

## Supplementary Information

### Ryanodine receptors are part of the myospryn complex in cardiac muscle

Matthew A. Benson<sup>1</sup>, Caroline L. Tinsley<sup>2</sup>, Adrian J. Waite<sup>2</sup>, Francesca A. Carlisle<sup>2</sup>, Steve M. M. Sweet<sup>3</sup>, Elisabeth Ehler<sup>4</sup>, Christopher H. George<sup>5</sup>, F. Anthony Lai<sup>5,6</sup>, Enca Martin-Rendon<sup>7</sup> and Derek J. Blake<sup>2,\*</sup>

### Supplementary Figure Legends

**Supplementary Figure S1. Sequence and conceptual translation of minispryn.** The nucleotide sequence of mouse minispryn (clone 7E) and its conceptual translation (open reading frame, nucleotides 139 to 2289) are shown. The 6.1kb complete cDNA encodes a protein of 716 amino acid protein, minispryn. The italicised sequences correspond to dinucleotide repeats (GA)<sub>n</sub> and (CA)<sub>n</sub> in the 3'-untranslated region of the transcript. Coloured text corresponds to the amino acids forming the BBOX' (blue), BBC (green) FN3 (purple) and SPRY domains (red) in Fig. 1A.

### Supplementary Figure S2. Comparative genomics of the genes encoding minispryn and myospryn.

(A) Genomic organisation of the *Fsd2* (minispryn) and *Cmya5* (myospryn) genes in mouse. The organisation of both paralogs is remarkably similar diverging only at exons 1 and 2. Note that genes are not draw to scale. (B) Genomic organisation of the human and pufferfish (*Tetraodon nigroviridis*) *CMYA5* and *FSD2* gene clusters. Arrows indicate the direction of transcription. For clarity, only the *CMYA5*, *HOMER1*, *JMY* and *AP3B1* genes and their paralogs have been shaded. Abbreviations: *JMY*, junction-mediating and regulatory protein; *WHAMM*, WAS protein homolog associated with actin, Golgi membranes and microtubules; *SCAMP1*, secretory carrier-associated membrane protein 1); *LHFPL2*, lipoma HMGIC fusion partner-like 2; *ARSB*, arylsulfatase B; *DMGDH*, dimethylglycine dehydrogenase precursor; *BHMT2*, betaine-homocysteine methyltransferase-2; *BHMT*, betaine-homocysteine methyltransferase; *THBS4*, thrombospondin 4; *PAPD4*, PAP-associated domain-containing 4; *MTX3*, metaxin 3; *SERINC5*, serine incorporator 5; *SCARNA15*, small Cajal body-specific RNA 15.

**Supplementary Figure S3. Sequence coverage of peptides derived from RyR2, myospryn and minispryn.** Tryptic peptides (red) spanning the entire protein sequence

derived from RyR2, myospryn and minispryn (Table 1) are represented on the primary sequence of each protein. Proteins were purified directly from mouse heart using anti-minispryn 819-conjugated antibody beads (Fig. 3A).

**Supplementary Figure S4. Immunoaffinity purification of the myospryn complex with the anti-myospryn antibody des122.** (A) Proteins eluted from anti-myospryn-conjugated protein A beads after incubation with RIPA-extracted cardiac muscle were separated by PAGE and stained with colloidal Coomassie blue. This profile was compared to the control lane where protein A alone was incubated with the cardiac muscle extract. Unique bands were excised and processed for MS (Table 1 and Supplementary Table S1). (B) Western blots of fractions obtained from each immunoaffinity purification showed the specific enrichment of myospryn with the anti-myospryn beads and not with the protein A beads. Similarly, minispryn was specifically enriched with the anti-myospryn-conjugated beads. Comparison of the lysate with the flow through for each column showed that myospryn and minispryn were immune-depleted by incubation with the des122-conjugated beads.  $\alpha$ -actinin was not detected in the eluate from the myospryn-conjugated beads despite its abundance in the starting RIPA-extracts of cardiac muscle.

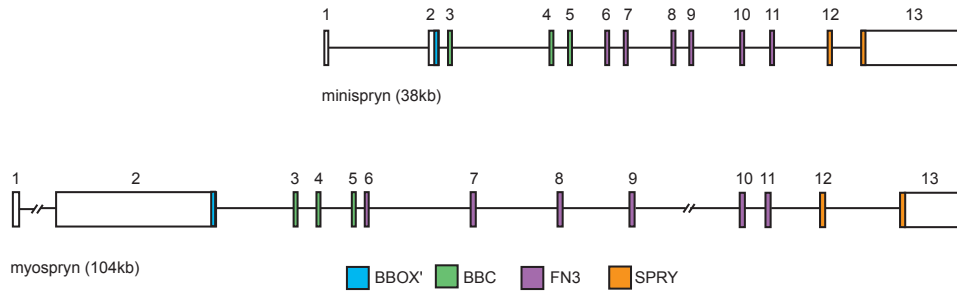
**Supplementary Figure S5. Immunoaffinity purification of cardiac RyRs using the 34C monoclonal antibody.** Immunoaffinity purified protein complexes (10% (v/v)) were western blotted using the indicated antibody. 0.1% (v/v) of the heart RIPA extract is shown for comparison. RyRs are highly enriched in the 34C immunoaffinity purified protein mixture with both myospryn and minispryn co-purifying with the RyR. Marker sizes (M) are indicated in kDa. Asterisks represent endogenous mouse IgG purified by the protein G sepharose detected by the anti-mouse secondary antibody.

