

Supplementary Material Tables 1 – 7 Gene acronyms, full names and functions in signal pathways (to accompany Figures 4, 5, 7, 9 and S8 Fig.).

Table 1 Insulin/IGF signaling (IIS) pathway components and pathway regulators in *D. melanogaster*

Acronym	Gene name	CG number	Function/description of gene product	Reference
<i>dilp2</i>	<i>Drosophila insulin-like peptide 2</i>	CG8167	<i>dilp2</i> is expressed in a set of median neurosecretory cells (mNSC), known as insulin-producing cells (IPCs); regulates growth, metabolism, stress and aging	[1-3]
<i>dilp1</i>	<i>Drosophila insulin-like peptide 1</i>	CG14173	<i>dilp1</i> transcripts are detected in larval-pupal IPCs; expression and function in adult are unknown	[4,5]
<i>dilp4</i>	<i>Drosophila insulin-like peptide 1</i>	CG6736	<i>dilp4</i> expression is not detected in adult flies; functions are unknown	[1,5]
<i>dilp3</i>	<i>Drosophila insulin-like peptide 3</i>	CG14167	<i>dilp3</i> is co-expressed with <i>dilp2</i> and <i>dilp5</i> in IPCs and in the muscle cells of the adult midgut	[1,4,6]
<i>dilp5</i>	<i>Drosophila insulin-like peptide 5</i>	CG33273	<i>dilp5</i> is expressed in IPCs and in follicle cells of the ovary as well as principal cells of the renal tubules	[1,4,7]
<i>dilp6</i>	<i>Drosophila insulin-like peptide 6</i>	CG14049	<i>dilp6</i> is expressed in adipose cells of the fat body	[8,9]
<i>dilp7</i>	<i>Drosophila insulin-like peptide 7</i>	CG13317	<i>dilp7</i> is expressed in about 20 neurons of the abdominal neuromeres; may function as <i>Drosophila</i> relaxin	[1,10,11]
<i>dilp8</i>	<i>Drosophila insulin-like peptide 8</i>	CG14059	<i>dilp8</i> is expressed in the imaginal discs of larvae; in adult <i>dilp8</i> expression is abundant in ovaries	[12,13]
<i>InR</i>	<i>Insulin-like receptor</i>	CG18402	Tyrosine-protein kinase with insulin-activated receptor activity; receptor of IIS signaling pathway	[14,15]
<i>Chico</i> (<i>IRS</i>)	<i>Chico</i> (<i>Insulin receptor substrate</i>)	CG5686	Insulin receptor substrate	[16]
<i>Lnk</i>	<i>Lnk</i>	CG17367	Insulin receptor adaptor protein	[17,18]
<i>Dp110</i> (<i>PI3K92E</i>)	<i>Dp110</i> (<i>PI3K92E</i>)	CG4141	Catalytic subunit of phosphatidylinositol 3-kinase (PI3K), a main upstream kinase in IIS	[19,20]
<i>Dp60</i> (<i>PI3K21B</i>)	<i>Dp60</i> (<i>PI3K21B</i>)	CG2699	Adaptive subunit of phosphatidylinositol 3-kinase (PI3K)	[21]
<i>step</i>	<i>steppke</i>	CG11628	PI3K upstream factor Steppke	[22]

<i>Akt1</i> (PKB)	<i>Akt1</i> (Protein kinase B)	CG4006	AKT, also known as protein kinase B, is a main downstream kinase in IIS, phosphorylates the transcription factor FOXO	[15]
<i>Pdk1</i>	<i>Phospho-inositide-dependent kinase 1</i>	CG1210	PDK-1 is a central mediator of the signaling between PI3K and various intracellular serine/ threonine kinases including Akt (PKB)	[23]
<i>melt</i>	<i>melted</i>	CG8624	Melted modulates IIS pathway in <i>Drosophila</i> interacting with both Tsc1 and FOXO and can recruit these proteins to the cell membrane	[24]
<i>foxo</i>	<i>forkhead box, sub-group O</i>	CG3143	FOXO is a key component of the insulin signaling cascade, which is phosphorylated by dAkt, leading to cytoplasmic retention and inhibition of its transcriptional activity	[25]
<i>sgg / GSK3</i>	<i>shaggy/ Glycogen Synthase Kinase 3</i>	CG2621	Shaggy is a <i>Drosophila</i> orthologue of glycogen synthase kinase-3; which regulates glycogen synthesis by inhibiting glycogen synthase	[26]
<i>GlyS (GS)</i>	<i>Glycogen synthase</i>	CG6904	Glycogen synthase is the main enzyme involved in converting glucose to glycogen	[27]
<i>Pepck</i>	<i>Phosphoenol-pyruvate carboxykinase</i>	CG17725	PEPCK is a key enzyme of both gluconeogenesis and glycerogenesis	[28,29]
<i>bmm</i> (<i>Atgl</i>)	<i>Brummer</i> (<i>adipocyte triglyceride lipase</i>)	CG5295	Triacylglyceride lipase Brummer, a homolog of human adipocyte triglyceride lipase (ATGL)	[30]
<i>Pdk</i>	<i>Pyruvate dehydrogenase kinase</i>	CG8808	PDK is responsible for an inactivation of pyruvate dehydrogenase complex and decrease of Krebs cycle turnover with a re-direction of pyruvate into anaerobic oxidation	[31]
<i>Cat</i>	<i>Catalase</i>	CG6871	Catalase is one of the key antioxidants enzymes; <i>Cat</i> expression is under FOXO control	[32,33]
<i>Sod2</i>	<i>Superoxide dismutase 2</i>	CG8905	SOD2 is a manganese/iron superoxide dismutase, participating in antioxidant defence; <i>Sod2</i> expression is under FOXO control	[32,33]
<i>Thor</i> (<i>4E-BP</i>)	<i>Thor</i> (<i>eukaryotic initiation factor 4 binding protein</i>)	CG8846	<i>Thor</i> encodes eukaryotic initiation factor 4 binding protein (4E-BP), an inhibitor of translation and is a FOXO transcriptional target, However, 4E-BP is also known to be under a control of the TOR-signaling pathway	[34,35]

