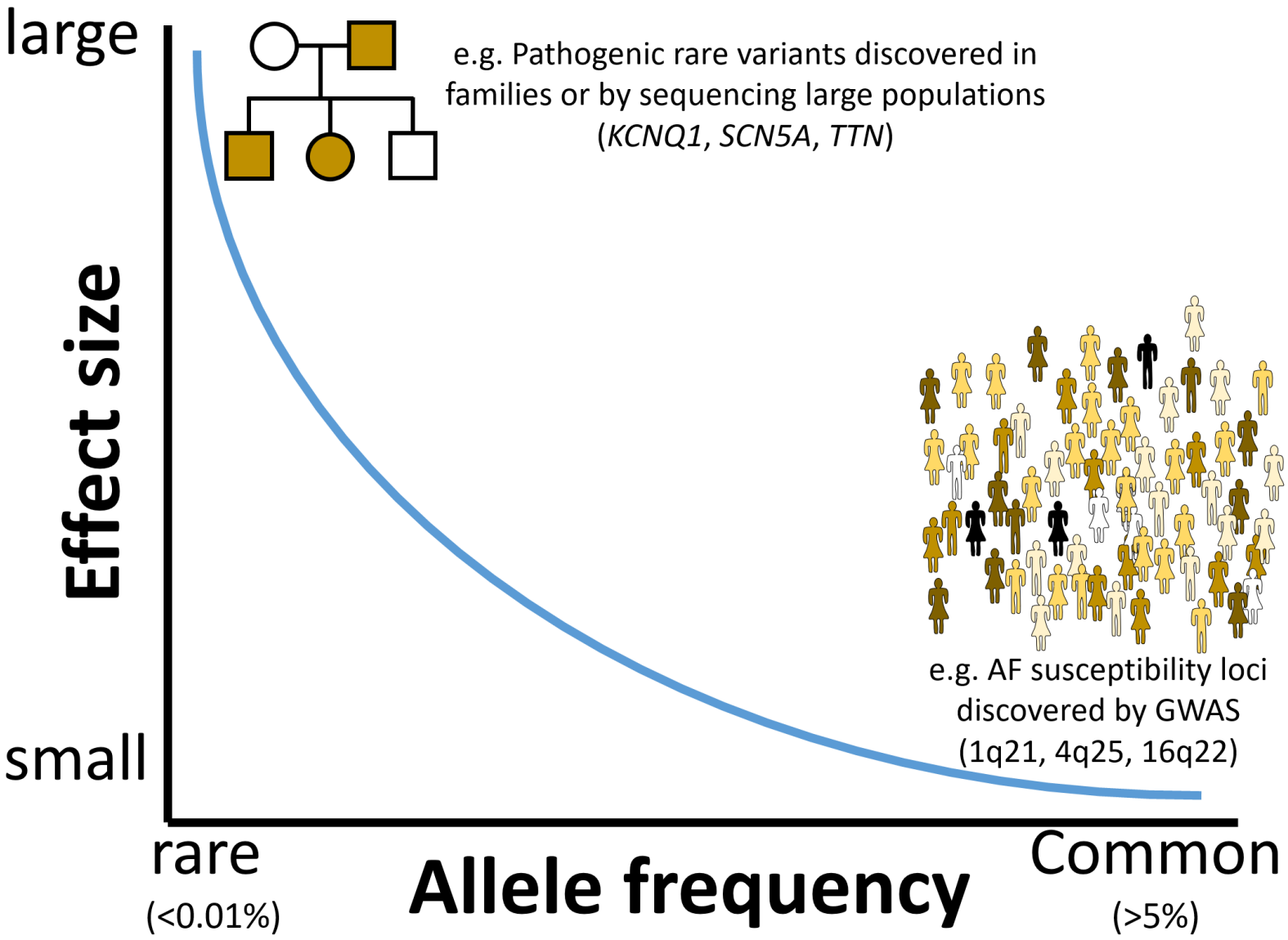
Supplementary Figure. The relationship between allele frequency and effect size in common diseases such as AF. KCNQ1, LMNA, and SCN5A are examples of 3 genes discovered by linkage analysis to possess monogenic causes of AF. 1q21, 4q25, and 16q22 are AF susceptibility loci discovered by GWAS which possess a small individual effect size (OR<2), but combine with thousands of other common variants across the genome to contribute greater effect for development of AF.

Supplementary Table I. Evaluation of AF in an inherited arrhythmia clinic focuses on historical features to suggest overlapping cardiomyopathy and arrhythmia syndromes. SOB- shortness of breath. DOE- dyspnea on exertion. VT/VF- ventricular tachycardia/ventricular fibrillation. ICD- implantable cardioverter defibrillator.

Supplementary Table II. Genetic loci associated with AF discovered using linkage analysis in families with AF. AV- atrioventricular. VT- ventricular tachycardia. PMID- Pubmed reference identification number.[67, 69, 72, 146-149]

Gene	Overlapping Syndromes	Year	1st Reference
LMNA	Sinus/AV nodal dysfunction, DCM	1999	69
KCNQ1	None	2003	146
NUP155	VT	2004	147
SCN5A	DCM	2005	148
NPPA	None	2008	149
MYL4	none	2016	67
GATA6	Septal defects	2017	72

Historical Feature	Suggests
History of Present Illness/Review of Systems	
Palpitations, fatigue, SOB/DOE,	AF-related symptoms
Syncope	Sinus node dysfunction/Conduction disease Ventricular arrhythmias
Orthopnea, edema, SOB/DOE	Congestive heart failure
Past Medical History/Family Medical History	
VT/VF ICD Sudden unexplained death syndrome Sudden infant death syndrome	Inherited channelopathy or cardiomyopathy with VT/VF
Pacemaker	Inherited channelopathy or cardiomyopathy with conduction disease
Seizures	Inherited channelopathy
Cardiomyopathy, heart failure	Inherited cardiomyopathy
Skeletal Muscle Weakness	Neuromuscular Disorder
Congenital deafness	Jervell-Lange Neilsen Syndrome
Cryptogenic stroke	Embolic stroke due to AF (possibly undiagnosed)


large
small
Effect size
e.g. Pathogenic rare variants discovered in families or by sequencing large populations (*KCNQ1*, *SCN5A*, *TTN*)
e.g. AF susceptibility loci discovered by GWAS (1q21, 4q25, 16q22)
rare
(<0.01%)
Allele frequency
Common
(>5%)