**Supplementary Figure S6. Immunolocalization of minispryn and myospryn in skeletal muscle.** Minispryn and myospryn were detected in longitudinal sections of guinea pig *tibialis anterior* muscle using indicated antibodies. Minispryn (819) and myospryn (des122) are found in two bands that flank the Z-line (labelled with anti- $\alpha$ -actinin). This staining pattern overlaps with the distribution of the ryanodine receptors (RyR, 34C) that also flanks the Z-line. Scale bar = 20 $\mu$ m.

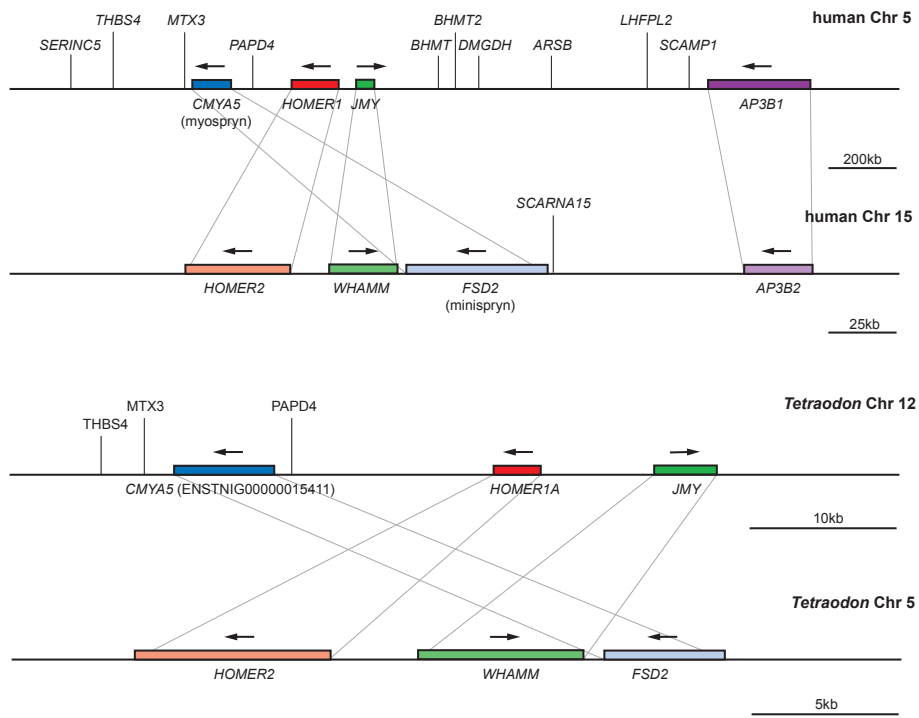
**Supplementary Table S1. Mass spectrometry data for minispryn and myspryn immunoaffinity purification from mouse heart.** Excel pivot table showing peptide sequences derived from RyR2, myspryn and minispryn following immunoaffinity purification of either minispryn (Fig. 3A) or myspryn (Supplementary Fig. S4) from mouse heart.



**a**



**b**



Supplementary Figure S2

**RyR2**

ryanodine receptor 2 [Mus musculus]

NCBI Reference Sequence:

NP\_076357.2

madagegede iqflrtddv vlcqtatihk egqklclaae **HAK**mplk**LLT** **NHYER**cwkyy clpggwgnfg aaseeelhis  
gfgnr**LCFLE** **STSN**SKnvpv dlsictfvle qslsvr**ALQE** rklfwgifda lsqk**KYEQEL** **FK**lalpclsa vagalppdym  
**MLANTVEK**se gqvdvkwwf mmktaqgggh r**LLYGHAIL** esnyvsmmek qssmdsegnf npqpvdtstni tipek**LEYFI**  
**LR**hsysgmyl cclstsrst dklafdvgll edttgeacww **NK**yaeshdk wsmdklangw iygeiysdss **KIQPLMKPYK**  
tihpaskqrs egkevrvgdd lilvsvsser ylhlsvgnss llsekekeiy rwpikeslkt mlawgwrier **TREGDSMALY**  
whvdaafggt lwsvapissg seaaggyllg gdvlrllhgh **NR**tr**RISQTS** **QVSDAAHG**Y **SPRAIDMSNV** **TL**SRdlhama  
mdectlvpvg ehgeeq**RTV** **HYEGGAVSVH** **AR**slwrletl emmaenyhni wakkkkelle sk**GGGNHPLL** **VPYD**TLTAKE  
r**VAMSGSHR** wggqfvlrhv ttgkylslme dknllmdeke kakkrekaqd ifkflqisgy vvsr**GFKDLD** **LD**TPSTEKRf  
kadvk**STAF**A **FR**sskekldv gvr**KEVDG**M **TSEIK**ygdsi aysflqqilir yvdeahgyil efdggsr**SKG** **BHF**PYEQEIK  
cyiqhvdtdgl wlytqvadvk sarmgsiqr**K** **AIMHHEGHMD** lardlyafyp ddyfknhrly flsaasrplc tgghasnk**EK**  
**DGLNLSR**sqh eesrtarvir **STVFLNRFI** r**GLDALS**KKV **EMV**TL**FLCKI** gvlvrhrisl fgndatsivn clhlilgqtdl  
kriptidipie svslslqdlly gyfhhpdehl ehedkqnrll artvmktgld svksalr**APL** **DNA**EDLEKt menlkggqft  
alknrqnlfq eegminlvle cidr**LHVYSS** **AAHFADVAGR** htrsdpkgvt qiinyttval lpmlsslfeh igqhqfgedl  
eageswksil nsllyellaal irgnrkncaq fsgslwdwlls iledqvscy r**IL**TS**LYALG** **TSKSIY**VERq rsalgeclaa  
rlerleassg ilevlhcvlv espealnik eghiksiisl fagafpiafl ethldkhnvy syntsrssre raalslpav  
ldkghrnhkv ldvlclslcvc hgavavr**SNQH** **LICDNLLPGR** edvcpnipsl ek**LMTEI**IEL **AESG**RYTqm pmmvmlvlp  
dillqtrlvn hvssmnpnif lgvsegsaqy kkwyyelmvd lcsymrwwv hgpnhpera emcctalnse hnttlgnil  
htepfvtaea thlrvgwast egyspyppgg eewgngvgd kiinynglid egawmkr**LAV** **FQOPI**LNKvk pglk**THFLP**  
dlfsygdgl hlwsqciart **VSSPNQHL**LR tddvisccld **LMEK**lkk**AA** **MV**SEEDHLK **AEAR**gdmsea ellildeftd  
lsapsisfri ngqpvqgmfe nfnidglfip vvsfsagikv lardlyafyp llir**FVDYNR** akwlk**ENP**AE **AE**ELFRmvae  
rfllggrhge fklfpppgya acyevlpke klkvehsrey vfiiywsksn fkreegnfvv qneinmsfl ldtckskmsk  
kqertytrld lgptvsltqa aftvpvdtst qivlpphler aaisdqerkk mkrkgdr**YSM** **Q**TL**LIV**AALK **R**llpjlgnic  
irerlaenh elwvnmkiel gwqygpvrdd nkrqhpclve apgdqelial aknr**FSLKDT** **E**EEV**RD**I**IR**s nihlqgk**LED**  
fcklpeqes**N** **YN**L**QMSLE**TL **K**llalagchv giadehaeek **PAIR**wmaly kdlpnrtedp sdpertvrv lgianvlfhl  
ENAHNVW**AR**d rir**QGW**TYGI **Q**Q**DV**Knrnrp r**LV**PY**TL**DD eqskytgrg yfslvehpqr skkavwhk**LL** **SKQ**KR**AV**VA  
**R**tkksnkds l reavrtllgy gyhleapdqd hasraevcsg **CFR**MAP**LYNL** **PR**hr**AV**N**FL** **Q**Q**VE**Kswiet eehfyfedk**LI**  
tgerfrifra ektyavkagr wyfefeavta gdmrvgwsrp **ED**L**K**PA**GAEL** **PE**DE**AM**Krv dplhqlillf srtalteck  
gcqpdlelgs ddr**AF**AF**DGF** **K**aqrwhqgne hygrswagad leedflymay adimakschd eedddgeev ksfeekemek  
vvgcmvdmne htmmtflnge illddsgeel afkdfvdgdg qk**LLYQ**Q**AR**l hdr**GA**EM**VL** **Q**T**S**AS**K**ET **G**PM**V**A**TL**KL  
fipvcslgva qvgr**MNF**GKD **V**ST**L**Kyftic glqgeyepfa **G**I**A**IL**NG**NS **T**V**Q**Q**K**LD**LYD** **K**ekkdvgffq slaglmgs  
vntnrldtmw lskrlpqlf vpsnehiev trid**GT**I**D**SS vldlnafer**Q** **N**K**A**E**L**GM**V**T **E**E**G**S**G**E**K**V**L**Q **D**D**E**F**T**CD**L**FR  
**P**CL**K**vtgk**F** **G**S**Q**NN**T**DI**M** **F**Y**R**LS**M**PI**E**C **A**E**V**F**S**K**S**V**A**G flqlclceghn sdfqnylrtq tgnnttvni istvdylrv  
**G**L**P**G**A**G**Y**G**F** **K**ndledfdvd sdfevlmkta hghlvpdrid gesisdfywy ysgk**DI**DE**Q** **G**Q**R**nfskaiq vakvfnltl  
kdketpkef nnhkdyaqek prlkrqfll rrtkpdystg eyiqqptgn qqslahsrllw davvgflhvf ahmqm**LSQ**D  