<i>Sik3</i>	Salt-inducible kinase 3	CG42856 (CG15072, CG18604)	SIK3 is a member of the AMPK family of Ser/Thr kinases, which play a critical role in energy balance. Being activated by AKT, SIK3 promotes lipid storage by blocking FOXO activity	[29]
<i>HDAC4</i>	<i>HDAC4</i>	CG1770	Gene encodes histone deacetylase class II, which regulates transcriptional activity of certain transcriptional factors, including FOXO	[29,36]
<i>HNF4</i>	<i>Hepatocyte nuclear factor 4</i>	CG9310	HNF4 is a nuclear receptor, which in association with the transcription factor FOXO activates expression of gluconeogenic genes	[37-39]

Table 2 TOR signaling pathway components in *D. melanogaster*

Acronym	Gene name	CG number	Function/Description of the gene product	Reference
<i>slif</i>	<i>slimfast</i>	CG11128	cationic amino acid transporter (CAT)	[40]
<i>path</i>	<i>pathetic</i>	CG3424	proton-assisted amino acid transporter (PAT)	[41]
<i>mind</i>	<i>minidisks</i>	CG3297	heterodimeric amino acid transporter (HAT)	[42]
<i>raptor</i>	<i>raptor</i>	CG4320	A rapamycin-sensitive TOR companion within TORC1 complex	(see [43])
<i>Tor</i>	<i>Target of rapamycin</i>	CG5092	TOR kinase, a main component of TORC1 and TORC2 complexes	(see [43])
<i>rictor</i>	<i>rapamycin-insensitive companion of Tor</i>	CG8002	A rapamycin-insensitive companion of TOR in TORC2 complex	(see [43])
<i>S6k</i>	<i>RPS6-p70-protein kinase</i>	CG10539	Ribosomal protein S6 kinase; a downstream target of TOR	(see [43])
<i>Thor</i>	<i>Thor/4E-BP</i>	CG8846	Eukaryotic translation initiation factor 4E binding; a downstream target of TOR	(see [43])
<i>RagA-B</i>	<i>Ras-related GTP binding A/B</i>	CG11968	Rag GTPases are activators of TORC1 in response to amino acid signals	[44,45]
<i>RagC-D</i>	<i>Ras-related GTP binding C/D</i>	CG8707	Rag GTPases are activators of TORC1 in response to amino acid signals	[44,45]
<i>Tsc1</i>	<i>Tsc1/tuberous sclerosis complex 1</i>	CG6147	A part of tuberous sclerosis complex (TSC), consisting of two subunits in <i>Drosophila</i> TSC1 and gigas (TSC2)	[46]
<i>gig</i>	<i>gigas (Tsc2)</i>	CG6975	A part of tuberous sclerosis complex (TSC) with an ability of TSC2 to act as a GTPase-activating protein to inactivate GTPase Rheb (Ras homologue enriched in brain), an ultimate activator of TOR kinase	[46]
<i>Rheb</i>	<i>Ras homologue enriched in brain</i>	CG1081	Small GTPase Rheb is a direct target of Tsc2 GAP activity	[47]

