Table S1: Defensive microbial symbionts in animals. Associations involving eukaryotic symbionts are highlighted with grey background.

Host phylum	Host taxon	Environment	Protected life stage of the host	Symbiont taxon	Symbiont localization	Means of defense	Chemistry of defense	Biosynthesis	Antagonist against which the defense is active	Evidence for defensive symbiosis	References
Porifera	*Halichondria okadai*	Marine	Adult	*Alteromonas* sp.	Unknown	Secondary metabolite production	Ubiquinones	Terpenoid	Predatory barnacles, e.g. *Balanus amphitite*	*In vitro* settlement inhibition of isolated compounds	1
Porifera	*Lissodendoryx isodictyalis*	Marine	Adult	*Winogradskyella poriferum*	Unknown	Secondary metabolite production	Polyether	Other	Biofilm forming bacteria that attract barnacle larvae, predatory barnacles, e.g. *Balanus amphitite & Hydroides elegans*	*In vitro* settlement inhibition of crude extracts and isolated compounds, *in vitro* antibacterial activity of isolated cultures, *in vitro* inhibition of bacterial biofilm formation	2, 3
Porifera	*Reniera japonica*	Marine	Adult	*Flexibacter* sp.	Unknown	Radical protection	3R,3'R-zeaxanthine	Terpenoid	Singlet oxygen, free radicals	*In vitro* production of zeaxanthine	4
Porifera	*Dysidea herbacea*	Marine	Adult	*Oscillatoria spongeliae*	Extracellular endosymbiont	Secondary metabolite production	Polychlorinated diketopiperazides, e.g. Herbadysolide, Dihydrodysamide C, Demethyl-dihydrodysamide C, 13-Demethylisodysidenin, Didechlorodihydrodysamide C	Other	Fish predators	Isolated compounds deter predatory fish in feeding assays with spiked food.	5-7
Porifera	*Dysidea herbacea, Lendenfeldia chondrodes, Phyllospongia papyracea*	Marine	Adult	*Oscillatoria spongeliae*	Extracellular endosymbiont	Secondary metabolite production	Polybrominated biphenylethers	Other	Fish predators, bacteria	Deter predatory fish in feeding assays with spiked food. *In vitro* antibacterial activity of extracted compounds	7-9
Porifera	*Dysidea herbacea, Lamellodysidea herbacea*	Marine	Adult	*Oscillatoria spongeliae*	Extracellular endosymbiont	Secondary metabolite production	dysidin, dysidenin, neodysidenin & related compounds	NRPS-PKS	Unknown	Phospholipase inhibition (-> microbial community regulation through immune system modulation?)	10-14
Porifera	*Dysidea herbacea*	Marine	Adult	*Synechocystis sp*	Extracellular endosymbiont	Secondary metabolite production	Dysiherbaine	Other	Unknown	*In vitro* neurotoxic activity of extracted compounds	15, 16
Porifera	*Pseudoceratina clavata*	Marine	Adult	*Salinispora sp.*	Unknown	Secondary metabolite production	Rifamycin B & SV	PKS	Bacteria	*In vitro* antibacterial activity of isolated cultures, Rifamycins are known antibiotics against Gram-posivive bacteria	17, 18
Porifera	*Plakortis simplex*	Marine	Adult	*Sphingomonas sp.*	Extracellular endosymbiont	Secondary metabolite production	Plakortins, Plakosides, Simplexides, Crasserides, Bacteriohopanoids	PKS Other Other Other terpenoid	bacteria, fish predators (e.g. *Carassius aurata*)	*In vitro* compound production by bacterial isolate *In vitro* antimicrobial & cytotoxic (antimalarial) activity, *In vitro* immunosuppressive activity, *In vitro* immunosuppressive activity, *In vitro* feeding deterrent	19-27
Porifera	*Psammocinia* aff. *bulbosa*	Marine	Adult	Unknown	Unknown	Secondary metabolite production	Psymberin (=ircinastatin)	*trans* AT PKS	Unknown	*In vitro* cytotoxic activity of extracted compound	28, 29
Porifera	*Mycale hentscheli*	Marine	Adult	Unknown	Unknown	Secondary metabolite production	Mycalamide A	*trans* AT PKS	Unknown	*In vitro* cytotoxic (antimalarial) activity of extracted compound	29-31
Porifera	*Theonella swinhoei*	Marine	Adult	Unicellular heterotrophic bacteria	Extracellular endosymbiont	Secondary metabolite production	Swinholide A	*trans* AT PKS	Unknown	*In vitro* cytotoxic activity of extracted compound	32, 33
Porifera	*Theonella swinhoei*	Marine	Adult	*Candidatus* Entotheonella palauensis	Extracellular endosymbiont	Secondary metabolite production	Theopalauamide, Theonellamide A	(NRPS?)	Unknown	*In vitro* antimycotic activity of extracted compound	33-37
Porifera	*Theonella swinhoei*	Marine	Adult	*Candidatus* Entotheonella sp	Extracellular endosymbiont	Secondary metabolite production	Polytheonamides Onnamides Pseudoonamide A Keramamides Nazuamide A Cyclotheonamide	Ribosomal NRPS-PKS	Unknown	*In vitro* antimycotic, antiviral and cytotoxic activity of some of the extracted compounds	38-44

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Porifera	*Discoderma calyx*	Marine	Adult	*Candidatus* Entotheonella sp?	Extracellular endosymbiont	Secondary metabolite production	Calyxamides A&B	(NRPS?)	Unknown	*In vitro* cytotoxic activity of extracted compound	45
