

Figure S3

# Flotillin 1

**SPFH-domain**

*Hsap* M-F-F-T-C-G-PNE-AMVVS-GF-CR-SPPV-MVAGGRV-FVLP-C-IQQI-QRIS-LNTLT-LNVKSEK-VYTRH-GVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMA  
*Mmus* M-F-F-T-C-G-PNE-AMVVS-GF-CR-SPPV-MVAGGRV-FVLP-C-IQQI-QRIS-LNTLT-LNVKSEK-VYTRH-GVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMA  
*Spur* MVF-F-EV-C-G-PNE-ALVVS-GC-CV-MKPL-LVPGGRV-FVWPV-FQK-LQRIS-LNTMT-LQVES-PCVYTS-QGVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG  
*Dmel* MTWG-FVT-C-G-PNE-ALVVS-GC-CV-MKPL-LVPGGRV-FVWPV-FQK-LQRIS-LNTMT-LQVES-PCVYTS-QGVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG  
*Nvec* MVF-F-EV-C-G-PNE-AMVVS-GF-CR-SPPV-MVAGGRV-FVLP-C-IQQI-QRIS-LNTLT-LNVKSEK-VYTRH-GVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG  
*Tadh* MVF-F-EV-C-G-PNE-AMVVS-GF-CR-SPPV-MVAGGRV-FVLP-C-IQQI-QRIS-LNTLT-LNVKSEK-VYTRH-GVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG  
*Ocar* MVW-F-EV-C-G-PNE-AMVVS-GF-CR-SPPV-MVAGGRV-FVLP-C-IQQI-QRIS-LNTLT-LNVKSEK-VYTRH-GVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG  
*Sros* MAF-V-S-G-PNE-ALVVS-GC-CV-MKPL-LVPGGRV-FVWPV-FQK-LQRIS-LNTMT-LQVES-PCVYTS-QGVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG  
*Mbre* MSF-V-T-C-G-PNE-ALVVS-GC-CV-MKPL-LVPGGRV-FVWPV-FQK-LQRIS-LNTMT-LQVES-PCVYTS-QGVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG  
*Cowc* MVF-R-K-C-G-PNE-AMVVS-GF-CR-SPPV-MVAGGRV-FVLP-C-IQQI-QRIS-LNTLT-LNVKSEK-VYTRH-GVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG

**hydrophobic stretch**

*Hsap* HMTVEE-IYKDRQKFS-EQVFK-VASSDLVNMGI-SVVS-YTL-KDIDHDDQDYLHSLGKARTAQVQK-DARIGEA-EAKRDAGI-REAKAKQEKVSAQYLS-EIEMAKAQRDYELKKAAYDIEVNTNR  
*Mmus* HMTVEE-IYKDRQKFS-EQVFK-VASSDLVNMGI-SVVS-YTL-KDIDHDDQDYLHSLGKARTAQVQK-DARIGEA-EAKRDAGI-REAKAKQEKVSAQYLS-EIEMAKAQRDYELKKAAYDIEVNTNR  
*Spur* TMTVEE-IYKDRQKFS-KNVFE-VASSDLFNMGI-SVVS-YTL-KDIRDENGELKALGMARTAEVKK-DARIGEA-EAKRDAGI-REAREAMEEKMAATYLS-AEVAKAKRDFELKKAAYDIEVQTK  
*Dmel* SMTVEE-IYKDRQKFS-KNVFE-VASSDLFNMGI-SVVS-YTL-KDIRDENGELKALGMARTAEVKK-DARIGEA-EAKRDAGI-REAREAMEEKMAATYLS-AEVAKAKRDFELKKAAYDIEVQTK  
*Nvec* TMTVEE-IYKDRQKFS-KNVFE-VASSDLVNMGI-SVVS-YTL-KDIRDENGELKALGMARTAEVKK-DARIGEA-EAKRDAGI-REAREAMEEKMAATYLS-AEVAKAKRDFELKKAAYDIEVQTK  
*Tadh* TMTVEE-IYKDRQKFS-KNVFE-VASSDLVNMGI-SVVS-YTL-KDIRDENGELKALGMARTAEVKK-DARIGEA-EAKRDAGI-REAREAMEEKMAATYLS-AEVAKAKRDFELKKAAYDIEVQTK  
*Ocar* TMTVEE-IYKDRQKFS-KNVFE-VASSDLVNMGI-SVVS-YTL-KDIRDENGELKALGMARTAEVKK-DARIGEA-EAKRDAGI-REAREAMEEKMAATYLS-AEVAKAKRDFELKKAAYDIEVQTK  
*Sros* TMTVEE-IYKDRQKFS-KNVFE-VASSDLVNMGI-SVVS-YTL-KDIRDENGELKALGMARTAEVKK-DARIGEA-EAKRDAGI-REAREAMEEKMAATYLS-AEVAKAKRDFELKKAAYDIEVQTK  
*Mbre* TMTVEE-IYKDRQKFS-KNVFE-VASSDLVNMGI-SVVS-YTL-KDIRDENGELKALGMARTAEVKK-DARIGEA-EAKRDAGI-REAREAMEEKMAATYLS-AEVAKAKRDFELKKAAYDIEVQTK  
*Cowc* TMTVEE-IYKDRQKFS-KNVFE-VASSDLVNMGI-SVVS-YTL-KDIRDENGELKALGMARTAEVKK-DARIGEA-EAKRDAGI-REAREAMEEKMAATYLS-AEVAKAKRDFELKKAAYDIEVQTK