<i>AMPKα</i> (<i>snf1a</i>)	<i>AMP-activated protein kinase α subunit (snf1a)</i>	CG3051	AMPK is a low ATP:ADP ratio sensor, which can directly phosphorylate TSC2, enhancing its GAP activity and, as result, leading to TORC1 inhibition	[48-50]
<i>Sesn</i>	<i>Sestrin</i>	CG11299	Sestrin transcription in <i>Drosophila</i> is under FOXO control and leads to AMPK activation and in turn an enhancement of Tsc1/Tsc2 inhibition of TORC1	[51]
<i>eIF-4E</i>	<i>Eukaryotic initiation factor 4E</i>	CG4035	Translation initiation factor that interacts with <i>Drosophila</i> eIF4E-binding protein (4E-BP)	[52]
<i>Tif-IA</i>	<i>Tif-IA</i>	CG3278 (CG5951)	TIF-IA protein is a Pol I transcription initiation factor	Reviewed [53]
<i>Atg1</i>	<i>Autophagy-related 1</i>	CG10967	Atg 1 is a main autophagy gene, whose kinase activity is known to be inhibited by TOR	Reviewed in [54]
<i>sima</i> (<i>HIF-1α</i>)	<i>similar</i> (<i>Hypoxia inducible factor 1α</i>)	CG45051 (CG7951)	One of the main hypoxia-inducible transcription factors, which represent <i>Drosophila</i> HIF1-a	[55]
<i>tgo</i> (<i>Arnt</i> , <i>HIF-1b</i>)	<i>tango</i> (<i>Arnt</i> , <i>Hypoxia inducible factor 1b</i>)	CG11987	One of the main hypoxia-inducible transcription factors, which represent <i>Drosophila</i> HIF1-b	[55]
<i>scyl</i>	<i>scylla</i>	CG7590	One of the hypoxia induced genes, homologue of mammalian REDD1	[56]
<i>chrb</i>	<i>charybde</i>	CG7533	One of the hypoxia induced genes, homologue of mammalian REDD2	[56]
<i>Dm</i> (<i>Myc</i>)	<i>diminutive</i> (<i>Myc</i>)	CG10798	Diminutive is a <i>Drosophila</i> Myc homologue; a transcriptional factor, whose expression and activity is under FOXO and TORC1 control, respectively, and involved in the transcriptional regulation of ribosome synthesis genes such as Pol I transcription factor <i>Tif-IA</i>	[57]
<i>saw</i> / <i>CG3071</i>	<i>saw/CG3071</i>	CG3071	An ortholog of human SAW; is under TOR-dependent transcriptional control and encodes a protein with conserved functional roles in growth (positive growth regulator)	[58]
<i>ash2</i>	absent, small, or homeotic discs 2	CG6677	An ortholog of human ASHL; is under TOR-dependent transcriptional control and encodes a protein, that is a negative growth regulator	[58]
<i>pit</i>	<i>pitchoune</i>	CG6375	Pitchoune is a helicase, required for cell growth and proliferation; a potential target of d-Myc	[59]
<i>ppan</i>	<i>peter pan</i>	CG5786	Required for mitotic proliferation, growth and some aspects of differentiation	[60]

<i>Nop60B</i> (<i>mnf</i>)	<i>Nucleolar protein at 60B</i> (<i>minifly</i>)	CG3333	Gene with pleiotropic effects on viability and fertility	[61]
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Table 3 Proposed AKH signalling pathway components in *D. melanogaster*, partly based on experimental findings from other insects

Acronym	Gene name	CG number	Function/Description of the gene product	Reference
<i>Akh</i>	<i>Adipokinetic hormone</i>	CG1171	AKH is produced by corpora cardiaca glandular cells; functional homolog of glucagon and regulates glucose homeostasis	[62,63]
<i>AkhR</i> (<i>GRHR</i>)	<i>Adipokinetic hormone receptor</i> (<i>Gonadotropin releasing hormone receptor</i>)	CG11325	AKHR belongs to the G protein-coupled proteins, structurally related to receptors of the vertebrate gonadotropin releasing hormone	[64]
<i>Plc21C</i>	<i>Phospholipase C at 21C</i>	CG4574	Activation of PLC21C is triggered by binding of AKH to AKHR, initiating a phospholipase-C/proteinkinase-C signalling cascade, when enhanced phospholipase C cleaves phosphatidylinositol (3,4,5)-trisphosphate (PIP ₃) into diacylglycerol (DAG) and inositol (1,4,5) phosphate (IP ₃), which, in turn, transduces a signal to protein kinase C	[65-67]
<i>Pkcδ</i>	<i>Protein kinase C delta</i>	CG42349 (CG10524)	Protein kinase C is activated by DAG as result of phospholipase C activation	[65,66]
Cam	<i>Calmodulin</i>	CG8472	Calmodulin is a calcium binding signal molecule that assists phospholipase-C/proteinkinase-C signalling cascade	[65]
<i>PhKγ</i>	<i>Phosphorylase kinase gamma</i>	CG1830	<i>Drosophila</i> phosphorylase kinase gamma is a putative homologue of the vertebrate phosphorylase kinase catalytic gamma-subunit, which is a target of phospholipase-C/proteinkinase-C signalling cascade and a direct activator of glycogen phosphorylase	reviewed in [66,68]
<i>GlyP</i> (<i>GP</i>)	<i>Glycogen phosphorylase</i>	CG7254	Glycogen breakdown enzyme	[69]
Ac13E	Adenylyl cyclase 35C	CG9210	Activation of adenylyl cyclase leads to elevation of cAMP, which activates protein kinase A (PKA)	Reviewed in [66,67]
<i>Pka/Pka-C1</i>	<i>Protein kinase A/cAMP-dependent protein kinase 1</i>	CG4379	PKA with assistance of calcium ions stimulates Plin1 and, in turn, hormone-sensitive lipase (HSL). In <i>Manduca sexta</i> binding of AKH by its receptor transduces a signal via cAMP to PKA, which phosphorylates Plin1, but the AKH/AKHR-mediated PKA activation is only	[70,71]

			partly confirmed for <i>Drosophila</i>	
<i>Lsd-1</i> (<i>plin1</i>)	Lipid storage droplet-1 (<i>Perilipin 1</i>)	CG10374	Perilipin 1 is a <i>Drosophila</i> lipid droplet surface protein that has opposite roles under normal and starvation conditions, preventing lipases from accessing lipid droplets under basal lipolysis, but promoting lipase access to lipids under starvation. Thus, under energy deficit Perilipin1 is phosphorylated by PKA in response to hormonal signals. Phosphorylated Perilipin1 facilitates maximal lipolysis by recruiting hormone-sensitive lipase (HSL). Plin1 is found to be downstream effector for AKH signalling. The mechanism is conserved for mammals and <i>Drosophila</i>	[70,72-74]
<i>Hsl</i>	Hormone-sensitive lipase	CG11055	Hormone-sensitive lipase is the sole homolog of mammalian HSL in <i>Drosophila</i>	[72,75]
<i>tobi</i>	target of brain insulin	CG11909	<i>tobi</i> expression was postulated to be under AKH signaling control through an unknown X transcription factor; <i>tobi</i> encodes alpha-1,4-glucosidase	[76]

