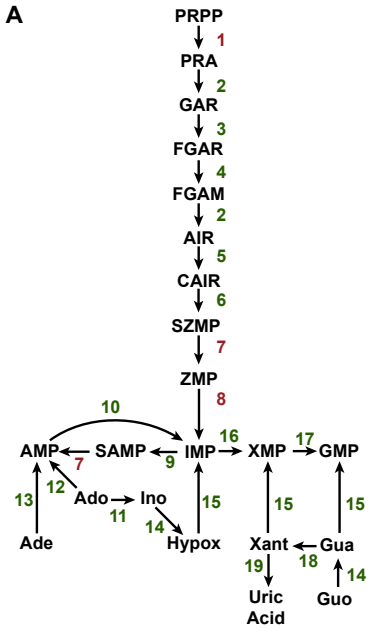
Supplementary Materials

Purine homeostasis is necessary for developmental timing, germline maintenance and muscle integrity in *C. elegans*

Roxane Marsac[1], Benoît Pinson[1], Christelle Saint-Marc[1], María Olmedo[2,3], Marta Artal-Sanz[2], Bertrand Daignan-Fornier[1] and José-Eduardo Gomes[1,4]

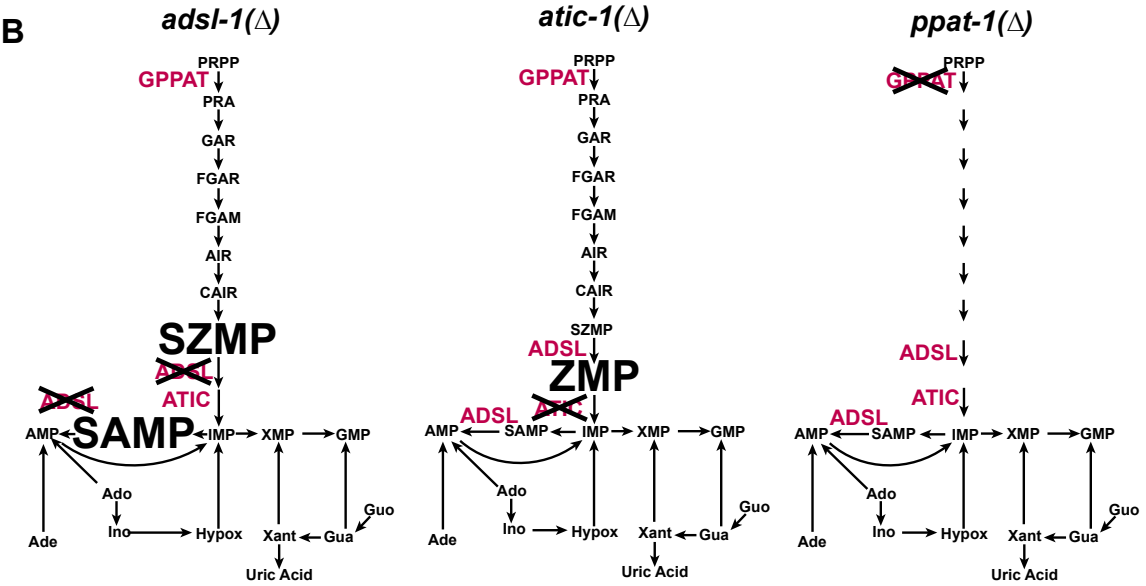
[1] - Institut de Biochimie et Génétique Cellulaires, Université de Bordeaux and CNRS UMR5095, 1 rue C. Saint Saëns, CS 61390, 33077 Bordeaux cedex, France
[2] - Andalusian Center for Developmental Biology, Consejo Superior de Investigaciones Científicas/Junta de Andalucía/Universidad Pablo de Olavide, Department of Molecular Biology and Biochemical Engineering. 41013, Seville, Spain
[3] - Current address: Department of Genetics, University of Seville, 41012, Seville, Spain
[4] - Correspondence: jose-eduardo.gomes@u-bordeaux.fr

A



	Enzyme	*C. elegans*	Human	% Similarity	% Identity	Yeast	% Similarity	% Identity
1	GPPAT	PPAT-1	PPAT	63	46	ADE4	51	32
2	GART/AIRS	F38B6.4 (N-ter)	GART	62	44	ADE5,7	58	39
3	GARS	F38B6.4 (C-ter)				ADE8	51	30
4	FGARAT	F10F2.2	PFAS	62	47	ADE6	52	34
5	AIRC	PACS-1 (C-ter)	PAICS	69	51	ADE2	47	32
6	SAICARS	PACS-1 (N-ter)				ADE1	40	20
7	ADSL	ADSL-1	ADSL	64	47	ADE13	61	43
8	ATIC	ATIC-1	ATIC	75	60	ADE16/17	72	57
9	ADSS	ADSS-1	ADSS	69	54	ADE12	70	51
10	AMPD	AMPD-1	AMPD	72	59	AMD1	67	49
11	ADOD	C06G3.5	ADA	58	40	-	-	-
12	ADOK	R07H5.8	ADK	69	51	ADO1	60	43
13	APRT	T19B4.3	APRT	65	46	APT1	61	43
14	PNP	K02D7.1	PNP	64	47	PNP1	56	40
15	HGPRT	HPRT-1	HPRT	62	49	HPT1	44	25
16	IMD	T22D1.3	IMPDH	73	57	IMD1	66	46
17	GMPS	GMPS-1	GMPS	65	51	GUA1	51	36
18	GDA	CPIN-1	GDA	38	22	GUD1	37	21
19	XO	GAD-3	XDH	50	35	-	-	-
19	XO	F15E6.6	XDH	55	38	-	-	-
19	XO	F55B11.1	XDH	61	47	-	-	-