Porifera	*Discoderma calyx*	Marine	Adult	*Candidatus* Entotheonella sp?	Extracellular endosymbiont	Secondary metabolite production	Calyculins	NRPS-PKS	Unknown	*In vitro* cytotoxic activity of extracted compound	46
Cnidaria: Anthozoa	*Pseudopterogorgia* spp. (*P. elisabethae* and *P. bipinnata*)	Marine	Mostly Adults	Dinoflagellates: *Symbiodinium* spp.	Intracellular endosymbiont	Secondary metabolite production	Pseudopterosins, and kallolide family of diterpenes	Terpenes	*Thalassoma bifasciatum* (fish)	Localization of compounds in symbiont cell fraction; labeling experiments; coral extracts unpalatable to fish predators	47-49
Cnidaria: Anthozoa	*Pseudopterogorgia americana*	Marine	Adults	Dinoflagellates?	Intracellular endosymbiont	Production of precursors of toxic compounds	Secosterols, including 9,11-secogorgosterol and 9,11-secodinosterol	Sterols	*Thalassoma bifasciatum* (fish)	Isolated dinoflagellates from several marine organisms produce gorgosterol and dinosterol; deterrence of secosterols to fish predator	50-52
Cnidaria: Anthozoa	unspecified soft coral	Marine	Adult?	Actinobacteria*:* *Micromonospora* sp. ACM2-092	Unknown	Secondary metabolite production	Thiocoraline	Other	Antimicrobial and cytotoxic activity	*In vitro* bioactivity of compounds	53
Cnidaria: Hydrozoa	*Hydra vulgaris*	Limnic	Adults	Complex community; mostly Beta-Proteobacteria	Ectosymbiont and extracellular endosymbiont	Unknown	Unknown	Unknown	Fungal pathogens	Experimental manipulation of microbiota affects protection against a fungal pathogen; some *in vitro* antifungal effects by individual bacterial isolates	54
Bryozoa	*Bugula neritina, B. simplex*	Marine	Mostly larvae and Adult reproductive tissue	Gamma-Prot.: '*Candidatus* Endobugula sertula'	Extracellular endosymbiont	Secondary metabolite production	Bryostatins 1-20	*Trans*-AT PKS	Multiple predators	Co-localization of bryostatins and symbionts *in vivo*; decrease in bryostatin concentrations after antibiotic treatment; identification of bryostatin biosynthesis gene cluster; deterrence of bryostatins against various predators	55-67
Bryozoa	*Sessibugula translucens, Bugula dentata*	Marine	Adult	*Pseudoalteromonas tunicata*	Extracellular endosymiont	Secondary metabolite production	Tambjamines	Other	Fish predators	Tambjamines isolated from bryozoans; deterrence against fish predators; identification of tambjamine biosynthesis gene cluster in *Pseudoalteromonas tunicata*; isolation of *P. tunicata* from some bryozoans	67-72
Bryozoa	*Amathia spp.*	Marine	Adult	Unidentified	Unknown	Secondary metabolite production	convolutamines, convolutindole	Other	Parasitic nematodes?	Intraspecific variability in bryozoans chemistry; structure of some of the compounds related to microbial metabolites; *in vitro* nematocidal activity	73
Bryozoa	*Amathia spp.*	Marine	Adult	Rod-shaped bacterium	Ectosymbiont	Secondary metabolite production	Amathamides and related compounds	Other	Unknown	Localization of amathamides correlated with bacteria	64, 74-76
Bryozoa	*Biflustra perfragilis*	Marine	Adult	Unknown	Unknown	Secondary metabolite production	Perfragilins	Other	Unknown	Similarity to microbial metabolites; *in vitro* cytotoxic activity	77
Bryozoa	*Flustra foliacea*	Marine	Adult	Unknown	Unknown	Secondary metabolite production	brominated indoles and diterpenoids	Other and terpenes	Unknown	Intraspecific variation in chemical composition of *F. foliacea*	78, 79
Bryozoa	*Phidolopora pacifica, Diaperoecia californica, Heteropora alaskensis, Tricellaria ternata,* and *Hippodiplosia insculpta*	Marine	Adult	Unknown	Unknown	Secondary metabolite production	phidolopins and other nitrophenols	Other	Fouling organisms	Occurrence in taxonomically diverse sympatric bryozoans; *in vitro* activity of compounds	80
Tunicata	*Atapozoa* sp. (=*Sigillina signifera*)	Marine	Adult	*Pseudoalteromonas tunicata*	Extracellular endosymbiont	Secondary metabolite production	Tambjamines	Other	Fish predators	Tambjamines isolated from *Atapozoa* sp.; deterrence against fish predators; identification of tambjamine biosynthesis gene cluster in *Pseudoalteromonas tunicata*; isolation of *P. tunicata* from some tunicates	67, 70-72, 81, 82
Tunicata	*Trididemnum solidum, Aplidium albicans*	Marine	Larvae	Cyanobacteria: *Synechocystis trididemni*	Ectosymbiont	Secondary metabolite production	Didemnins	NRPS/PKS	Fish predators	Didemnin B found in two phylogenetically distant ascidians; plasmid-localized didemnin gene cluster in a marine Alpha-Proteobacteria; deterrent activity against predatory fish	83-90
Tunicata	*Lissoclinum patella*	Marine	Adult	Cyanobacteria: *Prochloron didemni*	Ectosymbiont	Secondary metabolite production	Cyanobactins (Patellamides, Trunkamide, Patellins, and others)	Ribosomal	Unknown	Co-occurrence of cyanobactins and *Prochloron* symbionts; cyanobactin gene clusters identified in symbiotic and free-living cyanobacteria; *in vitro* cytotoxicity	87, 91-97