hsartledvl addrddyeil mgtstyysv rifpggepan **S**S**Q**IEL**L**K**E**L **M**D**L**Q**K**dmvum llsmlegnv ngtigtkgmvd  
vwwgitsdf hqydtgfdld rvr**TV**VT**L**G **D**E**K**gkvhesi mlvessnve milk**F**D**M**F**L** **K**L**K**D**L**T**S**S**D**T **F**K**E**Y**D**PD**G**Kg  
khlqlieps vfk**EA**AV**P**EE **E**G**G**T**P**E**K**eis iedaklegee viskrdfhka meshkhytqs etefllscae tdenetldye  
fiang**K**EL**ST** **Y**Q**V**EP**ST**KL fpavfaqats pnvfqlfelgr efvkrfhepa kdigfnvavl ltnlsehmpn dtrlqtfllel  
**I**N**V**M**L**S**A**G **L**F**K**sehknpv pqcprlhvq flshvlwsrm aesvlnfyq flgr**IE**IM**G**s **A**K**R**ier**V**Y**F**E **I**S**S**ERT**Q**WE  
pnqflkvds riserqgwlv qcldpqlfms lhipeenrv **K**P**Q**V**K**eskr**Q** **F**I**F**D**V**NE**G**G **E**K**E**K**M**elfvn fceditfemq  
dileltegee llqfhyhtlr **L**Y**S**AV**C**AL**G**N **H**R**V**ahalcsh laaaisedl ner**L**AN**K**E**S** **E**K**E**R**P**E**E**Q**A**P Rmgffllti  
vdepqlliai enkympgllr aggydlldi hlssyatar**L** qsalfalr**YN** **V**L**T**L**V**Rmllsl kslkkqkmrm kmtfvkdml  
**M**M**N**NE**F**I**V**M **T**E**R**T**S**itlf pdenk**H**GL**P** **G**I**G**L**S**T**S**LR**P** affssywsvf vtllhfvavsv crgffrivss lllgslvge  
**R**mrfspsfv sisndcyqys pefpldilk k**T**I**Q**ML**T**E**A**V akkikvaell anmpdptqde vrgdeeger kplesalpe  
**K**egslhardp vggttelflv pliklfytl imgifhned dltdlkelte esdlldsfif ldlkreggy kliphnpag  
khlqlieps vfk**EA**AV**P**EE **E**G**G**T**P**E**K**eis iedaklegee lsdlmtnpvp vpevqekfge qkakeekkek eektsepeka  
eakggkr**K**E **G**L**L**Q**M**K**L**pep vklqmcillq ylcdcoqvrhr egedgekek akdeksqkl rqlhthyge pevpesafwk  
eaiavfsdd fvaklqdnqr fr**Y**NE**V**M**Q**AL **N**M**S**A**A**L**T**ARK **K**I**I**AY**Q**Q**K**LL **N**Y**F**AR**N**fyym rmlalfvafa inifillfyk  
trefrspqge qinmlnlfkd dksecppee irdqlldfhe stssvvegke lptrtssdta **K**V**T**NS**L**D**S**SP **H**R**I**avhyvl  
dlmthogiel dedgsldgsn dltirgrlls lvekvtlykk eessgymept lrilailhti isffciigyy clk**V**PL**V**I**F**K  
kqaekpvasd srkcsslqql isetmvrwaq esviedpelv rekevarkle fdglyiteqp seddikqgdw rlvlntqsfp  
r**AM**V**L**H**R**Q **Y**D**G**I**G**L**V**RA lpktytingv svedtinlla nnywdkfvkr kvmdk**Y**E**F**Y **G**R**D**r**I**SEL**G** **M**D**K**A**A**L**D**F**S**D  
slgqirslls vr**M**G**K**EE**E**K**L** **M**I**R**GL**G**DI**M**N **N**K**V**F**Y**Q**H**PN**L** **A**REkkk**K**VD **S**S**L**S**A**V**L**NS**I** **D**V**K**ymkwklg vvftdnsfly  
**M**R**A**lgmhetv mevnmvlgv geskeitfpk mvancor**FLC** lawymtmsvl ghynnfffaa hlldiamgfk tlr**T**L**S**SV**T**  
**Y**FC**R**lsrqnq kamfdhlsyl lenssvglas pamrgstpld **H**NG**K**qlvltv gllavvlylv tvvafnfrk fynksedgdt  
vaaasvmdnn elalalrepl lekvv**Y**L**A**G **C**G**L**Q**S**C**Q**M**L**V **P**dmkcdmllt cymfhmyvgv raggigdei edpagdeyei  
**S**K**G**ypdigwn pveger**Y**L**D**F **L**R**F**avfcnge sveenanvvv yriifdtiff ffvivillai igqliidafg elr**D**Q**E**Q**V**K  
rllir**R**E**C**F **G**P**A**L**R**G**E**GG**N** **G**L**L**A**A**M**E**E**A**I **K**I**A**ED**P**SR**D**G **E**D**M**E**T**K**F**icf **I**gndyfdtv phgfethtlq ehnlanylff  
**P**SP**T**S**G**SS**K**t ldieeeddt ihmgnaimtf yaalidllgr lmylinkdet ehtgqesyvv kmqgercwef fpagdcfr**K**Q  
capemliha gkgeairirs ilrslipldg lvgvisiafq **Y**ED**M**S**A**G**F**C **P**D**H**K**A**amvlf ldrvygievq  
mptiakdg**V** **V**E**P**D**M**S**A**G**F**C **P**D**H**K**A**amvlf ldrvygievq dflhlhlevg flpdlraas ldtlaalsatd malaln**Y**L**C**  
tav**L**PL**L**TR**C** aplfagtehh aslidsllht vyrllskgcsl **T**AV**L**PL**L**TR**C** aplfagtehh aslidsllht vyrllskgcsl  
tkaqrdsiev cllsicgqlr psmmqhlrr **L**V**F**D**V**PL**L**NE