Table 4 JAK-STAT signaling pathway components in *D. melanogaster*

Acronym	Gene name	CG number	Function/Description of the gene product	Reference
<i>dome</i>	<i>domeless</i>	CG14226	Encodes cytokine-like receptor Dome, which expression is under Stat92E control	[77-80]
<i>hop</i>	<i>hopscotch</i>	CG1594	Encodes <i>Drosophila</i> Janus kinase (JAK)	[77-79]
<i>Stat92E</i>	Signal-transducer and activator of transcription protein at 92E	CG4257	Transcriptional factor Stat92E	[77-79]
<i>RanBPM</i>	Ran-binding protein M	CG42236 (CG11763)	The <i>Drosophila</i> homologue of <i>RanBP10</i> known to control signal-dependent nuclear translocation of Stat92E	[81]
<i>RanBP3</i>	Ran binding protein 3	CG10225	Control of the signal-dependent nuclear translocation of Stat92E	[81]
<i>Socs36E</i>	Suppressor of cytokine signaling at 36E	CG15154	The strongest negative effector of JAK/STAT signaling among three Socs. Involved in both lysosomal degradation of Dome and preventing its phosphorylation by hop; participates in a negative feedback loop: <i>Socs36E</i> expression is transcriptionally activated by JAK signaling	[82-85]
<i>Socs16D</i>	Suppressor of cytokine signaling at	CG8146	<i>Socs16D</i> is a negative regulator of JAK-STAT signalling	[82,83]

	<i>16D</i>			
<i>Socs44A</i>	<i>Suppressor of cytokine signaling at 44A</i>	CG2160	Socs44E is a negative regulator of JAK-STAT signalling through hop	[82,83]
<i>Ptp61F</i>	<i>Protein tyrosine phosphatase 61F</i>	CG9181	Ptp61F is a transcriptional target of Stat92E, which also functions via a negative feedback and deactivates hop	[78,81]
<i>Su(var)2-10</i>	<i>Suppressor of variegation 2-10 (zimp, dPIAS)</i>	CG8068	The <i>Drosophila</i> PIAS (protein inhibitors of activated STATs) homolog, responsible for binding and blocking of Stat92E dimers	[86]
<i>os/upd1</i>	<i>outstretched (unpaired 1)</i>	CG5993	Receptor Dome ligand	[87]
<i>upd2</i>	<i>unpaired 2</i>	CG5988	Receptor Dome ligand	[87]
<i>upd3</i>	<i>unpaired 3</i>	CG33542 (CG5963, CG15062)	Receptor Dome ligand	[87]
<i>Cnot4</i>	<i>Cnot 4 homologue</i>	CG31716 (CG5251)	Transcription regulation complex subunit, needed for proper Stat92E DNA binding	[88]
<i>BRWD3</i>	<i>bromo-domain-containing protein</i>	CG31132 (CG6400)	A positive regulator with an elusive function	[79,89]
<i>ken</i>	<i>ken and barbie (ok)</i>	CG5575	Stat92E transcriptional antagonist	[79]
<i>Diedel</i>	<i>Diedel</i>	CG11501	A suggested negative regulator of JAK/STAT signalling with unclear molecular mechanism	[89,90]
<i>et</i>	<i>eye transformer (latran)</i>	CG14225	A negative regulator of JAK/STAT signaling	[91]
<i>dally</i>	<i>division abnormally delayed (gem)</i>	CG4974	A glypican involved in Upd distribution, responsible in activating of JAK/STAT pathway	[92]
<i>dlp</i>	<i>dally-like protein</i>	CG32146	An activator of JAK/STAT pathway by participating in Upd distribution	[92]
<i>TotA</i>	<i>Turandot A</i>	CG31509	Stress-inducible humoral factor, known to play an important role in stress tolerance and immune response	[87,93]
<i>Nop56</i>	<i>Nop56</i>	CG13849	A JAK/STAT target gene with Stat92E binding sites; a growth regulator	Reviewed in [94]
<i>Jheh2</i>	<i>Juvenile hormone epoxide hydrolase</i>	CG15102	A JAK/STAT target gene with Stat92E binding sites; JHEH is mainly involved in xenobiotic biotransformation, not just in juvenile hormone metabolism in <i>D. melanogaster</i>	Reviewed in [94,95]
<i>ftz-f1</i>	<i>ftz transcription factor 1</i>	CG4059	A JAK/STAT target gene with Stat92E binding sites; zinc finger, nuclear hormone receptor-type	Reviewed in [94]
<i>H</i>	<i>Hairless</i>	CG5460	A JAK/STAT target gene with Stat92E binding sites; negative regulator of Notch	Reviewed in [94]