Tunicata	*Lissoclinum patella*	Marine	Adult	Alpha-Prot.:	Intracellular	Secondary	Patellazoles	*Trans*-AT PKS	Unknown	Inconsistent occurrence across *L. patella* individuals; metagenomic	98-102

				'Candidatus Endolissoclinum faulkneri	endosymbiont	metabolite production				and genomic analyses and identification of the patellazole gene cluster in the otherwise eroded symbiont genome; *in vitro* cytotoxicity	
Tunicata	*Lissoclinum bistratum*	Marine	Adult	Cyanobacteria: *Prochloron didemni*	Ectosymbiont	Secondary metabolite production	Bistramides	PKS	Unknown	Enrichment of bistramides in *Prochloron* cell fraction; *in vitro* cytotoxicity	103-106
Tunicata	*Synoicum adareanum*	Marine	Adult	Unknown bacterium	Unknown	Secondary metabolite production	Palmerolides	*Trans*-AT PKS/NRPS	Unknown	Putative bacterial palmerolide PKS fragments sequenced; *in vitro* cytotoxicity	107
Tunicata	*Ecteinascidia turbinata*	Marine	Adult	'*Candidatus* Endoecteinascidia frumentensis'	Intracellular endosymbiont	Secondary metabolite production	Ecteinascidin-743	NRPS	Unknown	Bacterial NRPS cluster likely responsible for ET-743 production assigned to the symbiont genome by analysis of codon usage; *in vitro* cytotoxicity of ET-743	108-110
Tunicata	*Eudistoma toealensis*	Marine	Adult	Possibly actinobacterial associates	Unknown	Secondary metabolite production	Staurosporines	Other	Unknown	Production of staurosporines by some terrestrial and marine Actinobacteria (*Streptomyces* spp.); presence of Actinobacteria (*Salinispora* and *Verrucosispora*) in ascidian tissue	111
Acoelomorpha: Convolutidae	*Amphiscolops spp.*	Marine	Unknown	Dinoflagellates: *Amphidinium* spp.	Unknown	Secondary metabolite production	Amphidinolides A-H	PKS	Predators?	*In vitro* production of cytotoxic amphidinolides by isolated dinoflagellates	reviewed in 112
Acoelomorpha: Convolutidae	*Amphiscolops spp.*	Marine	Unknown	Dinoflagellates: *Symbiodinium* sp.	Unknown	Secondary metabolite production	Zooxanthellatoxins A and B	PKS?	Unknown	*In vitro* production of vasoconstrictive zooxanthellatoxins & cytotoxic symbiodinolide by isolated dinoflagellates	reviewed in 112
Nemertea	*Cephalothrix simula*	Marine	Adult	*Bacillus sp.*	Extracellular(?) endosymbiont	Secondary metabolite production	Tetrodotoxin	Unknown	Predators	In vitro cytotoxic activity of extracted compound	113-117
Mollusca, Gastropoda	*Crysomallon squamiferrum*	Marine	Adult	[illegible]- and [illegible]-proteobacteria	Ectosymbiont	Mineral armor	Pyrite and greigite	Other	Predators	Hardening of scales	118-120
Mollusca, Gastropoda	*Conus pulicarius & Conus sp.*	Marine	Adult	*Streptomyces sp*	Intracellular endosymbiont	Secondary metabolite production	Aerugine, Pulicatins, Watasemycin	Other	Unknown	*In vitro* compound production by bacterial isolate *In vitro* antimicrobial *In vitro* anti-inflamatory *In vitro* anti-hypotensive	121, 122
Mollusca, Gastropoda	*Conus tribblei & Chicoreus nobilis*	Marine	Adult	*Streptomyces sp.*	Unknown	Secondary metabolite production	Nobilamides	(NRPS?)	Unknown	*In vitro* compound production by bacterial isolate *In vitro* anti-inflamatory	123
Mollusca, Gastropoda	*Conus circumcisus & Conus sp*	Marine	Adult	*Gordonia sp*	Unknown	Secondary metabolite production	Circumcins	Unknown	Unknown	*In vitro* compound production by bacterial isolate *In vitro* neuroactive	124
Mollusca, Gastropoda	*Conus tribblei & Conus rolani*	Marine	Adult	*Nocardiopsis alba*	Unknown	Secondary metabolite production	Nocapyrones	PKS	Unknown	*In vitro* compound production by bacterial isolate Structurally related compounds are shown to be defensive	125, 126
Mollusca, Gastropoda	Teredinidae ("shipworms")	Marine	Adult	Teredinibacter turnerae	Ectosymbiont	Secondary metabolite production	Tartrolons	*Trans* AT PKS	Bacteria, Boron	*In vitro* antimicrobial activity of isolated compounds, (controlling boron concentration, which is cytotoxic in high levels?)	127-132
Mollusca, Gastropoda	*Lienardia totopotens*	Marine	Adult	*Streptomyces sp.*	Unknown	Secondary metabolite production	Lobophorins	PKS	Bacteria, Predators(?)	*In vitro* compound production by bacterial isolate *In vitro* antibacterial *In vitro* cytotoxic	133
Mollusca, Cephalopoda	*Hapalochlaena* sp.	Marine	Adult	Variable bacteria	Variable locations	Secondary metabolite production	Tetrodotoxin	Unknown	Predators	Extraction and structure elucidation of cytotoxic tetrodotoxin derivatives, *In vitro* production of tetrodotoxin by variable isolates	116, 134, 135
Mollusca, Cephalopoda	*Euprymna scolopes*	Marine	Adult	*Vibrio fisherii*	Ectosymbiont	Light emission	Luziferase	Other	Predators and prey	Camouflage through counterillumination	136-139
Mollusca, Cephalopoda	*Loligo* sp., *Sepia* sp., *Euprymna scolopes*	Marine	Egg	[illegible]- and [illegible]-proteobacteria, *Bacteroidetes* bacteria (esp. *Roseobacter* in *Loligo* and *Sepia*, *Phaeobacter* in *Euprymna*)	Unknown endosymbiont	Secondary metabolite production	Unknown	Unknown	Unknown	*In vitro* antimicrobial activity of extracts from symbiont populated glands and eggs	140-151