B



C

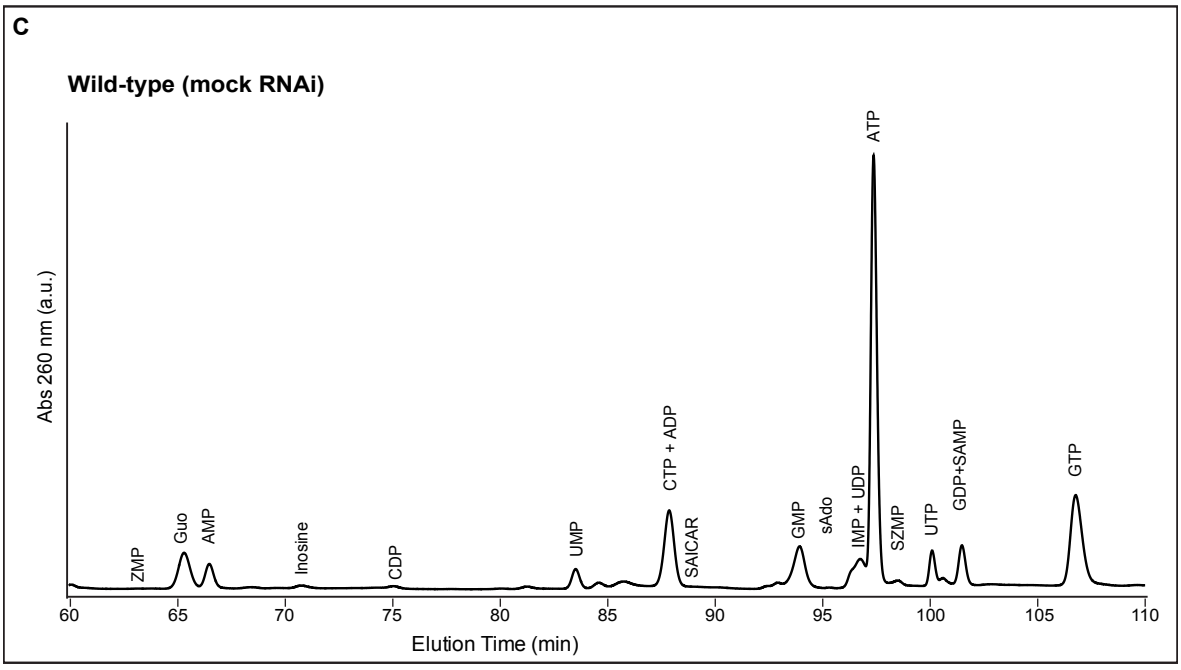


Figure S1

Purine biosynthesis pathway conservation in *C. elegans*. (A) Schematics of the Purine Biosynthesis pathways in *C. elegans* based on sequence homology, and table of comparison with both human and yeast (*S. cerevisiae*) orthologues. Enzymes subject to functional analysis are in red. (B) Schematics of predicted purine biosynthesis pathways in *adsl-1(Δ)*, *atic-1(Δ)* and *ppat-1(Δ)* mutants; large font represents intermediate metabolite accumulation. (C) Representative example of a chromatogram, absorbance at 260 nm, of wild-type worms, in mock (control) RNAi condition.

PPAT-1

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C. elegans   ------------------------------------------------------------MCGLFGIVAAGNYEHL---NVLAANGLAALQHRG  31
H. sapiens   ------------------------------------------------MELEEIGIREECGVFGCIAEGEWPTQLDVPHVITLGLVGLQHRG  44
R. norvegicus ------------------------------------------------MELEESGIREECGVFGCIAEGDWPTQLDVPHVITLGLVGLQHRG  44
D. melanogaster MMAQSDSGNCCAKLNKDECCQKTKDVILSGVSPKMFPDKIYKSVQPKGEDATGMTCECGVFAAIAGDYPTQLDIAQMICLGLVALQHRG  90
S. cerevisiae ------------------------------------------------------------MCGILGIVLANQTT---FVAPELCDGCIFLQHRG  31

C. elegans   TESTGLVGSDGITRDHVEIKGHGLVRDVITEDNISRMNGQSIILGHNRYSTAGKKKSGINCVQPFVVYTAMGTVATAHNGELVDAKQER 121
H. sapiens   QESAGIVTSDGSSVPTFKSHKGMGLVNHVFTEDNLKKIYVSNLGIGHTRYATTGKC--ELENCQPFVVFTLHGKIAVAHNGELVNAARLR 132
R. norvegicus QESAGIVTSDGSSVPTFKVHKGMGLVNHVFTEDNLKKIYVSNLGIGHTRYATTGKC--ELENCQPFVVFTLHGKIAVAHNGELVNAARLR 132
D. melanogaster QESAGIVTSIGKSSKTSVHKGMGMINNIFNDEAIRKI-KGNLGIGHTRYSTAAAS--EVVNCQPFVVFTAHGAIAIAHNGELVNCESLR 177
S. cerevisiae QDAAGIATCGS--RGRIYQCKGNGMARDVFTQQRVSGI-AGSMGIAHLRYPTAGSS--ANSEAQPFYVNSPYG-INLAHNGNLVNIASLK 115

C. elegans   KEVIHE-GVGLSTDIDSELIAQMIAKAIALNVKCKYGQEMGDITRELAVTMSALNMSYSLI-VMTFDRLYAIRDPFGNRPLCVGTVYSK- 208
H. sapiens   KKLIRH-GIGLSTSSDSEMTQLLAYTFPQ-E----QDDTPDWVARIKNLMKEAETAYSLI-IMHRDVIYAVRDPYGNRPLCIGRLIPYS 215
R. norvegicus KKLIRH-GIGLSTSSDSEMTQLLAYTFPQ-E----QDDTPDWVARIKNLMKEAEAAYSLV-IMHRDVIYAVRDPYGNRPLCIGRLMPYS 215
D. melanogaster REVIER-GVGLSTHSDSELIAQSLCCAPEDVS----EHDGENWFARIRHFMTIAEPSYSLV-YMHKDKIYAVRDSYGNRPLCIGKIVPVD 261
S. cerevisiae RYMDEDVHRHINTDSDSELLNIFAAELEKHN--KYRVNNEVFHALEGVYRLCRGGYAGYGLLAGFALFGFRDEMGTRPLLFGEREN-- 201

