

Supplementary Material:

Loss-of-Function Variants in Cytoskeletal Genes Are Associated with Early-Onset Atrial Fibrillation

Oliver Bundgaard Vad ^{1,2}, Christian Paludan-Müller ^{1,2}, Gustav Ahlberg ^{1,2},
Silje Madeleine Kalstø ³, Jonas Ghouse ^{1,2}, Laura Andreassen ^{1,2}, Stig Haunsø ^{2,4}, Arnljot Tveit ^{3,5}, Ahmad
Sajadieh ⁶, Ingrid Elisabeth Christophersen ^{3,7}, Jesper Hastrup Svendsen ^{2,4} and Morten Salling Olesen ^{1,2}

¹ Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen N, Denmark;

² Laboratory for Molecular Cardiology, Department of Cardiology, Centre for Cardiac, Vascular, Pulmonary and Infectious Diseases, Rigshospitalet, Copenhagen University Hospital, 2100 Copenhagen O, Denmark;

³ Department of Medical Research, Bærum Hospital, Vestre Viken Hospital Trust, 3004 Drammen, Norway;

⁴ Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen N, Denmark;

⁵ Department of Cardiology, Institute of Clinical Medicine, University of Oslo, 0450 Oslo, Norway;

⁶ Department of Cardiology, Copenhagen University Hospital, Bispebjerg, 2400 Copenhagen NV, Denmark;

⁷ Department of Medical Genetics, Oslo University Hospital, 0450 Oslo, Norway;

*Correspondence: mortensol@sund.ku.dk; Tel.: +4535330753

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Table S1 Descriptive information on studies used for genetic correlation analysis of AF and other traits.

Trait	Study	No. of participants:	Ancestry of participants	Reference
Alcohol dependence	Trans-ancestral GWAS of alcohol dependence reveals common genetic underpinnings with psychiatric disorders	28,757	European	(1)
Angina	www.nealelab.is/uk-biobank/	337,159	European	(2)
BMI	www.nealelab.is/uk-biobank/	336,107	European	(2)
Coronary heart disease	Identification of 64 novel genetic loci provides an expanded view on the genetic architecture of coronary artery disease	400,961	European	(3)
Depression	Meta-analysis of genome-wide association studies for neuroticism in 449,484 individuals identifies novel genetic loci and pathways	357,957	European	(4)
Diabetes type 2	Large-scale association analysis provides insights into the genetic architecture and pathophysiology of type 2 diabetes	69,033	European	(5)
Ever smoked	www.nealelab.is/uk-biobank/	336,067	European	(2)
Hand grip strength	www.nealelab.is/uk-biobank/	335,821	European	(2)
Heart failure	Phenotypic refinement of heart failure in a national biobank facilitates genetic discovery	394,156	European	(6)
Height	www.nealelab.is/uk-biobank/	336,474	European	(2)
Hypertension	www.nealelab.is/uk-biobank/	361,194	European	(2)
Non-ischemic cardiomyopathy	Phenotypic refinement of heart failure in a national biobank facilitates genetic discovery	390,142	European	(6)
Overall health rating	www.nealelab.is/uk-biobank/	336,020	European	(2)

Table S2. All affected isoforms of *DMD*, *FKTN*, and *PDLIM3*.

Gene	Genomic Position	Amino-Acid Change	RefSNP	Effect	Transcript	Consequence
<i>DMD</i>	ChrX:31140001_31140013	delTCTGCCCAAATC A	rs752332058	Frameshift variant	ENST00000343523	p.D1113Efs*6
					ENST00000358062	p.D1366Efs*6
					ENST00000359836	p.D1210Efs*6
					ENST00000361471	p.D602Efs*6
					ENST00000378680	p.D505Efs*6
					ENST00000378723	p.D615Efs*6
					ENST00000474231	p.D1223Efs*6
<i>DMD</i>	ChrX:31196048	C>T	rs145603325	Splice donor	ENST00000357033	c.10262+1G > A
					ENST00000378677	c.10250+1G > A
					ENST00000378702	c.1058+1G > A
					ENST00000378705	c.632+1G > A
					ENST00000378707	c.2882+1G > A
					ENST00000378723	c.1058+1G > A
ENST00000474231	c.2882+1G > A					
<i>FKTN</i>	Chr9:108358933	C>T	NA	Nonsense variant	ENST00000223528	p.Q54*
					ENST00000357998	p.Q54*
					ENST00000448551	p.Q54*
					ENST00000540160	p.Q54*
<i>PDLIM3</i>	Chr4:186425651_186425652	delCA	NA	Frameshift variant	ENST00000284770	p.C294*fs*1
					ENST00000284771	p.C246*fs*1

Table S3. Summary of protein-protein interactions of *DMD*, *FKTN*, and *PDLIM3*.