Crustacea	*Palaemon macrodactylus*	Marine	Egg	*Alteromonas* sp.	Ectosymbiont	Secondary metabolite production	2,3-indolinedione (isatin)	Other	Fungal pathogen: *Lagenidium callinectes*	Aposymbiotic eggs are susceptible but isolated compound restores protective effect upon application to aposymbiotic eggs	152
Crustacea	*Homarus americanus*	Marine	Egg	Rod-shaped, Gram-negative bacteria	Ectosymbiont	Secondary metabolite production	4-hydroxyphenethyl alcohol (tyrosol)	Other	Fungal pathogen: *Lagenidium callinectes*	*In vitro* inhibition of *L. callinectes* growth by extracted compound	153

Crustacea	Isopoda: *Santia spp.*	Marine	Adult	Cyanobacteria: *Synechococcus, Prochlorothrix* and *Synechocystis*	Ectosymbiont	Secondary metabolite production	Unknown	Unknown	Fish predators	Aposymbiotic isopods are not rejected by fish but methanolic extract from symbiotic animals restores protection	154
Nematoda	various *Heterorhabditis* spp. and *Steinernema* spp. (Rhabditida)	Terrestrial , within Insect	All life stages	Various *Photorhabdus luminescens* and *Xenorhabdus nematophila*	Ectosymbiont	Secondary metabolite production	Rhabduscin	Other	Potential activity against fungi	Defensive compound elucidated	155
Nematoda	various *Heterorhabditis* spp. (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	Various *Photorhabdus* spp.	Ectosymbiont	Secondary metabolite production	Carbapenem (beta-lactam antibiotic)	Other	Activity against distantly related bacteria, yeasts, fungi	Defensive compound elucidated, *in vitro* defensive activity	156-158
Nematoda	various *Heterorhabditis* spp. (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	*Photorhabdus luminescens*	Ectosymbiont	Secondary metabolite production	Carbapenem-like molecule	Other	Broad-spectrum activity against Gram-negative bacteria	Defensive compound elucidated, *in vitro* defensive activity	157
Nematoda	various *Heterorhabditis* spp. (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	*Photorhabdus luminescens*	Ectosymbiont	Secondary metabolite production	Genistine	Other	Unknown	Defensive compound elucidated	159
Nematoda	various *Heterorhabditis* spp. (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	*Photorhabdus luminescens* and others	Ectosymbiont	Secondary metabolite production	Isopropylstilbenes (e.g. 3,5-dihydroxy-4-isopropylstilbene)	Other	Activity against Gram-positive and Gram-negative bacteria, fungi, nematodes	Defensive compounds elucidated, *in vitro* defensive activity	160-166
Nematoda	various *Heterorhabditis* spp. (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	*Photorhabdus luminescens*	Ectosymbiont	Secondary metabolite production	Anthraquinones (red pigments color cadaver) (e.g. 1,3,8-trihydroxy-9,10-anthraquinone)	PKS	Activity against microorganisms assumed,[167] tested only against *E. coli*	Defensive compounds elucidated	159, 161, 162, 168
Nematoda	*Heterorhabditis bacteriophora* (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	*Photorhabdus luminescens*	Ectosymbiont	Secondary metabolite production	Photobactin	Other	Antibacterial	Defensive compounds elucidated, *in vitro* defensive activity	158
Nematoda	*Heterorhabditis* sp. (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	*Photorhabdus aeruginosa*	Ectosymbiont	Secondary metabolite production	Lumicins	Unknown	Broad-spectrum bacteriocins to outcompete other *Photorhabdus* spp. and strains as well as other bacteria	Defensive compounds elucidated, *in vitro* defensive activity	169, 170
Nematoda	various *Heterorhabditis* spp. (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	Various *Photorhabdus* strains	Ectosymbiont	Secondary metabolite production	Photorhabdicins (bacteriophage-related R- and F-type pyocins)	Unknown	Broad-spectrum bacteriocins to outcompete other *Photorhabdus* spp. and strains as well as other bacteria	Defensive compounds elucidated, *in vitro* defensive activity	169, 171
Nematoda	various *Heterorhabditis* spp. (Rhabditida: Heterorhapditidae)	Terrestrial , within Insect	All life stages	*Photorhabdus luminescens*	Ectosymbiont	Secondary metabolite production	Small, extracellular, possibly nonproteinacious compound(s)	Unknown	Ants	Defensive compounds elucidated, *in vivo* fitness benefits	172-175
Nematoda	various *Steinernema* spp. (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus budapestensis* and *X. szentirmaii*	Ectosymbiont	Secondary metabolite production	Fabclavines (peptide-polyketide-polyamino hybrids)	PKS/NRPS	Broad-spectrum activity against bacteria, yeasts and protozoa	Defensive compounds elucidated, *in vitro* defensive activity	176