C. elegans   --------NGNEEAFIASSESCAEPA-NAKLDFEVRPGEIVELSTCGIKSVWQ---MKFNTPLAMCIFEYVYFARNDSELPGCQVCTVEE 286
H. sapiens   DINDKEKKTSETEGWVVSSESCSFLSIGARYREVLPGEIVEISRHNVCTLDI-ISRSEGNPVAFCIFEYVYFARPDSMFLQMVYTVEY 304
R. norvegicus DINDKEKKSSETEGWVVSSESCSFLSIGARYCHEVKPGEIVEISRHGVRTLDI-IPRSNGDPVAFCIFEYVYFARPDSMFLQMVYTVEY 304
D. melanogaster AGH-ANINDQLAEGWVVSSESCGFLSIGARYVREVEPGEIIELSRNGYRTVDI-VERFDYKRMAFCIFEYVYFARSDSMFEGQMVYSAEL 349
S. cerevisiae --------PDGKDYMLASESVWKAHNFTKYRDLKPGEAVIIPKNCSKGEPEFKQVVPINSYRPDLFEYVYFARPDSVLDGISWVHTEL 283

C. elegans   PCGKTMAL-----EDDLEADVGNVTDSSLSAALGYAGQSGLTVEPVLHRNSYVGRSPIEPNDEMRQNAIKMKFGVLKKKIHGGRIVLVD 371
H. sapiens   RCGCQLAI-----EAPVDADLVSTVPESATPAALAYAGKCGLPYVEVLCKNRYVGRTFIQPNMRLRQLGVAKKFGVLSDNFKGKRIVLVD 389
R. norvegicus RCGCQLAV-----EAPVEADLVSTVPESATPAALGYAEKCGLPYVEVLCKNRYVGRTFIQPNMRLRQLGVAKKFGVLSDNFKGKRIVLID 389
D. melanogaster QCGRQLAR-----ESPLDADLVSSVPESTTAAAFGYARESGLPFCEVLCKNRYVGRTFIQFSTRLRQLGVAKKFGALAQNYEGKRIVLVD 434
S. cerevisiae AMGSKLAENILKQLKEEIDVVIPVPDTARTGAIECANVLGKPYRGGFYKNRYVGRTFIMPNQREEVSSVRRKLNPMESEFGKKVLIVD 373

C. elegans   DSIVRGNTMRTLVKLRDAGAKEVHFRIASPPVRGPCFMGINIPTTKELIAAEKTIPEICQFVGASSVRYLSVDGLVSSVQKGIER---- 457
H. sapiens   DSIVRGNTISPIIKLLKESGAKEVHIRVASPPIKYPCFMGINIPTKEELIANKPEFDHLAEYIGANSVYYLSVEGLVSSVQEGIKFKKQK 479
R. norvegicus DSIVRGNTISPIIKLLKESGAKEVHIRVASPPIKPCFMGINIPTKEELIANKPEFEYLAEYIGANSVYYLSVEGLVSSVQEGIKFKKQK 479
D. melanogaster DSIVRGNTIGPIIKLLRDAGAFEVHIRIASPPICYPCVMGINIPTREELIANKLNADQLADHVGAGSLAYLSVEGLVKAVCMNKAH---- 520
S. cerevisiae DSIVRGTSKEIVNMAKESGATRVYFASAAFAIRYNHIYGIDLIDTKNLIAYNRIDEEVAEVGCERVAVCGEPDLIDCCKTDKIKFE- 462

C. elegans   ---------------AANFSPGHCTACLTGKYPVAIDL-------------------------------------------- 480
H. sapiens   EKKHDIMIQENGNGLECFEKSGHCTACLTGKYPV----ELEW-------------------------------------- 517
R. norvegicus VKKRDITIQENGNGLEYFEKTGHCTACLTGCYPV----DLEW-------------------------------------- 517
D. melanogaster ---------------VNPLKAGYCTACLTGEYPGGLPEELSW-------------------------------------- 547
S. cerevisiae ------------------------DGVFTGNVTGVEDGYIQELEEKRESIANNSSDMKAEVDIGLYNCADY 510
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ADSL-1

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C. elegans   ------MASEDKFESVLSGRYCKNSPLVSILSSTNKATLWRQLWTWLAEAEKELGLKQVTQDAIDEMKSNRDV--FDWPFIRSPERKLRH 82
H. sapiens   MAAGGDHGSPDSYRSPLASRYASP-EMCFVFSDRYKFRTWRQLWLWLAEAEQTLGLPTT-DEQIQEMKSNLEN--IDEKMAAEEEKRLRH 86
R. norvegicus MAASGDPACAESYRSPLAARYASH-EMCFVFSDRYKFRTWRQLWLWLAEAEQTLGLPTT-DEQIQEMRSNLSN--IDEQMAAEEEKRLRH 86
D. melanogaster -----MASNYEGVRSPLSTRYASK-EMCFVFSDCNKFSTWRRLWVWLAKAESRLGLPSS-DAQIAEMELQTSN--IDEEAAAEERLTRH 81
S. cerevisiae ------MPDYDNYTTPLSSRYASK-EMSATFSLRNRFSTWRKLWLNLAIAEKELGLTVVTDEIAKEQMRKHVEITDDEIAKASAQEAIVRH 83