**myospryn (Cmya5)**  
stretch-responsive fibronectin  
protein type 3 [Mus musculus]  
GenBank: CAD53474.1

```

mvavqrEDSG ITWETNSSR stpwasgesq tsgiclegs
altspgsvs fimdevkrtr krtqkskrqs psllrrkgskk
rnslesqdlv tnqedgpsis espvlniene KSSIGTYDKT
rrkkTASNTP PITGAIYKeh kplvlkpvyi gtvgykikmf
nsvkeelipl qfygtlplkgy vikeihyrng kdssislepdp
lsgngsnivp qrKLQAQSPEE DKVRelappv rgalskgsrT
SIFSHEEQK TYADSNLNVP SSTHEAFPSS ARNDTADQEE
NLSLFPQMMPQ QPADESKthr MEPPSIPATM VLERAKELE
QNAQKesse ddasvltgsa ddvqqeglvsv vnhsmpwaeae
kesletgppr papaiqekFE PMEGLEPIS TEKTEQASEY
VTSSEPIVHR EEEHAFEPIV HREEHAFEP IVHREEHAF
EPIVHReeeh apesivhree ehapesivqr eeehapepes
ivhreeehap gpvpihvree ehvpelesiv hrGEEHAFEP
IVHRDEGHAP EPIVHReeeh vpepivhrDE GHAPEPIVHR
eeehvpepes ivhreeehap epmvlrkaql ergvetstpi
tdttedpess leeeiieldy pesplaskET SPSPLSPEVE
HRKEPILPTQ MTFTPERitl seereenes vstdsafvse
ysvlqdnht pekleveavs vsdvkssnep avfseddeer
eayspamtvs seqslspstt ektsaiqspl fstvsvplsg
deasesvchs pesesaaeys vpahaqelll kTGDHKLPLK
sqrivsepiiq aedekeidigl lppaalsqav lsesedslsg
fsaedsLFP KPSVSQNATR espqkTDDM PQFKPRGLSD
PATLLEEKEe aigvlgsssn evsavecalp pgttellses
happwaisss eqvvqseegs rdqqrGSFSS TFELGHTSPL
LLKgassptg lseggqeedn igplspdsaf asefsfspyp
tqelekreig rdsplcltsp seqtvlssded teeadifspd
sasqvslppy rIAETEONKV EPDELLPRs apdyppfsea
deeeagssvv tpvpehseps qereesspcr pvfedisl1lp
sadtktgaet msdvptists vseylilaqq ektqaslepe
aedlvpppts gwekrdakss lpavtiaaass salssvvkee
ttsvlptsqp svspstcvl kpegeptapl tltsadeqma
lvrvrEKAV LDSQEATAHK SQDQTPPERL PNVPGSGMKY
SVLSDLDGEP KADVKNLNLAP TVTSELEQRm lskNEPEVAK
PHSPPEETSI SGPKVlsavk tevqkeskit rELPAASSGR
ergaehsppa ppalpalmee mgkdeatass attvpvtkld
snstklGRDE VLTDPSLAP VEHPGLKgvg kSELGSLPL
PSMSTSEVLR PEPKlpvnsg veverednep pplqvsptsk
ptvpndkhee itrspdsenv vsddlaptll alrhemnrga
eetspvpvgs flsgeqelik LPPEPEKhkQ LSEVPTAGSE
LIDSRdrdrS LGIEPVKPIG TEPGSILEK GPAELQRrgk
eqeenrklpv pasapletas fdplieqkep krtlheggav
evpdessssa dkpelgvkql aekKENLEQP KPFVTTERas
vtgskVKESL ISPKdntwml ekpdglvnhq edrKPFTGQL
ESSESTDLMS EKLGAAPLDT DHTSETRNQE TSKAPVSGEK
lsgeprrvqs kavddseegr KLASGNVEVL TQSKsvpavk
akATPQPPEP PEVTPQKPEK SLVTEQGLPA EKGkgkissf
kswmssllfg ssiidskVSD NEDLETRPGP SVEKAVPAIE
PKGtvpaevn iaekpavhsl pevtvklae kpgvsvkSSI
SQDLKEKLF LSNEDVLKQP Knsenygqk elpgfsegmg
eslatsvgdk hpgihpcspm gekVGMEEAQ NMAPLHITES
QRrkqpevss psmwnisark eepssdhket wlsssdvdr
mpgkpkSAQS AFTRMNEEP ASMILPVESK GSLSDLGEDR
LRgempkpts lehceeever pteekdgwet rSFSLAGKRG
LAERQEIMAP LELRENEAVG ELQRMPESRP FKLEESKaae
rieqrispte klmekpsktl aldrrekevg ewvfsegeqk
eyppaampvp gasavslcka qphllaktp vvekpehivt
evypeirerK AAETQHPQE EKGTLVektk vsrVESPHGE
ETDGHSLTQE GNLELEKsge srvdлкеer rfvmpelslg
asvaaedgsv qprplskaa rvsdmtdetk hlgtptqps
avepqtllvg tsvehvkkq etwsdrptvh tfqtskDYTE
EMLKQSVLIS KHHLEAVEDV HRneppssaa snytqfmlsa
seisadgvpp mggtaqepg tsvkdeefsv tskpaglseq
qksafsiise gceilnihap afipsvdqee seqmqdkLQY
LEEKasfksi svhdekkaaa shktqkSKLE VPDRKITSLK
ENETKethkt keeiatdsgm gafftiqptv sgeedfyeky