**hydrophobic stretch**

**Flotillin-domain**

*Hsap* RAQADLALYQLQVAKTKQIE-EQRVQVQVVERAQVAVQEQE-IARREKLEAARVKKPAEAERYKLERLA-EAEKSLIMQAEAEASVVRMRGEAEFAIGARARAEAEQMAKKAFAFQL  
*Mmus* RAQADLALYQLQVAKTKQIE-EQRVQVQVVERAQVAVQEQE-IARREKLEAARVKKPAEAERYKLERLA-EAEKSLIMQAEAEASVVRMRGEAEFAIGARARAEAEQMAKKAFAFQM  
*Spur* KATSELALEYLQAAKTKQAEKEEEMQKLVVERSSQAKKIQVQEQE-IARREKLEAATVKKPAEAERYRLETTIANANMKRVMLLEAEAEASIRVKGEEAEYAI-EQKAKAEAEQMAKKAFAWKM  
*Dmel* KAEAEEMAYELQAAKTKQRIKEEEMQKLVVERSSQAKKIQVQEQE-IARREKLEAATVKKPAEAERYRLETTIANANMKRVMLLEAEAEASIRVKGEEAEYAI-EQKAKAEAEQMAKKAFAWKM  
*Nvec* NATSQMAYNLQAAVTKQRIKEEEMQKLVVERSSQAKKIQVQEQE-IARREKLEAATVKKPAEAERYRLETTIANANMKRVMLLEAEAEASIRVKGEEAEYAI-EQKAKAEAEQMAKKAFAWKM  
*Tadh* KAEAEELSYELQAAKTKQRIKEEEMQKLVVERSSQAKKIQVQEQE-IARREKLEAATVKKPAEAERYRLETTIANANMKRVMLLEAEAEASIRVKGEEAEYAI-EQKAKAEAEQMAKKAFAWKM  
*Ocar* KAESELALEYLQAAKTKQAEKEEEMQKLVVERSSQAKKIQVQEQE-IARREKLEAATVKKPAEAERYRLETTIANANMKRVMLLEAEAEASIRVKGEEAEYAI-EQKAKAEAEQMAKKAFAWKM  
*Sros* QATNALADLQAAKTKQRIKEEEMQKLVVERSSQAKKIQVQEQE-IARREKLEAATVKKPAEAERYRLETTIANANMKRVMLLEAEAEASIRVKGEEAEYAI-EQKAKAEAEQMAKKAFAWKM  
*Mbre* KAVAAALADLQAAKTKQRIKEEEMQKLVVERSSQAKKIQVQEQE-IARREKLEAATVKKPAEAERYRLETTIANANMKRVMLLEAEAEASIRVKGEEAEYAI-EQKAKAEAEQMAKKAFAWKM  
*Cowc* RAQADLALYDLSAAKLTQGI-REGEIQVVERQKQIEVQEQE-IARREKLEAATVKKPAEAERYRLETTIANANMKRVMLLEAEAEASIRVKGEEAEYAI-EQKAKAEAEQMAKKAFAWKM

*Hsap* YQEAALDMLLEKLPQVAEEISGPLTSANKITLVSSGSGTGAAGKVTGEVLDLIRLPESVERLTGVSISQVNHKPLRRTA- - - - -  
*Mmus* YQEAALDMLLEKLPQVAEEISGPLTSANKITLVSSGSGTGAAGKVTGEVLDLIRLPESVERLTGVSISQVNHKPLRRTA- - - - -  
*Spur* YQDAAMVDMVLDVLPKJAAEAAPLSQAKKITMVS SGTGDVGAQKLTGEVMDIMDRIPLLLVENMTSVNISKAIKAT- - - - -  
*Dmel* YQDAAMVEMLDLTPKVAEEAAPLSQAKKITMVS SGTGDVGAQKLTGEVMDIMDRIPLLLVENMTSVNISKAIKAT- - - - -  
*Nvec* YQEAALDMLLEKLPQVAEEISGPLTSANKITLVSSGSGTGAAGKVTGEVLDLIRLPESVERLTGVSISQVNHKPLRRTA- - - - -  
*Tadh* YQDAAMVDMVLDVLPKJAAEAAPLSQAKKITMVS SGTGDVGAQKLTGEVMDIMDRIPLLLVENMTSVNISKAIKAT- - - - -  
*Ocar* YQDAAMVDMVLDVLPKJAAEAAPLSQAKKITMVS SGTGDVGAQKLTGEVMDIMDRIPLLLVENMTSVNISKAIKAT- - - - -  
*Sros* YQDAAMVDMVLDVLPKJAAEAAPLSQAKKITMVS SGTGDVGAQKLTGEVMDIMDRIPLLLVENMTSVNISKAIKAT- - - - -  
*Mbre* YQDAAMVDMVLDVLPKJAAEAAPLSQAKKITMVS SGTGDVGAQKLTGEVMDIMDRIPLLLVENMTSVNISKAIKAT- - - - -  
*Cowc* YQDAALVGMVLELTPKVAEEAHPPLTSVKKITMVS SGNVEGASKLTGVELLDLIRLPESVERLTGVSISQVNHKPLRRTA- - - - -