			pathway	
<i>Tom</i>	<i>Twin of m4 (barbu)</i>	CG5185	A JAK/STAT target gene with Stat92E binding sites; negative regulator of Notch pathway	Reviewed in [94]
<i>Paip2</i>	<i>polyA-binding protein interacting protein 2</i>	CG12358	A JAK/STAT target gene with Stat92E binding sites; negative regulator of translation	Reviewed in [94]
<i>Zfh-1</i>	<i>zinc finger homeodomain 1</i>	CG1322	A JAK/STAT target gene with Stat92E binding sites; transcription factor that binds E box sequences and acts as an active transcriptional repressor	[96,97]
<i>eve</i>	<i>even skipped</i>	CG2328	A JAK/STAT target gene that functions in development	[98]
<i>chinmo</i>	<i>chronologically inappropriate morphogenesis</i>	CG31666 (CG17156)	A functional effector of the JAK/STAT pathway that regulates eye development, tumor formation, and stem cell self-renewal in <i>Drosophila</i>	[99]
<i>TotC</i>	Turandot C	CG31508	Stress-inducible humoral factor, known to play an important role in stress tolerance and immune response	[93]
<i>TotM</i>	Turandot M	CG14027	Stress-inducible humoral factor, known to play an important role in stress tolerance and immune response	[93]
<i>TotX</i>	Turandot X	CG31193	Stress-inducible humoral factor, involved in response to heat and oxidative stress as well as bacterial infection	[93]
<i>vir-1</i>	<i>virus-induced RNA-1</i>	CG31764	A JAK/STAT readout gene, known to be required for antiviral protection	[100]
<i>Tep2</i>	<i>Thioester-containing protein 2</i>	CG7052 (CG18589)	Resembles the vertebrate complement factors and α -macroglobulin family of protease inhibitors, and is known to be expressed mainly in hemocytes under JAK/STAT signalling control	[77,101]
<i>Tep3</i>	<i>Thioester-containing protein 3</i>	CG7068	Resembles the vertebrate complement factors and α -macroglobulin family of protease inhibitors, and is known to be expressed mainly in hemocytes under JAK/STAT signalling control	[77,101]
<i>Tep4</i>	<i>Thioester-containing protein 4</i>	CG10363	Resembles the vertebrate complement factors and α -macroglobulin family of protease inhibitors, and is known to be expressed mainly in hemocytes under JAK/STAT signalling control	[77,101]

Table 5 Toll signaling pathway in *D. melanogaster*

Acronym	Gene name	CG number	Function/Description of the gene product	Reference
<i>PGRP-SA</i>	<i>Peptidoglycan recognition protein SA</i>	CG11709	Pattern recognition receptor for Gram-positive bacteria, cooperates with GGBP1	[74]
<i>PGRP-SD</i>	<i>Peptidoglycan recognition protein SD</i>	CG7496	Pattern recognition receptor for Gram-positive bacteria	[102]
<i>GGBP1</i>	<i>Gram-negative bacteria binding protein 1</i>	CG6895	Pattern recognition receptor for Gram-positive bacteria, cooperates with PGRP-SA	[74]
<i>GGBP3</i>	<i>Gram-negative bacteria binding protein 3</i>	CG5008	Pattern recognition receptor for fungal cell wall components	[95]
<i>modSP</i>	<i>modular serine protease</i>	CG31217	Protease from protease cascade leading to processing spatzie	[84]
<i>grass</i>	<i>Gram-positive Specific Serine protease</i>	CG5896	Protease from activation cascade leading to processing spatzie	[103]
<i>spheroide</i>	<i>spheroide</i>	CG9675	Protease from activation cascade leading to processing spatzie	[69]
<i>spirit</i>	<i>spirit</i>	CG2056	Protease from activation cascade leading to processing spatzie	[69]
<i>sphinx1/2</i>	<i>sphinx1/ sphinx2</i>	CG32383/ CG32382	Proteases from activation cascade leading to processing spatzie	[69]
<i>nec</i>	<i>necrotic</i>	CG1857	Serine proteinase inhibitor, inhibitor of persephone	[104]
<i>psh</i>	<i>persephone</i>	CG6367	Serine protease activated by several virulence factors	[105]
<i>SPE</i>	<i>Spätzle-Processing Enzyme</i>	CG16705	Serine protease responsible for spätzle cleavage	[106]
<i>spz</i>	<i>spätzle</i>	CG6134	Toll receptor ligand	[105]
<i>Tl</i>	<i>Toll</i>	CG5490	Toll receptor	[105]
<i>mop</i>	<i>myopic</i>	CG9311	Endocytosis complex component	[107]
<i>Myd88</i>	<i>Myd88</i>	CG2078	Adaptor protein of Toll receptor, part of heterotrimeric DD complex	[105]
<i>tub</i>	<i>tube</i>	CG10520	Adaptor protein of Toll receptor, part of heterotrimeric DD complex	[105]
<i>pll</i>	<i>pelle</i>	CG5974	Adaptor protein of Toll receptor, part of heterotrimeric DD complex	[105]
<i>pli</i>	<i>Pellino</i>	CG5212	Pelle/IRAK interacting protein	[108]
<i>Gprk2</i>	<i>G protein-coupled receptor kinase 2</i>	CG17998	Cactus interacting protein	[109]
<i>cact</i>	<i>cactus</i>	CG5848	I κ B factor	[59]
<i>Dif</i>	<i>Dorsal-related</i>	CG6794	NF- κ B transcription factor	[110]