C. elegans   DVMAHNHAFGKLCPAAGIIHLGATSCFVQDNADLIAYRDSIPHIKRPATVIDRLAFSLKNMEVVTVGRTHVQTASLVFVGKRGVLVA 172
H. sapiens   DVMAHVHTFGHCCPAAGIIHLGATSCYVGDNTDLIIRNALDLLLPKLARVISRLAGFAMERASLPTLGFTHFQPAQLTTVGKRCCLWI 176
R. norvegicus DVMAHVHTFGHCCPAAGIIHLGATSCYVGDNTDLIIRNAFDLLLPKLARVISRLADFAMERADLPTLGFTHFQPAQLTTVGKRCCLWI 176
D. melanogaster DVMAHVHYFAKCCPSAPVIHLGATSCYVGDNTDLIVRDAIKLLLPRVASVIARISQFAQSYKDQPTLGFTHIQPAQLTTVGKRACLWI 171
S. cerevisiae DVMAHVHTFGECCPAAGIIHLGATSCFVTDNADLIFIRDAVDIIIPKLVNVINRLAFAMSYKDLPVLGWTHFQPAQLTTLGKRATLWI 173

C. elegans   QELLMAFCCLSEFRKMRFRGIKGATGTCDSFLTLFAGDESKVEALDELVTKANSSNRFLITGQTYSEQCSQLVFSLSLLGAAAKKVC 262
H. sapiens   QDLCMDLQNLKRVRDDLRFRGVKGTTGTQASFLQLFEGDDHKVEQLDKMVTEKAGFKEAFIITGQTYTRKVDIEVLSVLASLGASYHKIC 266
R. norvegicus QDLCMDLQNLKRVRPELRFRGVKGTTGTQASFLQLFEGDHKVEQLDKMVTEKAGFKEAYIITGQTYTRKVDIEVLSVLASLGASYHKIC 266
D. melanogaster QDLHMDERALSRCLEDLRFRGVKGTTGTQASFLQLFNGDGEKVEQLDQMVTEIAGFKEAYAVTGQTYSRKVDVEIVAFLASLGTTHKVC 261
S. cerevisiae QELLWDLRNFERARNDIGLRGVKGTTGTQASFLALFHGNHDKVEALDEFVTELLGFDKVYPVTGQTYSRKIDIDVLAFLSSFAATAHKMA 263

C. elegans   TDIRVTQAFGELLEPFEKDQIGSSAMPYKKNPMKSERCCATSRNFINAPQEATILADCGLERTLDDSAGREMLIPDVLTTAEALTTLQ 352
H. sapiens   TDIRLLANLKEVEEPFEKCQIGSSAMPYKRNPMRSERCCSLARHLMTLVMPELQTASVQWFERTLDDSANRRICTAEAFLTATTINTLQ 356
R. norvegicus TDIRLLANLKEVEEPFEKCQIGSSAMPYKRNPMRSERCCSLARHLMSLTMPELQTASVQWFERTLDDSANRRICTAEAFLTATTITTLQ 356
D. melanogaster SDLRILASKKEVEEPFESTQIGSSAMPYKRNPMRSERCCALARHLITLFSSAANTHATQWIERTLDDSANRRLTTSEAFLAADAALTTLI 351
S. cerevisiae TDIRLLANLKEVEEPFEKSQIGSSAMAYKRNPMRGERVCSLARHLGSLFSDAWQTASVQWFERTLDDSAIRRISTPSAFLTADILISTLI 353

C. elegans   NIFEGTSVQTDNVKKIVEDEAFLGEKAMVMLTEEGWDRQQAAVIRKTALEAKQLQA---TQKVDFRQTMAPFPDSVRDRVVGLVNN 439
H. sapiens   NISEGLVVYPKVIERRIQQELPFMATENIIMAMVKAGGSRQCHEKIRVLSQQAASVVKQEGGDNDLIERIQVDAYFSPIHSQLDH-LLD 445
R. norvegicus NVSEGLVIYPKVIERRIQQELPFMATENIIMAMVKAGGSRQCHEKIRVLSQQAAAVVKQEGGDNDLIERIRADAYFSPIHSQLEQ-LLD 445
D. melanogaster NISCGLVVYPKVIERRIQQELPFMSTENIIMAMVKAGGERQCVCHEKIRVLSQEAGACVKQHGKDNDLVFRVRKDFYFSPILEQLDT-LLD 440
S. cerevisiae NISSGLVVYPKVIERRIKGELPFMATENIIMAMVEKNASRQEVHERIRVLSEQAAAVVKEEGGENDLIERVKRDFFFRPIWEELDS-LLE 442

C. elegans   EINTTGRCVSQTESGIAHSLKPTIDKVLDKSAGNVQL--DV 478
H. sapiens   PSSTTGRAQQQVQRLEEEVYPLIKPYESVMKVKAELGL-- 484
R. norvegicus PSSTTGRAQQQVHRLEEEVYPLIKPYGSVMAVKAELGL-- 484
D. melanogaster AKTTTGRASDQVGEPVKEEVEPVIARYSEALKNVQDVKLNI 481
S. cerevisiae PSTTVGRAQQQVEKSVQKDVNNALCPFQKYLNDE-QVRLNV 482
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ATIC-1

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C. elegans   MTDGKSLAIISVSDKTGLIPLAHGLVSAGLTTIASGGTAKAIRDGGLDVHDVADVTKFPEMLGGRVKTLHPAVHGGILARDTPSDRKGLE 90
H. sapiens   -MAFGQLAIFSVSDKTGLVEFARNLTALGLNLVASGGTAKAIRDAGLAVRDVSETTGFPEMLGGRVKTLHPAVHAGILARNIPEDVADVA 89
R. norvegicus -MASSQLAIFSVSDKTGLVEFARNLASLGLSLVASGGTAKAIRDAGLAVRDVSETTGFPEMLGGRVKTLHPAVHAGILARNIPEDVADVA 89
D. melanogaster -MSSSKIALISVSDKTGLLLTGKSLVALGFDLVASGGTATSLRQAGLKVRDVSETTGFPEMLGGRVKTLHPAVHAGILSRTTPSDADKR 89
S. cerevisiae MANYTKTALISVYDKTGLLLLARGLIEKNVRILASGGTARMIRDAGFPIEDVSALTHAPEMLGGRVKTLHPAVHGGILARDIPSDEKELK 90