# Flotillin 2

**SPFH-domain**

*Hsap* MGNCHTVGPNALVVS-GG-CGSDYKQVYFGGAWAWWV-LSDTQRISLEIMTLQPRCEDVETAEGVALVTVTGVAQVKIMTE- - - - -KELLAVACEQFLGKNVQDIKNVVL  
*Mmus* MGNCHTVGPNALVVS-GG-CGSDYKQVYFGGAWAWWV-LSDTQRISLEIMTLQPRCEDVETAEGVALVTVTGVAQVKIMTE- - - - -KELLAVACEQFLGKNVQDIKNVVL  
*Spur* MGSCHTVGPNALVVS-GG-CGSAEKYVMGAWAWWV-LVTDVQRISLEIMTLQPRCEDVETAEGVALVTVTGVAQVKIMTE- - - - -EGLLAQACEQFLGKSVSEIETVVL  
*Dmel* MGNCHTVGPNALVVS-GG-CGSAEKYVMGAWAWWV-LVTDVQRISLEIMTLQPRCEDVETAEGVALVTVTGVAQVKIMTE- - - - -EGLLAQACEQFLGKSVSEIETVVL  
*Nvec* MGNCHTVGPNALVVS-GG-CGSAEKYVMGAWAWWV-LVTDVQRISLEIMTLQPRCEDVETAEGVALVTVTGVAQVKIMTE- - - - -EGLLAQACEQFLGKSVSEIETVVL  
*Tadh* MGNCHTVGPNALVVS-GG-CGSAEKYVMGAWAWWV-LVTDVQRISLEIMTLQPRCEDVETAEGVALVTVTGVAQVKIMTE- - - - -EGLLAQACEQFLGKSVSEIETVVL  
*Ocar* MGNCHTVGPNALVVS-GG-CGSAEKYVMGAWAWWV-LVTDVQRISLEIMTLQPRCEDVETAEGVALVTVTGVAQVKIMTE- - - - -EGLLAQACEQFLGKSVSEIETVVL  
*Sros* MGNVHVGPDPQVMVVS-GG-CGNATKNTLIGGCWAWWV-LVTDVQRISLEIMTLQPRCEDVETAEGVALVTVTGVAQVKIMTE- - - - -EGLLAQACEQFLGKSVSEIETVVL  
*Mbre* M-SFYTCGPNALVVS-GG-CG-SKPRLVPGGRV-FVWPV-FQK-LQRIS-LNTMT-LQVES-PCVYTS-QGVPI-SVTGIAQVQK-IQQNK-EMLAAC-QMFLGKTEAE-IAHIA-LETTLEGHQRAIMG  
*Cowc* MGNVHTVGPNEALVVS-GG-CG-SGARVYVIGGAWAWWV-LVSDIKRLLTLEVLTLLEPVCNDVETKQGVAVSVSAVAQVKFLTE- - - - -RALLEKAMEQFLGKSTREIQDVIIV

**hydrophobic stretch**

*Hsap* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Mmus* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Spur* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Dmel* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Nvec* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Tadh* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Ocar* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Sros* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Mbre* ETLEGHQRAIMGMTMVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL  
*Cowc* QTLEGLHRLSILGTLTVEEIQYQDRDQFAKLVREVAAPDVVGRMGIEILSFTIKDVIDYKVDYLSLGGKTQAVVQRDADIGVAEAEERDAGIREAECKKEMLDVKKFMDATKIADSKRAFEL

**Flotillin-domain**

*Hsap* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Mmus* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Spur* LKAGYFAEVNKKKQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Dmel* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Nvec* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Tadh* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Ocar* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Sros* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Mbre* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA  
*Cowc* QKSAFSEEVNIKTAAEQALAYELQGAAREQKQIRQEEIEIEVQVQRKQIAVEAQEILRTDKELIATVRRPAAEAEAHRIQQIAEGEKVQKVLQAQAEAEKIRKIGEAFAAVIEAMGKAEAA

*Hsap* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Mmus* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Spur* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Dmel* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Nvec* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Tadh* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Ocar* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Sros* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Mbre* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -  
*Cowc* ERMKLEKAEAYQKYGDAAKMALVLEALPQIAAKIAAPLTKVDEIVVLSGDN- - - - -SKVTSEVNRLLAELPASHVHALTGVDLSKIPLIKATGVQV- - - - -