	<i>immunity factor</i>			
<i>dl</i>	<i>dorsal</i>	CG6667	NF-κB transcription factor	[105]
<i>Deaf1</i>	<i>Deformed epidermal autoregulatory factor-1</i>	CG8567	Transcription factor	[111]
<i>Drs</i>	<i>Drosomycin</i>	CG10810	Antimicrobial protein (AMP)	[112]
<i>Drsl5</i>	<i>Drosomycin-like 5</i>	CG10812	AMP-like protein	[113]
<i>IM1</i>	<i>Immune induced molecule 1</i>	CG18108		[113]
<i>IM2</i>	<i>Immune induced molecule 2</i>	CG18106		[113]

Table 6 Torso/MAPK signaling pathway components in *D. melanogaster*

Acronym	Gene name	CG number	Function/Description of the gene product	Reference
<i>tsl</i>	<i>torso-like</i>	CG6705	Torso-like is a <i>Drosophila</i> membrane attack complex/perforin-like protein. It binds the receptor tyrosine kinase Torso (Tor) and activates the Torso signaling cascade during terminal patterning of <i>Drosophila</i> embryo. A role of Tsl in control of body size and development, independent on Torso signaling.	[103,114,115]
<i>tor</i>	<i>torso</i>	CG1389	The Torso receptor tyrosine kinase (RTK) is distributed throughout the membrane in the embryo and activated by its ligand, like torso-like. Upon activation, two neighboring Torso receptors dimerize and transphosphorylate each other, recruiting corkscrew and the adaptor molecule Drk.	[116]
<i>trk</i>	<i>trunk</i>	CG5619	Trunk (expressed in the embryo) is a putative ligand of Torso receptor, responsible for the spatially restricted Tor activation. Trunk must be cleaved under control of Torso-like (Tsl) secretion at embryo pole in order to bind Tor. Torso-like independent cleavage of Trunk has also been found.	[117]
<i>boss</i>	<i>bride of sevenless</i>	CG8285	Boss is a G protein-coupled receptor (GPCR) that was first identified as a ligand for the Sevenless tyrosine kinase, which is involved in eye differentiation in <i>Drosophila</i> . Recently a role of Boss in glucose sensing and regulation of sugar and lipid metabolism was shown.	[118,119]
<i>sev</i>	<i>bride of sevenless</i>	CG18085	Sevenless is a receptor tyrosine kinase (RTK), initiating the signaling pathway responsible for	[120,121]

			differentiation of ommatidial cells during development.	
<i>drk</i>	<i>downstream of receptor kinase</i>	CG6033	Drk is an adaptor molecule that couples receptor tyrosine kinase (RTK) to son-of-sevenless (Sos). The association of Drk, Sos and RTK allows Sos to interact with membrane-bound Ras1.	[122]
<i>csw</i>	<i>corkscrew</i>	CG3954	Corkscrew is a non-receptor protein tyrosine phosphatase, homologous to the mammalian SHP-2 protein.	[123]
<i>Sos</i>	<i>Son of sevenless</i>	CG7793	Sos encodes a guanine-nucleotide exchange factor, which exchanges inactive GDP-Ras I for active GTP-Ras I.	[124]
<i>βggt-1</i>	<i>β subunit of type I geranylgeranyl transferase</i>	CG3469	A factor involved in RAS posttranslational modification (prenylation); a positive regulator of MAPK signaling.	[125,126]
<i>Fnta</i>	<i>Farnesyl transferase α</i>	CG2976	FNTA is <i>Drosophila</i> ortholog of the mammalian alpha farnesyltransferase subunit, an enzyme responsible for RAS farnesylation, which is required for Ras membrane localization and cell transforming activity.	[102,126]
<i>Hmgcr</i>	<i>Hydroxymethyl-glutaryl-(HMG) Coenzyme A reductase</i>	CG10367	HMGCR functions is required for farnesylation of RAS membrane-associated proteins.	[126]
<i>Ras85D (Ras1)</i>	<i>Ras oncogene at 85D (Ras 1)</i>	CG9375	Ras I associates with Raf1 serine/threonine kinase, recruiting it to the plasma membrane.	[127]
<i>phl (Raf1)</i>	<i>pole hole (Raf1)</i>	CG2845	Pole hole, a <i>Drosophila</i> Raf1 that may function as the first molecule in the MAPK cascade, phosphorylating and activating Dsor 1 (<i>Drosophila</i> MEK).	[109,128]
<i>Dsor1 (MEK)</i>	<i>Downstream of raf1</i>	CG15793	Dsor (MEK) is MAPKK, which is phosphorylated by Raf1 (MAPKKK), in turn, phosphorylates and activates rolled/ERK (MAPK).	[111]
<i>rl (ERK, MAPK)</i>	<i>rolled (Mitogen-activated protein kinase)</i>	CG12559	Rolled encodes a <i>Drosophila</i> MAPK – a central kinase in the MAPK signalling cascade, which phosphorylates a number of transcriptional factors and cytoplasmic targets.	[129]
<i>ksr</i>	<i>kinase suppressor of ras</i>	CG2899	<i>ksr</i> encodes a protein kinase, which is a general and evolutionarily conserved component of the RAS signaling pathway that acts between RAS and RAF.	[107]
<i>cnk</i>	<i>connector enhancer of ksr</i>	CG6556	<i>cnk</i> encodes a protein containing several protein-protein interaction domains, suggesting	[106]