Nematoda	various *Steinernema* spp. (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus bovienii* and *X. nematophilus*	Ectosymbiont	Secondary metabolite production	Xenorhabdins (dithiolopyrrlones; member of pyrothine family)	Unknown	Activity against Gram-positive bacteria, little effect against Gram-negative bacteria, some with activity against fungi	Defensive compounds elucidated, *in vitro* defensive activity	156, 162, 177
Nematoda	various *Steinernema* spp. (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	Various *Xenorhabdus* spp.	Ectosymbiont	Secondary metabolite production	Xenorxides (oxidized products of Xenorhabdins)	Unknown	Broad-spectrum activity against Gram-positive bacteria, yeast, fungi	Defensive compounds elucidated, *in vitro* defensive activity	178
Nematoda	*Steinernema* sp. (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus* sp. PB30.3	Ectosymbiont	Secondary metabolite production	Xenobactin (hexadepsipeptide)	(NRPS?)	Activity against protozoa and Gram-positive bacteria, not effective against Gram-negative bacteria	Defensive compounds elucidated, *in vitro* defensive activity	179

Nematoda	*Steinernema carpocapsae* (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus nematophilus* and others	Ectosymbiont	Secondary metabolite production	Xenocoumacins (peptide-polyketide origin ; benzopyran-1-one derivatives)	NRPS-PKS	Activity against Gram-positive bacteria	Defensive compounds elucidated, *in vitro* defensive activity	180
Nematoda	*Steinernema carpocapsae* (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus nematophilus*	Ectosymbiont	Secondary metabolite production	Xenematide (cyclodepsipeptide)	NRPS	Antibacterial activity	Defensive compounds elucidated, *in vitro* defensive activity	181, 182
Nematoda	*Steinernema carpocapsae* (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus nematophilus*	Ectosymbiont	Secondary metabolite production	Benzylideneaceton e (monoterpenoid)	Terpenoid	Specific activity against Gram-negative bacteria	Defensive compounds elucidated, *in vitro* defensive activity	183
Nematoda	*Steinernema carpocapsae* (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus nematophilus*	Ectosymbiont	Secondary metabolite production	Nematophins (indole derivatives)	Other	Activity against Gram-positive and Gram-negative bacteria as well as a few fungi	Defensive compounds elucidated, *in vitro* defensive activity	160, 184
Nematoda	*Steinernema carpocapsae* (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus nematophilus*	Ectosymbiont	Secondary metabolite production	Xenorhabdicins (phage related R-type pyocin)	Unknown	Narrow-spectrum bacteriocins to outcompete *Xenorhabdus* spp., *P. luminescens* and sister taxon *Proteus*	Defensive compounds elucidated, *in vitro* defensive activity, in vivo fitness benefits	169, 185-187
Nematoda	*Steinernema carpocapsae* (Rhabditida : Steinernematidae)	Terrestrial , within Insect	All life stages	*Xenorhabdus nematophilus*	Ectosymbiont	Secondary metabolite production	ant-deterent factor (ADF)	Unknown	Deter ants	Defensive compounds elucidated, *in vivo* fitness benefits	175
Insecta, Blattodea,	Fungus-farming Macrotermitinae	Terrestrial	Fungal cultivars	*Termitomyces* sp.	Ectosymbiont	Secondary metabolite production	Unknown mycocins	Unknown	Related cultivar species and strains	*In vitro* defensive activity	188
Insecta, Blattodea	Fungus-farming termites (Termitidae)	Terrestrial	Fungal cultivars	Various Actinobacteria	Ectosymbiont	Secondary metabolite production	Unknown	Unknown	Competing fungi (*Pseudoxylaria*, *Trichoderma*)	*In vitro* defensive activity	189
Insecta, Blattodea	Fungus-farming *Microtermes* sp.	Terrestrial	Fungal cultivars	*Streptomyces* sp.	Ectosymbiont	Secondary metabolite production	Microtermolides A and B	PKS-NRPS	Unknown	Defensive compounds elucidated	190
Insect, Orthoptera	Locust: *Schistocerca gregaria*	Terrestrial	Adult	*Pantoea agglomerans* (ϒ-proteobacteria)	Ectosymbiont	production of bioactive compound	Quinines	Other	Pathogenic fungi (*Metarhizium anisopliae)*	*In vivo* fitness benefits, in vitro defensive activity and elucidation of defensive compounds	191-193
Insecta, Hemiptera	Whitefly: *Bemisia tabaci*	Terrestrial	Adult	*Rickettsia* sp.	Intra- and extracellular endosymbiont	Unknown	Unknown	Unknown	Bacterial pathogen (*Pseudomonas syringae)*	*In vivo* fitness benefits in laboratory conditions	194
Insecta, Hemiptera	Aphid: *Myzus persicae* (Aphididae)	Terrestrial	Nymph and Adult	*Regiella insecticola* (ϒ-proteobacteria)	Intra- and extracellular endosymbiont	Unknown	Unknown	Unknown	Parasitoid wasp (*Aphidius colemani*)	*In vivo* fitness benefits	195
Insecta, Hemiptera	Aphids: *Acyrthosipon pisum, Aphis craccivora* and *Aphis fabae* (Aphididae)	Terrestrial	Nymph and Adult	*Hamiltonella defensa* (ϒ-proteobacteria) (APSE bacteriophage encoded genes)	Intra- and extracellular endosymbiont	production of bioactive compound, and possibly complementary mechanisms	Shiga-like toxin, cytolethal distending toxin, and YD-repeat toxins (possibly others as well)	(Ribosomal peptide?) (Ribosomal peptide?) (Ribosomal peptide?)	Parasitoid wasps (*Aphidius ervi* , *Aphidius eadyi, Lysiphlebus fabarum)*	*In vivo* fitness benefits	196-202