Gene	Interaction (confidence score)	Gene	Interaction (confidence score)	Gene	Interaction (confidence score)
<i>DMD</i>	<i>DAG1</i> (0.997)	<i>FKTN</i>	<i>FKRP</i> (0.992)	<i>PDLIM3</i>	<i>NEB</i> (0.877)
<i>DMD</i>	<i>SNTG2</i> (0.989)	<i>FKTN</i>	<i>ISPD</i> (0.991)	<i>PDLIM3</i>	<i>TNNC2</i> (0.875)
<i>DMD</i>	<i>SNTB1</i> (0.987)	<i>FKTN</i>	<i>POMK</i> (0.977)	<i>PDLIM3</i>	<i>PDLIM7</i> (0.873)
<i>DMD</i>	<i>CAV3</i> (0.987)	<i>FKTN</i>	<i>POMGNT1</i> (0.958)	<i>PDLIM3</i>	<i>MYL1</i> (0.866)
<i>DMD</i>	<i>SGCD</i> (0.986)	<i>FKTN</i>	<i>POMT1</i> (0.952)	<i>PDLIM3</i>	<i>CAV3</i> (0.852)
<i>DMD</i>	<i>SNTA1</i> (0.982)	<i>FKTN</i>	<i>POMT2</i> (0.950)	<i>PDLIM3</i>	<i>MYBPC3</i> (0.810)
<i>DMD</i>	<i>SGCB</i> (0.979)	<i>FKTN</i>	<i>DAG1</i> (0.870)	<i>PDLIM3</i>	<i>ACTN2</i> (0.789)
<i>DMD</i>	<i>LAMA2</i> (0.977)	<i>FKTN</i>	<i>THEM5</i> (0.852)	<i>PDLIM3</i>	<i>SRL</i> (0.705)
<i>DMD</i>	<i>AGRN</i> (0.975)	<i>FKTN</i>	<i>POMGNT2</i> (0.840)		
<i>DMD</i>	<i>TTN</i> (0.972)	<i>FKTN</i>	<i>DPM3</i> (0.824)		



Figure S1. DMD isoform expression.

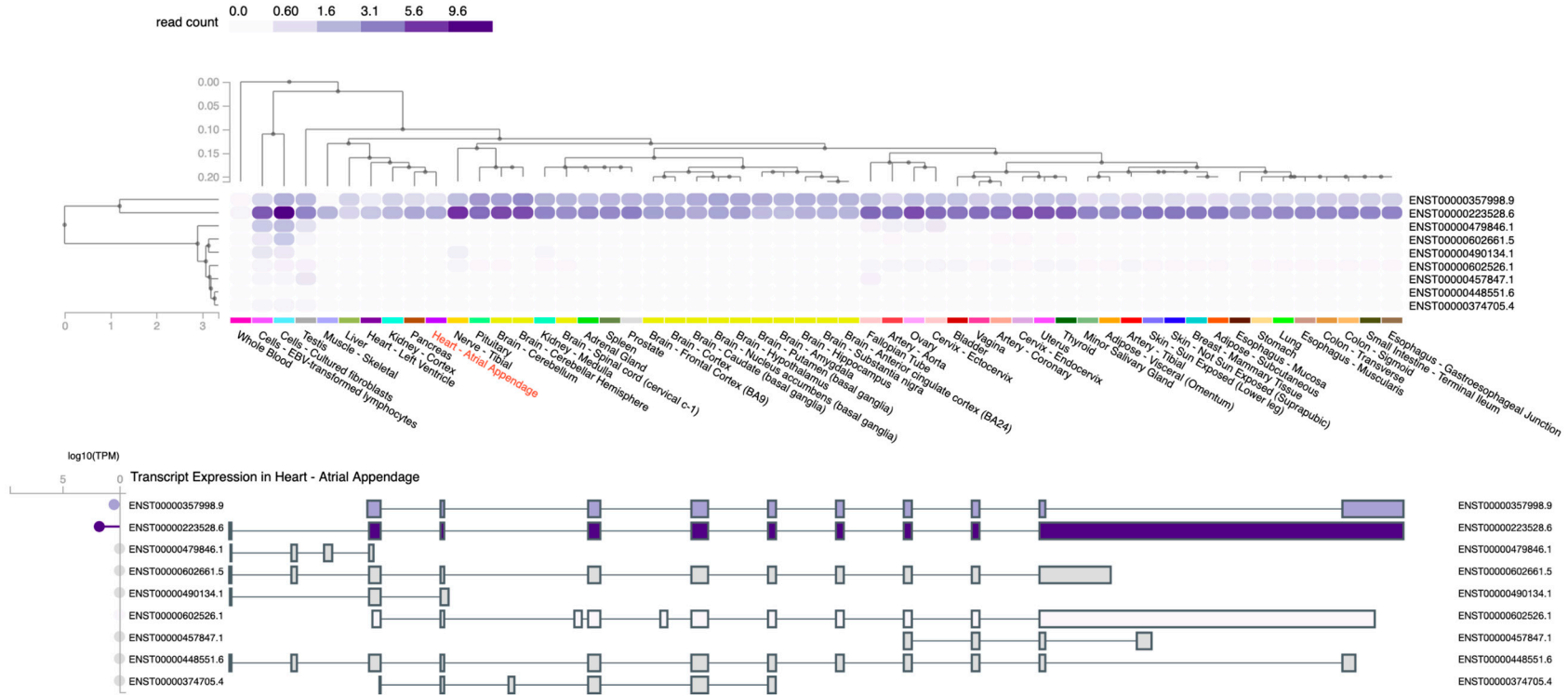


Figure S2. *FKTN* isoform expression.



Figure S3. *PDLIM3* isoform expression.

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