			that it brings different signaling molecules together.	
<i>Ave</i> (<i>HYP</i>)	<i>Aveugle</i> (<i>Hyphen</i>)	CG30476	Hyphen (Aveugle) is a sterile alpha motif domain-containing protein, which in association with CNK interacts with KSR and that leads to stimulation of the RAS-dependent RAF activating.	[130,131]
<i>alph</i>	<i>alphabet</i>	CG1906	<i>alph</i> encodes a protein phosphatase 2C (PP2C) family member, which negatively regulates the MAPK signaling pathway.	[132]
<i>14-3-3ε</i>	<i>14-3-3ε</i>	CG31196	<i>14-3-3ε</i> is a member of 14-3-3 protein family, an activator of Ras.	[133]
<i>14-3-3ζ</i>	<i>14-3-3ζ</i>	CG17870	<i>14-3-3ζ</i> is a member of the 14-3-3 protein family, an activator of Ras with a partly redundant function with <i>14-3-3ε</i> .	[133]
<i>Cdc37</i>	<i>Cdc37</i>	CG12019	A positive regulation of Raf1.	[134]
<i>mago</i>	<i>mago nashi</i>	CG9401	A positive effector of <i>rl</i> (<i>MAPK</i>) transcription.	[126,135]
<i>eIF4AIII</i>	<i>eIF4AIII</i>	CG7483	A positive effector of <i>rl</i> (<i>MAPK</i>) transcription.	[126,135]
<i>Cdk12</i>	<i>Cyclin-dependent kinase 12</i>	CG7597	Cdk12 is RNA polymerase II C-terminal domain kinase, which provides phosphorylation required for transcription elongation, RNA processing, and splicing; Cdk12 is a modulator of <i>rl</i> (<i>MAPK</i>) transcription.	[126,136]
<i>Fip1</i>	<i>Fip1</i>	CG1078	FIP1 is a modulator of <i>rl</i> (<i>MAPK</i>) transcript processing, probably regulating splicing efficiency; FIP1 yeast ortholog encodes a component of a yeast pre-mRNA polyadenylation factor that directly interacts with poly(A) polymerase.	[126,137]
<i>CG1603</i>		<i>CG1603</i>	<i>CG1603</i> encodes a protein of unknown function that contains MADF type zinc finger domains; modulator of <i>rl</i> (<i>MAPK</i>) transcription.	[126]
<i>CG4936</i>		<i>CG4936</i>	<i>CG4936</i> encodes a zinc finger protein of unknown function that is related to human BCL-6 like transcription factor that is expressed in hematopoietic tissues; effector of MAPK signalling in <i>Drosophila</i> acting as MEK downstream .	[126,138]
<i>PTP-ER</i>	<i>Protein tyrosine phosphatase-ERK/Enhancer of Ras1</i>	CG9856	Negative regulator of MAPK signalling; transcription of <i>PTP-ER</i> is found to be under <i>CG4936</i> control.	[126]
<i>gfzf</i>	<i>GST-containing FLYWCH zinc-finger protein</i>	CG33546 CG10065 CG31492	GFZF affects MEK expression, presumably by regulating mek transcription	[126]

		CG31329	
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Table 7 JNK signaling pathway components in *D. melanogaster*

Acronym	Gene name	CG number	Function/Description of the gene product	Reference
<i>Src64B</i>	<i>Src oncogene at 64B</i>	CG7524	A non-receptor tyrosine kinase of the Src family; an upstream kinase in “canonical” JNK signalling pathway	[108]
<i>Btk29A</i>	<i>Btk family kinase at 29A</i>	CG8049	A non-receptor tyrosine kinase of the Src family; an upstream kinase in “canonical” JNK signalling pathway	[108]
<i>Src42A</i>	<i>Src oncogene at 42A</i>	CG44128	A non-receptor tyrosine kinase of the Src family; an upstream kinase in “canonical” JNK signalling pathway	[108]
<i>shark</i>	<i>SH2 ankyrin repeat kinase</i>	CG18247	Tyrosine kinase Shark plays a crucial role in JNK-mediated dorsal closure, where it acts upstream of JNK	[139]
<i>Dok</i>	<i>Downstream of kinase</i>	CG2079	Dok is an adaptor protein of Shark with ability to bind Shark SH2 domains in a tyrosine phosphorylation-dependent fashion; Dok tyrosine phosphorylation is Src dependent	[140]
<i>slpr</i>	<i>slipper</i>	CG2272	JUN kinase kinase kinase (JNKKK), known as Mixed Lineage Kinase (MLK)	[112]
<i>msn</i>	<i>misshapen</i>	CG16973	JUN kinase kinase kinase kinase (JNKKKK), kinase associated with MLK	[141]
<i>Rac1</i>	<i>Rac1</i>	CG2248	A small GTPase; a main activator of MLK	[141]
<i>egr (TNF)</i>	<i>eiger (tumor necrosis factor)</i>	CG12919	A TNF superfamily ligand that triggers the <i>Drosophila</i> JNK pathway	[142]
<i>wgn (TNFR)</i>	<i>wengen (tumor necrosis factor receptor)</i>	CG6531	The receptor of Eiger	[143]
<i>Traf4 (TRAF1)</i>	<i>TNF-receptor-associated factor 4 (Drosophila homolog of mammalian TRAF1)</i>	CG3048	Tumor necrosis factor receptor-associated factor, functioning as a signal mediator of cell surface receptor	[144]
<i>Traf6 (TRAF2)</i>	<i>TNF-receptor-associated factor 4 (Drosophila homolog of mammalian TRAF2)</i>	CG10961	Tumor necrosis factor receptor-associated factor, functions as a signal mediator of cell surface receptor	[144]
<i>Tab2</i>	<i>TAK1-associated-binding protein 2</i>	CG7417	Adaptor protein, linking dTRAF1 to the JNKKK dTAK1	[145]