C. elegans   KHNISFVSVVVCNLYPFFKTVQSEDCSVEEAVENIDIGGVTLLRAAAKNHERVSVLGPADYDHITSEIKSG---GTRFRPRQLLALKAF 177
H. sapiens   RLEENLIRVVACNLYPFFKTVASFGVTVEEAVEQIDIGGVTLLRAAAKNHARVTVVCEPEDYVVVSTEMQSSESKDTSLETRRQLALKAF 179
R. norvegicus RLEENLIRVVVCNLYPFFKTVASPDVTVEEAVEQIDIGGVTLLRAAAKNHARVTVVCEPEDYGAVAAEMQGSGNKDTSLETRRHLALKAF 179
D. melanogaster KQGFLLIQLVVCNLYPFASTVAKPDVTIADAVENIDIGGVTLLRAAAKNHQRVTVVCEAVDYDRVISEIKAS--GNQTVETRQALALKAF 177
S. cerevisiae EQHIEKMDYVVCNLYPFKETVAKVGVTIPEAVEEIDIGGVTLLRAAAKNHARVTILSDPKDYSEFISEISSN--GETTQDLRNRLALKAF 178

C. elegans   EHTTSYDESISGFMERRFAGNGERALFLRYGANPHQKDDAELYIVEDEMPPKVLNGSPGYINILDGLNGWQLVKELSDATKMPAAASFKH 267
H. sapiens   THTAQYDEAISDYFRKQY-SKGVSQVPLRYGMNPHQTPAQLYT-LQPKLPITVLNGAPRYGMNPHQTPAQLYT-LKPKLPITVLNGAPGFINLCDALNAWQLVKELKEALGTPAAASFKH 267
R. norvegicus THTAQYDEAISDYFRKQY-SKGISQVPLRYGMNPHQTPAQLYT-LKPKLPITVLNGAPGFINLCDALNAWQLVTELRGAVDIPAAASFKH 267
D. melanogaster THTATYDDAISDYFRKQY-GSGVSQVPLRYGMNPHQKPAQLYT-QLAKLPLTVLNGSPGFINLCDALNGWQLVRELKKALQLPAAGSFKH 265
S. cerevisiae EHTADYDAAISDFFRKQY-SEGQAQITLRYGANPHQKPAQAYVSQQDSLPFKVLGGSPGVINIIDALNSWPLVKELSASLNLPAAASFKH 267

C. elegans   VSPAGAAVGIPLNEEAAGCMVSDLPIDTKKPSLAAAYARARGADRMSSFGDFIALSEKCDEITAKIIRREVSDGVVAPDEEGAALSIIA 357
H. sapiens   VSPAGAAVGIPLSEEAAVCMVYDLYK--TLTPISAAYARARGADRMSSFGDFVALSDVCDVPTAKIISREVSDGIIAPGYEEEALTILS 355
R. norvegicus VSPAGAAVGVPLSEEAAVCMVYDLYP--TLTPLAIAYARARGADRMSSFGDFVALSDVCDVPTAKIISREVSDGIVAPGYEEAIKILS 355
D. melanogaster VSPAGAAVGVPINPAQAKLCMVDDLYE--QLTPLATAYARARGADRMSSFGDFVALSDVCDVYTANIISREVSDGIIAAGYEPEAIEIIK 353
S. cerevisiae VSPAGAAVGIPLSDVEKQVYHVAII-E--NLSPLACAYARARGADRMSSFGEWIALSNIVDVPTAKIISREVSDGVIAPGYEPEAIAILS 354

C. elegans   KKKNGNYCVLKINPNYLSEHEERTVEGIRLSQKRNNAVINAETGANVVGSANEINKQAIDLIVATIATKYAQSNSVCFAHRGQVIGGG 447
H. sapiens   KKKNGNYCVLQMDQSYKPDENEVRTFGLHLSQKRNNGVVDKSLFSNVVTKNKDLPESALRDLIVATIAVKYTQSNSVCYAKNGQVIGIG 445
R. norvegicus KKKNGSYCVLQMDQSYKPDENEVRTTFGLRLSQKRNNGVVDKSLFSNIVTKNKDLPESALRDLIVATIAVKYTQSNSVCYAKDGQVIGIG 445
D. melanogaster KKKNGGYCVLQMDPNYEESAVERKTFGLTLSQKRNDAVIDASLFSNVVSRRGPLPEVAVRDLIVATIAIKYTQSNSVCYARDGQVVGIG 443
S. cerevisiae KKKGGKYCVLQIDPNYVEEAVERRQVYGVTLSQKRNDALINQSTHSKEIVSQNRNTTEGAIIDITVATIAIKYTQSNSVCYARNGMVVGIG 444

C. elegans   AGQQSRIHCTRLAGDKANNWWLRQHPTVLSLPWKNATKRSEKSNAIDVLCSGVLGSEI-AIDQWQQYSNEPVEPPAGDDRKCWLSQQTGV 536
H. sapiens   AGQQSRIHCTRLAGDKANYWWLRHPQVLSMKFKGGVKRAEISNAIDQYVTGTIGEEG-DIIKWKALFEEVPELLTEAEKKEWVEKLTEV 534
R. norvegicus AGQQSRIHCTRLAGDKANSWWLRHPRVLSMKFKAGVKRAEVSNAIDQYVTGTIGEGG-DIVKWKALFEEVPELLTEAEKKEWVDKLSGV 534
D. melanogaster AGQQSRIHCTRLAGEKANNWWLRQHPVAGMKFKAGVKRAEISNAIDNYVNGTVGKDM-PISQFEGMPDKAPAQLTSEGKWEWLKQISGV 532
S. cerevisiae AGQQSRIHCTRLAGDKANNWFRQHPRVEIRWAHGVKRFEKSNAIDLFVTGQPTTEPPESEVQSKFEEIEKFTPEEKEWLSKLTEV 534

