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***Abstract:** DESCRIPTION (provided by applicant): Atrial fibrillation (AF) causes significant morbidity, disability, and mortality related to heart disease and stroke in the human population. Dilated cardiomyopathy (DCM) is characterized by ventricular dilatation and systolic contractile dysfunction and is an important cause of heart failure. In some canine breeds, DCM is a relatively common, lethal disease. A recent study of 500 Irish Wolfhounds (IW) found that 24% had DCM; 88% of these affected dogs also had AF. The DCM/AF phenotype appears to be inherited as an autosomal dominant trait. We have collected DNA and clinical data from a large family of IW in which AF and progressive DCM is segregating. Our hypothesis is that a mutation in a single gene causes DCM/AF in IW, and we propose to map this gene by linkage analysis and to use the tools of positional cloning and candidate gene analysis to identify the gene. One of the most common genetic causes of human DCM is mutation in the lamin A/C gene. The phenotype caused by lamin A/C mutations in such patients also includes conduction system disease and therefore resembles the DCM/AF phenotype in IW. In preliminary studies, we have excluded lamin A/C as the locus of the defect in IW. Hence our proposed work presents an ideal opportunity to identify a novel DCM/AF disease gene. If successful, this may lead to improved knowledge of the mechanisms of DCM and AF in humans.*