<i>Tak1</i>	<i>TGF-β activated kinase 1</i>	CG18492	JUN kinase kinase kinase (JNKKK)	[146]
<i>Pk92B (ASK1)</i>	<i>Protein kinase at 92B (Apoptotic signal-regulating kinase 1)</i>	CG4720	JUN kinase kinase kinase (JNKKK)	[110,147]
<i>Mekk1 (MEKK4)</i>	<i>Mekk1 (MEKK4)</i>	CG7717	Stress-induced MAP kinase kinase kinase (MKKK), an activator of JNK pathway	[148]
<i>hep (MKK7)</i>	<i>Hemipterous (MAP kinase kinase 7)</i>	CG4353	JUN kinase kinase (JNKK)	[149]
<i>Mkk4</i>	<i>MAP kinase kinase 4</i>	CG9738	JUN kinase kinase (JNKK)	[149]
<i>bsk</i>	<i>basket</i>	CG5680	Encodes a single <i>Drosophila</i> JNK	[150]
<i>Jra (c-Jun)</i>	Jun-related antigen	CG2275	A homolog of mammalian c-Jun; in association with Kayak forms AP-1 transcriptional complex	[151]
<i>kay (c-Fos)</i>	<i>kayak</i>	CG33956	A homolog of mammalian c-Fos; in association with Jra forms AP-1 transcriptional complex	[151]
<i>Cka</i>	<i>Connector of kinase to AP-1</i>	CG7392	Encodes a scaffold molecule suggested to form a complex with Hemipterous and Basket	[148]
<i>dpp</i>	<i>decapentaple-gic</i>	CG9885	<i>dpp</i> is a main AP-1 target gene, encoding the <i>Drosophila</i> member of transforming growth factor- β (TGF- β) family, a ligand for Dpp signalling	[152,153]
<i>puc</i>	<i>puckered</i>	CG7850	A JNK-specific phosphatase that restricts JNK activity in a negative feedback loop	[154,155]
<i>chic</i>	<i>chickadee</i>	CG9553	A JNK signaling responsible gene, homolog of vertebrate regulator of actin cytoskeleton profilin	[156]
<i>Mmp1</i>	<i>Matrix metallo-proteinase 1</i>	CG4859	A primary function of Mmp1 in the JNK pathway control is to promote basement membrane repair, which in turn may permit cell migration and the restoration of tissue	[113]
<i>Fer1HCH</i>	<i>Ferritin 1 heavy chain homologue</i>	CG2216	A JNK signaling responsible gene; free radical scavenger	[104]
<i>MtnA</i>	<i>Metallothione-in A</i>	CG9470	A JNK signaling responsible gene; antioxidant	[104]
<i>Sesn</i>	<i>Sestrin</i>	CG11299	A JNK signaling responsible gene; antioxidant	[51]
<i>NLaz</i>	<i>Neural Lazarillo</i>	CG33126	A JNK signaling responsible gene; lipocalin	[157]
<i>l(2)efl</i>	<i>lethal (2) essential for life</i>	CG4533	A JNK signaling target gene; a small heat shock protein, antioxidant	[104]
<i>GstD1</i>	<i>Glutathione-S-transferase D1 homologue</i>	CG10045	A JNK signaling target gene; an antioxidant enzyme	[104]

<i>Hsp68</i>	<i>Heat shock protein 68</i>	CG5436	A JNK signaling target gene; <i>Drosophila</i> HSP70	[104]
<i>Jafrac1</i>	<i>thioredoxin peroxidase 1</i>	CG1633	Jafrac1, a JNK signaling target gene, is a <i>Drosophila</i> homolog of human Peroxiredoxin II (hPrxII), known to act as a downstream effector of JNK/FOXO signaling in neurons that enhance stress resistance and extends life span	[158]
<i>aop</i> (<i>Yan</i>)	<i>anterior open</i>	CG3166	Negative regulator of JNK pathway, which represses transcriptional activity of AP-1 complex	[151]
<i>scaf</i>	<i>scarface</i>	CG11066	Inhibitor of JNK pathway, which acts in negative feedback loop as an extracellular pathway regulator	[159]
<i>raw</i>	<i>raw</i>	CG12437	Negative regulator of JNK signalling pathway, whose molecular mechanisms remain unclear	[160]
<i>peb</i>	<i>pebbled</i>	CG12212	Inhibitor of JNK signalling pathway with an elusive mechanism	[160]

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