```

```

TLIDYNLSPG SGKQKSTVEE SSEATKtl t sfpessaega
ldheynlvkL DESFYGPED DSKlshaemq kSLAIQKPPD
Rnapkgisrd vsdrSPGMPL FDVEEGVLSK RQIFPTTPKa
vnpelleepp alsffykdy egaggekneg etasegdsvd
setsfprhrs dtddgpgmyf ekyilkddil hdetvtqedq
gggleekpvg eedsqqlrva ereirRKPET FWEKnleeq
hkvvgrEGEP TGHMETLDEA AMQKAPITE QVRavtgkms
yavpfgdtrc vlesepsgg neagnaspdv nlnvpqvsf
peeesaagat yapevlqerL VPSVSRERL hntpvqdeyd
fvgslnqaaa sqallpeepg sesspkEVLS QGSSEFEHIR
EQELTSEGEP RMSASQEVWD RTEDQSAREs vtaktqkep
KTQAESYCYT CKSLVSEMDK aldihkDHEV SALDTAISAV
KVQLGEFLEN LQEKslria fvseiesffn tieekcskne
KRLEMQNEEM MKRVLQAYDE KAQSFEVek kkmeflhdgm
vhflqsmpta kDTLETIVRg akeldetvfl asfeinerl
lsamestaal enmpaafslf ehdyddsars dqmlkQVAVP
QPPRlepqep ssatsttiav ywsvnkedvv dsfgvycvee
pqddqinel veeyrltvKE SCCIEFEDLEP DRcyyvwvma
vnftgcslps eraifrtaps tavihvedct vcwnatvrv
rpanpeatet ytleycrqhs pegeglrsfs gikgqlkvn
lppndnyffy vrATNASGTS EQSEAALIST Rgtrflllre
tahpalqisa ngtvisfser rrlteipsvl geelpacqgh
ywettvadsp ayrLGICTSS AVRagalqgg etswvnhcse
pqrytffysg ivsevhatar parVIGLLDY TNQRllfina
esgqllfivr hrFNEGVHFA FALEKPGRCT LHLGLEPPDS
Vrhk