Insecta; Hemiptera	Pea aphid: *Acyrthosipon pisum* (Aphididae)	Terrestrial	Adult	*Regiella insecticola, Rickettsiella* sp. (ϒ-proteobacteria) *Rickettsia* sp. (α-proteobacteria)	Intra- and extracellular endosymbiont	Unknown	Unknown	Unknown	Fungal pathogen (*Pandora neoaphidis*)	*In vivo* fitness benefits	203-205
Insecta, Hemiptera	Asian citrus psyllid: *Diaphorina citri* (Psylidae)	Terrestrial	Adult	*Candidatus* Profftella armatura (β-proteobacteria)	Intracellular endosymbiont	production of bioactive compound	Diaphorin (polyketide)	*trans*-AT PKS	Unknown	Defensive compound elucidated and present in 100% of individuals at potentially cytotoxic concentrations	206
Insecta, Hemiptera	Red gum lerp psyllid: *Glycaspis brimblecombei* (Psylidae)	Terrestrial	Adult	*Arsenophonus* sp.	Intracellular endosymbiont	Unknown (proposed: phage-mediated)	Unknown	-	Parasitoids	Positive correlation between presence of symbiont and natural enemy in the field	207
Insecta, Coleoptera	Some *Euops* Leaf-rolling weevils (Attelabidae)	Terrestrial	Larva, Pupa	*Penicillium herquei*	Ectosymbiont	Secondary metabolite production	Scleroderolide	PKS	Fungal and bacterial pathogens	Defensive compounds elucidated, *in vitro* defensive activity, *in vivo* fitness benefits	208-210
Insecta,	*Dendroctonus*	Terrestrial	All life stages	*Ogataea pini*	Ectosymbiont	Volatile organic	Ethanol, carbon	Other	*Beauvaria bassiana* insect	Defensive compounds elucidated, *in vitro* defensive activity	211

Coleoptera	*brevicomis* (Curculionidae)			(Saccharomycetales: Saccharomycetaceae)		compound production	disulfide (CS2), delta-3-carene	Other Terpene	pathogen		
Insecta, Coleoptera	*Dendroctonus frontalis* (Curculionidae)	Terrestrial	Fungal cultivars	*Streptomyces thermosacchari* (Actinobacteria)	Ectosymbiont	Secondary metabolite production	Mycangimycin (polyene)	Other (Polyene)	Competing fungi	Defensive compounds elucidated, *in vitro* defensive activity	212, 213
Insecta, Coleoptera	*Dendroctonus frontalis* (Curculionidae)	Terrestrial	Fungal cultivars	*Streptomyces* sp.	Ectosymbiont	Secondary metabolite production	Frontalamides A and B	PKS-NRPS	Unknown	Defensive compounds elucidated	214
Insecta, Coleoptera	Fungus-farming *Euwallacea validus* (Curculionidae)	Terrestrial	Fungal cultivars	Unknown cultivar fungus	Ectosymbiont	Secondary metabolite production	Cerulenin, Helvolic acid	Other Terpenoid	Fungal pathogens of cultivars	Defensive compounds elucidated, *in vitro* defensive activity	215
Insecta, Coleoptera	Alfalfa weevil: *Hypera postica* (Curculionidae)	Terrestrial	Not specified	*Wolbachia* (α-proteobacteria) (and/or others)	Intracellularendosymbiont	Unknown	Unknown	Unknown	Parasitoid wasp (*Microctonus aethiopoides*)	*In vivo* fitness benefits (specificity of association not confirmed)	200, 216
Insecta, Coleoptera	Rove beetles: *Paederus* spp. (Staphylinidae)	Terrestrial	Larvae (potentially others)	*Pseudomonas* sp. (β-proteobacteria)	Extracellular endosymbiont	Production of bioactive compound	Pederin (polyketide)	*trans*-AT PKS	Wolf spiders (Araneae: Lycosidae, Salticidae)	*In vivo* fitness benefits (decreased predation)	217-224
Insecta, Hymenoptera	*Microplitis demolitor* and other parasitoid wasps (Braconidae, Ichneumonidae)	Terrestrial	Egg and larva	*Brachovirus* and *Ichnovirus* (Polydnaviruses)	Endosymbiont	Immunosuppression in parasitized host	Apoptosis induction, haemocyte clumping, phenoloxidase inhibition (various genes)	-	Parasitized host immune system (usually Lepidoptera larvae)	*In vivo* fitness benefits, characterization of genes responsible for protective function	225-227
Insecta, Hymenoptera	Various fungus-farming Attine species (Formicidae)	Terrestrial	Fungal cultivars	*Pseudonocardia* spp. (Actinobacteria)	Ectosymbiont	Secondary metabolite production	Dentigerumycin, five angucyclines and a nystatin-like compound	(NRPS-PKS?) (depsipeptide)	Specific activity against pathogen of fungal cultivars(*Escovopsis* sp.)	Defensive compounds elucidated, in vitro defensive activity, in vivo fitness benefits	228-236
Insecta, Hymenoptera	Various fungus-farming Attine species (Formicidae)	Terrestrial	Fungal cultivars	*Streptomyces* spp., *Amycolatopsis* spp. (Actinobacteria)	Ectosymbiont	Secondary metabolite production	Streptomyces: Candicidin	PKS	Competing fungi	Defensive compounds elucidated, *in vitro* defensive activity	235, 237-240
Insecta, Hymenoptera	*Allomerus* ants (Formicidae)	Terrestrial	Fungal cultivars	*Streptomyces* spp. *Amycolatopsis* spp. (Actinobacteria)	Ectosymbiont	Secondary metabolite production	Unknown	Unknown	Competing fungi	defensive compounds elucidated, *in vitro* defensive activity	241