C. elegans   VMSSDAFLPFRDNVDCAKQFGVSVVAHPGSVRPDDIKEACDEHGTTLHTCLRLFHH 594
H. sapiens   SISSDAFFPFRDNVDRAKRSGVAVIAAPSGSAADKVVIEACDEHGIILAHTCLRLFHH 592
R. norvegicus SVSSDAFFPFRDNVDRAKRSGVAVIVAPSGSTADKVVIEACDEHGIVLAHTCLRLFHH 592
D. melanogaster ALGSDAFFPFRDNIDRASLSGVSVIASPAGSTNPAGVIAACDEHGIVMAHTCLRLFHH 590
S. cerevisiae SISSDAFFPFPDNVGRAVKSGVKVIAAPSGSVMDKVVFSAAESFDLVYVENPIRLFHH 592
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Figure S2

Sequence alignment of *C. elegans* PPAT-1, ADSL-1 and ATIC-1 with closest orthologue in humans, rat (*Rattus norvegicus*), fly (*Drosophila melanogaster*) and yeast (*S. cerevisiae*). Grey boxes indicate similar residues, black boxes indicate identical residues.

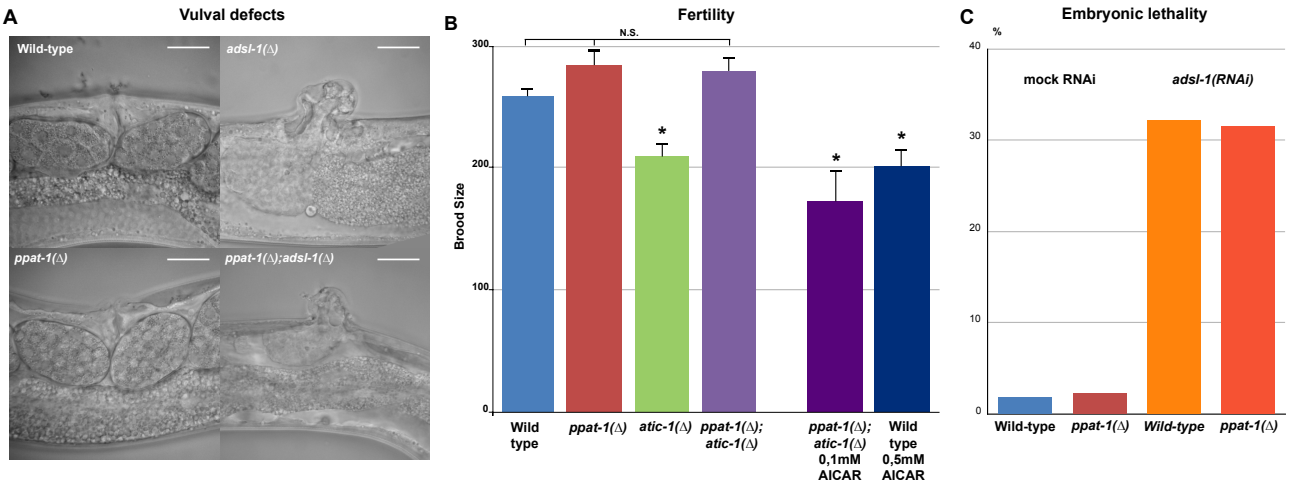

Figure S3

Developmental defects in purine mutants. (A) Representative DIC micrographs of the vulva region in young adults of wild-type, *ppat-1(Δ)*, *adsl-1(Δ)* and *ppat-1(Δ); adsl-1(Δ)* genotypes (bar= 20μm). (B) Graph depicting the average number of eggs laid by the *de novo* pathway mutants, and AICAR treated *ppat-1(Δ); atic-1(Δ)* (0.1 mM) and wild-type (0.5 mM) worms (error bar - standard error of the mean; n= 30 in all samples; * - statistically significant difference relative to wild-type - Student's t-test). (C) Graph displaying the percentage of embryonic lethality (unhatched eggs) upon *adsl-1(RNAi)* and mock (control) RNAi in both wild-type and *ppat-1(Δ)*.