```

**minispryn (Fsd2)**  
fibronectin type III and SPRY  
domain-containing protein 2 [Mus  
musculus]  
NCBI Reference Sequence:  
NP\_766492.2

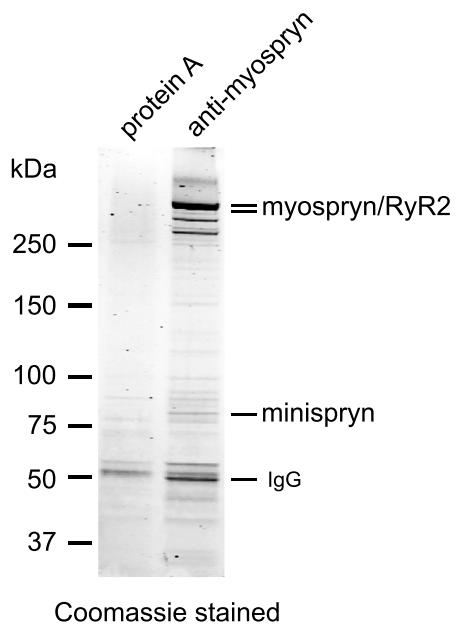
```

meeeaeesg lgrsaapkDF HFYHMDLYDS EDRLQLFPGD
SSRirREVTQ AEDDRELGDE FVDEHRLGTL GYPYSGMRrr
dpgreprdwg eaaeaedlgy gggggpldq dldrearyt
hgraseyec yvipeeade epadvfctc ktpvrTEKD
FDTHKEHEVT PISKALEHAK DEVHKNMCKL eqqiemenf
ashleevfit veenfrgreq nfechyngil etlaqYEEK
IQALGEKkre klealygqlv scgenldacr ELMETVEEMC
HEEKVEFLKD AVAMTDRlgk flkktdvel saqpefedqt
ldfsdveqlm daintipaps apvinpqpap satgsvrvrc
wslsddtve syqlsyrpvq dsssgkDRAE FTMMVKetyc
svtlnleptq yefwvraqn TGSPPCSEHA VYMTAPSPPS
IKteairsce eavlicwesg nlnpdsytv eliaquetpa
sgvtesvvgi ptcesliql prHSYTYIVR ALNVGTSAR
SEPATVHTTG SYFQLNKdtc hpwltisedg ftvvrsekks
frKELPSKt qftrCVAVMG NLPVRgrghy wevevaeild
ytvgvacedv pkQEDLGANS LSWCMrhftv skrHRYEFLH
NKmtpdirit vaprKIGVLL DYENAKlsff nvdiaghlyt
fscqlhfvhv pcfsleksqg lkICNGISMP Khvtff

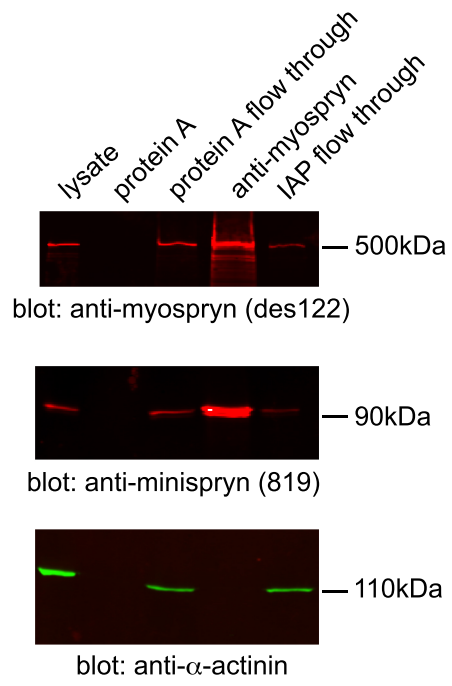
```