Insecta, Hymenoptera, Formicidae	Fungus-farming *Atta sexdens, Atta texana* (Formicidae)	Terrestrial	Fungal cultivars and all life stages	Various killer yeasts (Basidiomycota, Ascomycota)	Ectosymbiont	Secondary metabolite production	Unknown mycocins	Unknown	Fungal pathogens of cultivars and insects	*In vitro* defensive activity	242, 243
Insecta, Hymenoptera	Fungus-farming *Cyphomyrmex costatus* (Formicidae)	Terrestrial	Fungal cultivars	*Lepiota* sp.	Ectosymbiont	Secondary metabolite production	Lepiochlorin	Other	Bacteria and fungi?	Defensive compounds elucidated	244
Insecta, Hymenoptera	Fungus-farming *Cyphomyrmex minutus* (Formicidae)	Terrestrial	Fungal cultivars and all life stages	*Tyridiomyces formicarum*	Ectosymbiont	Secondary metabolite production	Several diketopiperazines	Other (peptide)	Fungal pathogens of cultivars and insects	Defensive compounds elucidated	245
Insecta, Hymenoptera	Fungus-farming *Atta colombica* (Formicidae)	Terrestrial	Fungal cultivars	*Leucocoprinus gongylophorus* (Lepiotaceae, Basidiomycota)	Ectosymbiont	Secondary metabolite production	Unknown	Unknown	Endophytic fungi within plant substrate of fungal cultivars	*In vitro* defensive activity	246
Insecta, Hymenoptera	*Philanthus* spp., *Trachypus* spp., *Philantinus* spp. (Crabronidae)	Terrestrial	Larva, Pupa	*Streptomyces philanthi* (Actinobacteria)	Ectosymbiont	Secondary metabolite production	Cocktail containing streptochlorin and eight piericidin derivatives	PKS PKS	Fungal and bacterial pathogens	Defensive compounds elucidated, in vitro defensive activity, in vivo fitness benefits	247-251
Insecta, Hymenoptera	Honey bees: *Apis* spp. (Apidae)	Terrestrial	Larvae and Adult	*Lactobacillus* spp., *Bifidobacterium* (α-proteobacteria)	Ectosymbiont	Production of bioactive compounds	Organic acids (lactic, formic, and acetic acids), hydrogen peroxide and various volatiles (benzene, toluene, octane,	Other Lipid	Bacterial and fungal pathogens (*Melissococcus plutonius, Paenibacillus larvae Pseudomonas*, Enterobacteriocea, *Bacillus* and *Candida*)	*In vitro* defensive activity and In vivo fitness effects	252-259

							ethylbenzene and nonane), 3-OH fatty acids, 2-heptanone and various peptides	Other Peptides			
Insecta, Hymenoptera	Honey bees: *Apis* spp. (Apidae)	Terrestrial	Larvae and Adult	*Bacillus* spp. (Firmicutes)	Ectosymbiont	Unknown (Proposed: production of bioactive compounds)	Unknown	-	Pathogenic fungi Chalkbrood causative agent (*Ascosphaera apis*)	*In vitro* defensive activity	[253, 260, 261]
Insecta, Hymenoptera	Honey bees: *Apis* spp. (Apidae)	Terrestrial	Adult	Mucorales, Aspergilli, Penicilli	Ectosymbiont	Unknown (Proposed: production of bioactive compounds)	Unknown	-	Pathogenic fungi (*Ascosphaera apis*)	*In vitro* defensive activity	[252]
Insecta, Hymenoptera	Bumble bees: *Bombus* spp. (Apidae)	Terrestrial	Adult	*Gilliamella apicola*	Ectosymbiont	Unknown (Proposed: colonization resistance)	Unknown	-	Gut trypanosomatid parasite (*Crithidia bombi*)	Negative correlation between presence of symbiont and parasite in wild populations	[262-268]
Insecta, Diptera	Mosquitoes: *Aedes* spp. (Culicidae)	Terrestrial	Adult	*Wolbachia pipientis* (α-proteobacteria)	Intracellular endosymbiont	Stimulation of immune system	Induces Toll pathway and antimicrobial peptide production in host	-	Pathogenic viruses	*In vivo* reduction of virus titers and reduced transmission capacities	[269, 270]
Insecta, Diptera	Mosquitoe: *Culex quinquefasciatus* (Culicidae)	Terrestrial	Adult	*Wolbachia pipientis* (α-proteobacteria)	Intracellular endosymbiont	Unknown	Unknown	-	Pathogenic viruses	*In vivo* reduction of virus titers and reduced transmission capacities	[271]
Insecta, Diptera	Fruit flies: *Drosophila* spp. Drosophilidae)	Terrestrial	Adult	*Wolbachia pipientis* (α-proteobacteria)	Intracellular endosymbiont	Unknown hypothesized: stimulation of immune system and/or production of bioactive compound)	Unknown	-	Pathogenic viruses	*In vivo* fitness benefits	[270-274]
Insecta, Diptera	Fruit fly: *Drosophila hydei* (Drosophilidae)	Terrestrial	Larva and Adult	*Spiroplasma* sp. (Mollicutes)	Intra- and extracellular endosymbiont	Unknown	Unknown	-	Parasitoid wasp (*Leptopilina heterotoma*)	*In vivo* fitness benefits	[275]
Insecta, Diptera	*Drosophila melanogaster* (Drosophilidae)	Terrestrial	Food substrate	Various yeasts	Ectosymbiont	Secondary metabolite production	Unknown	Unknown	Aspergillus nidulans food competitor	*In vivo* fitness benefits	[276]
Insecta, Diptera	Fruit fly: *Drosophila neotestacea* (Drosophilidae)	Terrestrial	Adult	*Spiroplasma* sp. (Mollicutes)	Intra- and extracellular endosymbiont	Unknown	Unknown ribosomal-inactivating protein	-	Nematode (*Howardula aoronymphium*)	*In vivo* fitness benefits	[274, 277]