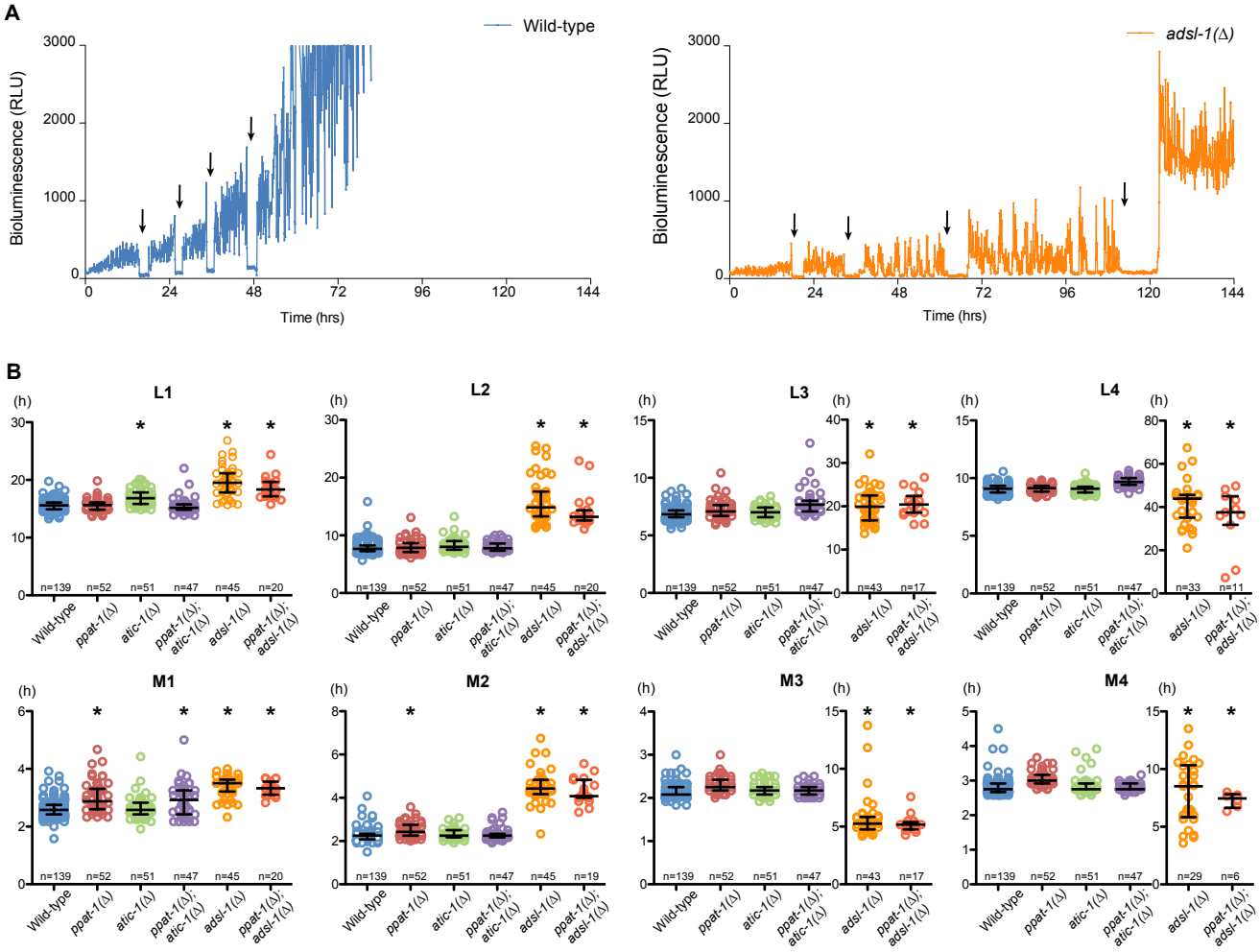

Figure S4

Post-embryonic development in purine mutants. (A) Representative bioluminescence profiles of a single wild-type (left, blue line) and *adsl-1(Δ)* mutant (right, orange line) individuals over time. Arrows indicate drop in luminescence observed during lethargus phase. (B) Detailed representation of the primary data presented in figure 3A, each circle corresponds to an individual observation, bars indicate median, 2nd and 3rd quartiles. L1 through L4 refer to the four larval stages and M1 though M4 refer to the lethargus phases following each larval stage. For better visualization *adsl-1(Δ)* and *ppat-1(Δ); adsl-1(Δ)* in L3, L4, M3 and M4 are represented on a different time scale. (* - statistically significant difference compared to wild-type; one-way ANOVA).