## Supplementary Figure S3

**a**

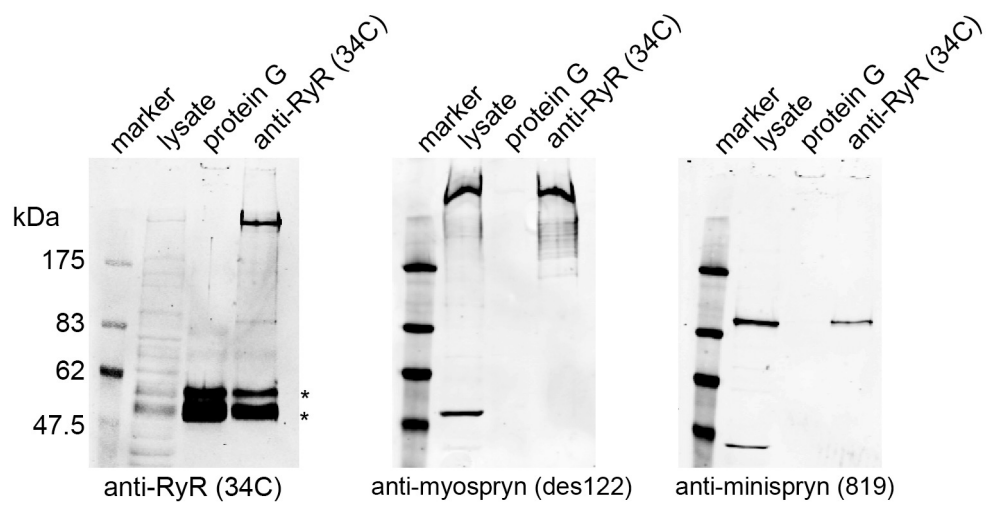


**b**

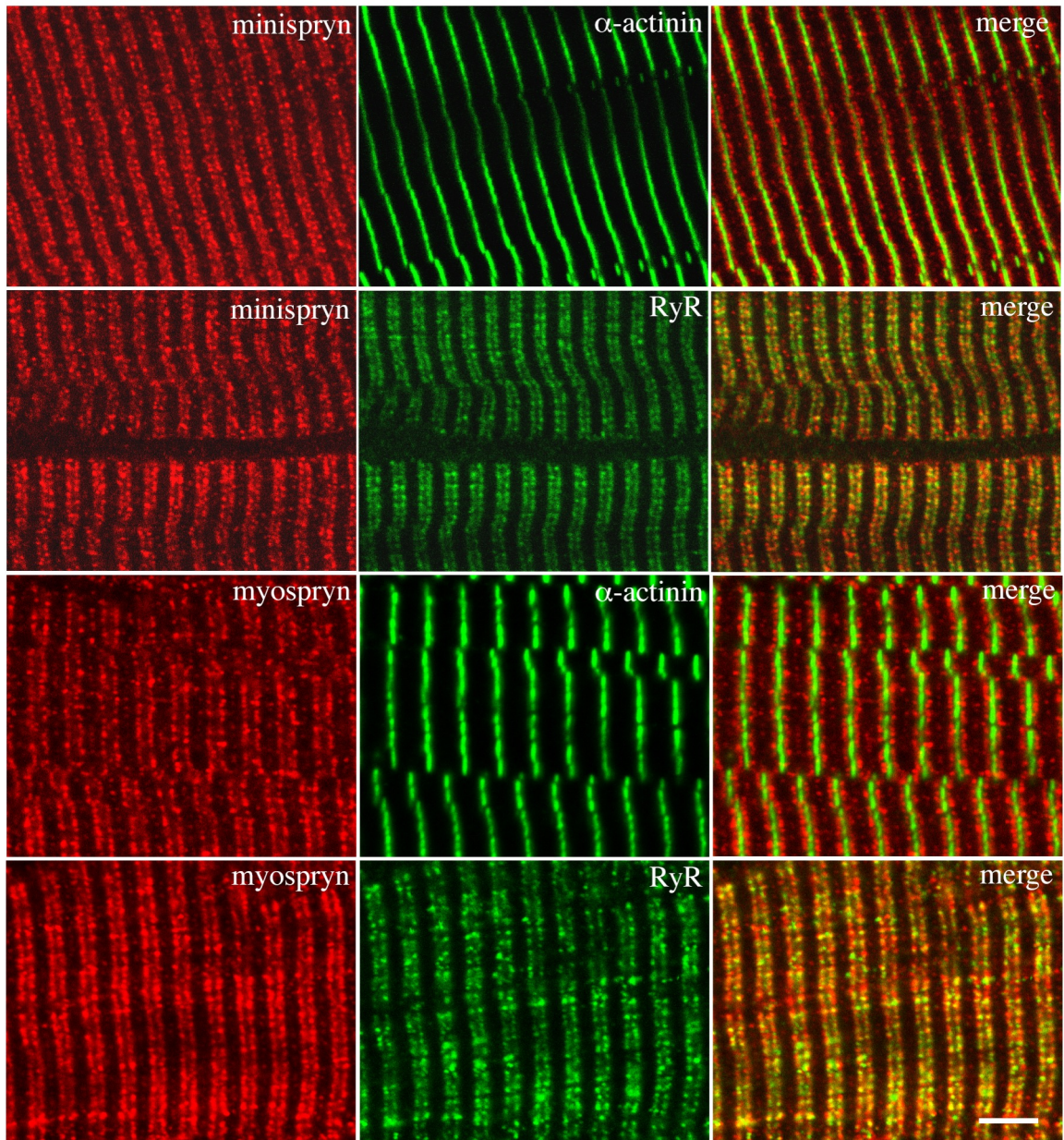


**Supplementary Figure S4**





**Supplementary Figure S5**



Supplementary Figure S6