Insecta, Diptera	House fly: *Musca domestica* (Muscidae)	Terrestrial	Larva	*Klebsiella oxytoca* (ϒ-proteobacteria), *Bacillus cereus* (Firmicutes)	Ectosymbiont	Unknown (proposed: colonization resistance or production of bioactive compounds)	Unknown	-	Fungi	*In vivo* fitness benefits	[278]
Chordata, Tetraodontiformes	Atlantic salmon *Salmo salar*, gilthead seabream *Sparus aurata*, flathead mullet *Mugil cephalus* and other fish species	Limnic/Marine	Adult (gut)	*Carnobacterium, Lactobacillus* and other Lactic acid bacteria (Firmicutes)	Ectosymbiont	Colonization resistance, stimulation of immune system, production of bioactive compounds	Bacteriocins (Carnocin UI49, Piscicocin V1, Divercin V41) and organic acids (lactic and acetic acid)	Ribosomal peptides , Other	Bacterial pathogens	*In vitro* defensive activity, *in vivo* fitness benefits, defensive compounds elucidated	[279-282]
Chordata, Tetraodontiformes	Puffer fish: *Spheroides rubripes* (Tetraodontidae) and several other marine organisms	Marine	Stage not specified	*Vibrio, Pseudomonas*, Actinomycetes and others (Proteobacteria, Actinobacteria, Firmicutes and Bacteroidetes)	Unknown	Secondary metabolite production	Tetrodotoxin	Other	Predators	Defensive compound elucidated	[113, 115, 117]

Chordata,	Newts and Salamanders: *Taricha* spp., *Cynops* spp. and others (Caudata, Ambystomatidae and Salamandridae) Frogs: *Atelopus* spp. and other anurans (Anura: Brachycephalidae, Dendrobatidae, Bufonidae and Rhacophoridae)	Limnic/Terrestrial	Adult, eggs and larvae (some species)	Unknown (bacterial origin uncertain)	Unknown	Secondary metabolite production	Tetrodotoxin	Other	Snake predators	Defensive compound elucidated, active secretion upon predator encounter, toxicity to predators, coevolutionary arms race with snake predators	113, 283-288
Chordata	Red back salamander: *Plethodon cinereus* (Caudata: Salamandridae)	Limnic/Terrestrial	Adult (skin and gut)	*Janthinobacterium lividum* (β-proteobacteria) *Lysobacter gummosus* (ϒ-proteobacteria)	Ectosymbiont	Secondary metabolite production	Indole-3-carboxaldehyde and violacein 2,4-diacetylphloroglucinol	Other	Fungal pathogen (*Batrachochytrium dendrobatidis*)	*In vitro* defensive activity , defensive compounds elucidated, co-occurrence of defensive compounds and symbiotic bacteria on host	289-293
Chordata	Mountain yellow-legged frog: *Rana muscosa* (Anura: Ranidae)	Limnic/Terrestrial	Adult (skin)	*Janthinobacterium lividum* (β-proteobacteria)	Ectosymbiont	Secondary metabolite production	Violacein	Other	Fungal pathogen (*Batrachochytrium dendrobatidis*)	*In vivo* fitness benefits, defensive compound elucidated	294
Chordata	Mountain yellow-legged frog: *Rana muscosa* (Anura: Ranidae)	Limnic/Terrestrial	Adult (skin)	*Pseudomonas fluorescens* (ϒ-proteobacteria)	Ectosymbiont	Synergistic effect of compound with host immune system	2,4-diacetylphloroglucinol	Other	Fungal pathogen Batrachochytrium dendrobatidis)	*In vitro* defensive activity , defensive compounds elucidated	295
Chordata	Hoopoe birds: *Upupa epops* (Coraciformes: Upupidae)	Terrestrial	Adult (feathers), and eggs	*Enterococcus faecalis* (Firmicutes)	Ectosymbiont	Secondary metabolite production	Bacteriocins (enterocin MR10 and AS-48) and mixture of volatiles (main: Butanoic acid, 2-methyl butanoic acid, 4-methyl pentanoic acid, indole, 3-phenyl propanoic acid and 4-chloro indole)	Ribosomal peptides , Other	Bacterial pathogens (*Bacillus licheniformis*, *Staphylococcus* and several Enterobacteriaceae)	*In vivo* fitness benefits, *in vitro* defensive activity , defensive compounds elucidated	296-301
Chordata	Human: *Homo sapiens* (Primates: Hominidae)	Terrestrial	Stage not specified (skin and nasal cavity)	*Staphylococcus epidermis* (Firmicutes)	Ectosymbiont	Secondary metabolite production, stimulation of immune system, colonization resistance	Epidermin, Pep5, epilancin K7 , modulin PSMγ and PSMδ, (thiolactone-containing pheromone AMPs), ESP serine protease	Ribosomal peptides	Pathogenic microbes (*Staphylococcus aureus*)	*In vitro* defensive activity, defensive compounds elucidated, rate of pathogen colonization decreased in presence of symbiont.	302-306
Chordata	Human: *Homo sapiens* (Primates: Hominidae)	Terrestrial	Stage not specified (intestine)	*Bacteroides fragilis* (Bacteroidetes)	Ectosymbiont	Modulation of immune system suppresses inflammatory response)	Polysaccharide A (PSA)	Other	Opportunistic bacterial pathogen (*Helicobacter hepaticus*)	*In vivo* fitness benefits, defensive compounds elucidated	307
Chordata	Laboratory mice *Mus musculus* (strain C57BL/6J) (Rodentia: Muridae)	Terrestrial	Not specified	Herpesvirus	Endosymbiont	Stimulation of immune system	Effect in immune system: prolonged production of the antiviral cytokine interferon-c and systemic activation of macrophages	-	Bacterial pathogens (*Listeria monocytogenes* and *Yersinia pestis*)	*In vivo* fitness benefits	308

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