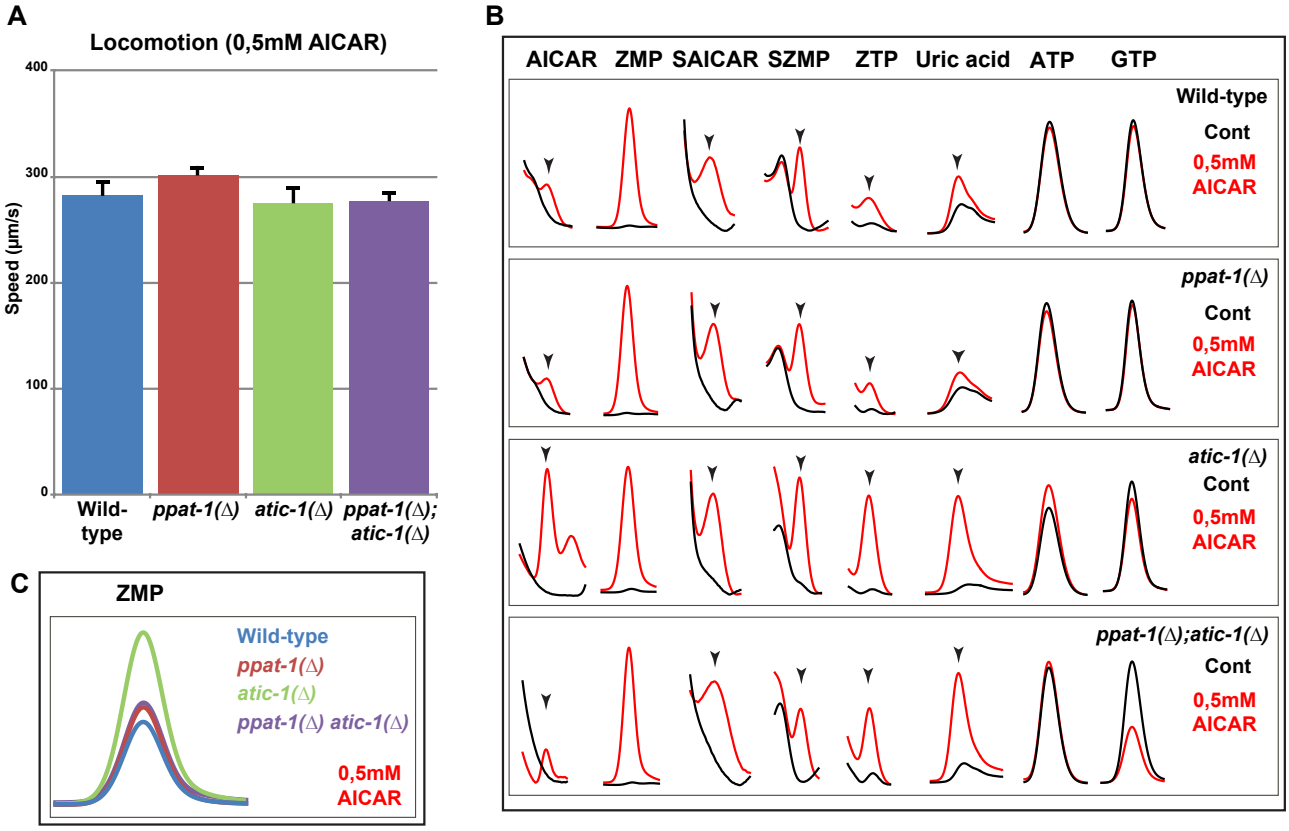

Figure S5

AICAR treatment and locomotion. (A) Graph depicting the average locomotion speed in *de novo* pathway mutants treated with AICAR (error bar - standard error of the mean; n= 30 in *ppat-1(Δ)* and *atic-1(Δ),* n= 40 in wild-type and *ppat-1(Δ); atic-1(Δ)*; * - statistically significant difference relative to wild-type - Student's t-test). (B) Zoom in on HPLC chromatogram peaks of specific metabolites AICAR, ZMP, SAICAR, SZMP, ZTP, uric acid, ATP and GTP, upon 0.5 mM AICAR treatment. (C) Zoom in on HPLC chromatogram peaks of ZMP upon 0.5 mM AICAR treatment, with the four genotypes analyzed represented on the sale scale.

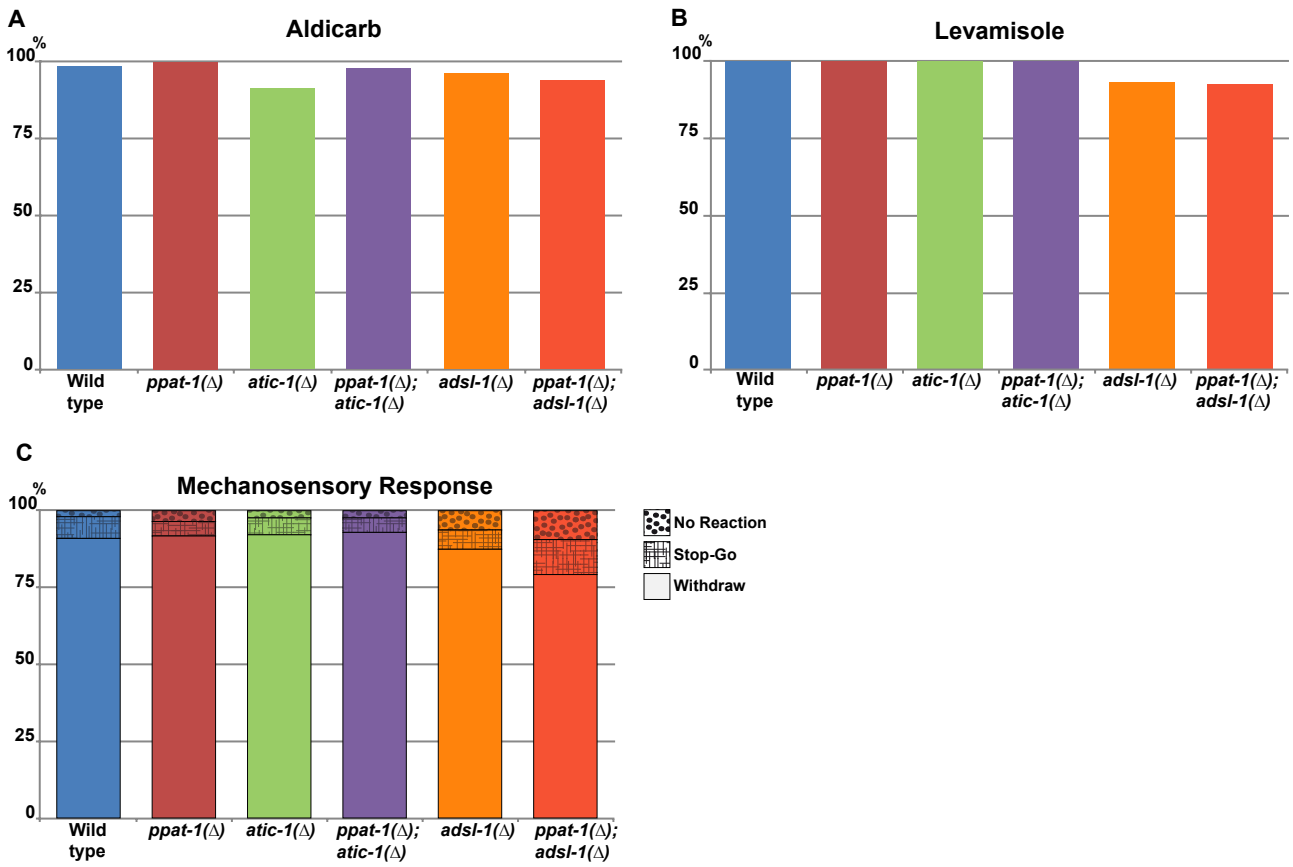

Figure S6

Neuromuscular function in purine mutants. (A) Percentage of paralysed worms upon Aldicarb treatment, in all studied genotypes (wild-type n= 136, *ppat-1(Δ)* n= 169, *atic-1(Δ)* n= 178, *ppat-1(Δ); atic-1(Δ)* n= 140, *adsl-1(Δ)* n= 54, *ppat-1(Δ); adsl-1(Δ)* n= 65). (B) Percentage of paralysed worms upon Levamisole treatment, in all studied genotypes (wild-type n= 50, *ppat-1(Δ)* n= 49, *atic-1(Δ)* n= 51, *ppat-1(Δ); atic-1(Δ)* n= 50, *adsl-1(Δ)* n= 104, *ppat-1(Δ); adsl-1(Δ)* n= 54). (C) Graph presenting the percentage of observed responses to mechanosensorial stimulation in all studied genotypes (wild-type n= 30, *ppat-1(Δ)* n= 30, *atic-1(Δ)* n= 30, *ppat-1(Δ); atic-1(Δ)* n= 30, *adsl-1(Δ)* n= 30, *ppat-1(Δ); adsl-1(Δ)* n= 30).