

Supporting Information

McFall-Ngai et al. 10.1073/pnas.1218525110

Suggested Readings

Erwin DH, et al. (2011) The Cambrian conundrum: Early divergence and later ecological success in the early history of animals. *Science* 334(6059):1091–1097.

McFall-Ngai M (2007) Adaptive immunity: Care for the community. *Nature* 445(7124):153.

[Editorial] (2011) Microbiology by numbers. *Nat Rev Micro* 9:628.

Siegl A, et al. (2011) Single-cell genomics reveals the lifestyle of Poribacteria, a candidate phylum symbiotically associated with marine sponges. *ISME J* 5(1):61–70.

Woese CR, Kandler O, Wheelis ML (1990) Towards a natural system of organisms: Proposal for the domains Archaea, Bacteria, and Eucarya. *Proc Natl Acad Sci USA* 87(12):4576–4579.

Wolfe N (2013) Small, small world. *Natl Geographic* 223:136–147.

Bacteria and the Origins of Animals. Abedin M, King N (2008) The premetazoan ancestry of cadherins. *Science* 319(5865):946–948.

Dayel MJ, et al. (2011) Cell differentiation and morphogenesis in the colony-forming choanoflagellate *Salpingoeca rosetta*. *Dev Biol* 357(1):73–82.

King N (2004) The unicellular ancestry of animal development. *Dev Cell* 7(3):313–325.

King N, Hittinger CT, Carroll SB (2003) Evolution of key cell signaling and adhesion protein families predates animal origins. *Science* 301(5631):361–363.

Matz C, Kjelleberg S (2005) Off the hook—How bacteria survive protozoan grazing. *Trends Microbiol* 13(7):302–307.

Michod RE (2007) Evolution of individuality during the transition from unicellular to multicellular life. *Proc Natl Acad Sci USA* 104(Suppl 1):8613–8618.

Thomas T, et al. (2010) Functional genomic signatures of sponge bacteria reveal unique and shared features of symbiosis. *ISME J* 4(12):1557–1567.

Intertwining Genomes. Caricilli AM, et al. (2011) Gut microbiota is a key modulator of insulin resistance in TLR 2 knockout mice. *PLoS Biol* 9(12):e1001212.

Danchin EG, et al. (2010) Multiple lateral gene transfers and duplications have promoted plant parasitism ability in nematodes. *Proc Natl Acad Sci USA* 107(41):17651–17656.

Flajnik MF, Kasahara M (2010) Origin and evolution of the adaptive immune system: Genetic events and selective pressures. *Nat Rev Genet* 11(1):47–59.

Human Microbiome Project Consortium (2012) Structure, function and diversity of the healthy human microbiome. *Nature* 486(7402):207–214.

Iyer LM, Aravind L, Coon SL, Klein DC, Koonin EV (2004) Evolution of cell-cell signaling in animals: Did late horizontal gene transfer from bacteria have a role? *Trends Genet* 20(7):292–299.

Koch H, Schmid-Hempel P (2011) Socially transmitted gut microbiota protect bumble bees against an intestinal parasite. *Proc Natl Acad Sci USA* 108(48):19288–19292.

Shin SC, et al. (2011) *Drosophila* microbiome modulates host developmental and metabolic homeostasis via insulin signaling. *Science* 334(6056):670–674.

Partners in Animal Development. Cash HL, Whitham CV, Behrendt CL, Hooper LV (2006) Symbiotic bacteria direct expression of an intestinal bactericidal lectin. *Science* 313(5790):1126–1130.

Fraune S, Bosch TC (2007) Long-term maintenance of species-specific bacterial microbiota in the basal metazoan *Hydra*. *Proc Natl Acad Sci USA* 104(32):13146–13151.

Goodman AL, et al. (2009) Identifying genetic determinants needed to establish a human gut symbiont in its habitat. *Cell Host Microbe* 6(3):279–289.

Hapfelmeier S, et al. (2010) Reversible microbial colonization of germ-free mice reveals the dynamics of IgA immune responses. *Science* 328(5986):1705–1709.

Hooper LV, et al. (2001) Molecular analysis of commensal host-microbial relationships in the intestine. *Science* 291(5505):881–884.

Orr HA (2005) The genetic theory of adaptation: A brief history. *Nat Rev Genet* 6(2):119–127.

Rawls JF, Mahowald MA, Ley RE, Gordon JI (2006) Reciprocal gut microbiota transplants from zebrafish and mice to germ-free recipients reveal host habitat selection. *Cell* 127(2):423–433.

Reikvam DH, et al. (2011) Depletion of murine intestinal microbiota: Effects on gut mucosa and epithelial gene expression. *PLoS ONE* 6(3):e17996.

Rhee KJ, Sethupathi P, Driks A, Lanning DK, Knight KL (2004) Role of commensal bacteria in development of gut-associated lymphoid tissues and preimmune antibody repertoire. *J Immunol* 172(2):1118–1124.

Turnbaugh PJ, et al. (2006) An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* 444(7122):1027–1031.

Uribe A, Alam M, Midtvedt T, Smedfors B, Theodorsson E (1997) Endogenous prostaglandins and microflora modulate DNA synthesis and neuroendocrine peptides in the rat gastrointestinal tract. *Scand J Gastroenterol* 32(7):691–699.

Interdomain Communication. Bäckhed F, et al. (2004) The gut microbiota as an environmental factor that regulates fat storage. *Proc Natl Acad Sci USA* 101(44):15718–15723.

Brown AJ, et al. (2003) The Orphan G protein-coupled receptors GPR41 and GPR43 are activated by propionate and other short chain carboxylic acids. *J Biol Chem* 278(13):11312–11319.

Chedid L (1983) Muramyl peptides as possible endogenous immunopharmacological mediators. *Microbiol Immunol* 27(9):723–732.

Cossart P, Boquet P, Normark S, Rappuoli R (2005) *Cellular Microbiology* (ASM Press, Washington, DC).

Francois F, et al. (2011) The effect of *H. pylori* eradication on meal-associated changes in plasma ghrelin and leptin. *BMC Gastroenterol* 11:37.

Fritz JH, Ferrero RL, Philpott DJ, Girardin SE (2006) Nod-like proteins in immunity, inflammation and disease. *Nat Immunol* 7(12):1250–1257.

Girardin SE, et al. (2003) Nod1 detects a unique muropeptide from gram-negative bacterial peptidoglycan. *Science* 300(5625):1584–1587.

Irie Y, Parsek MR (2008) Quorum sensing and microbial biofilms. *Curr Top Microbiol Immunol* 322:67–84.

Kimura I, et al. (2011) Short-chain fatty acids and ketones directly regulate sympathetic nervous system via G protein-coupled receptor 41 (GPR41). *Proc Natl Acad Sci USA* 108(19):8030–8035.

Ley RE, Turnbaugh PJ, Klein S, Gordon JI (2006) Microbial ecology: Human gut microbes associated with obesity. *Nature* 444(7122):1022–1023.

Said HM (2011) Intestinal absorption of water-soluble vitamins in health and disease. *Biochem J* 437(3):357–372.

Samuel BS, et al. (2008) Effects of the gut microbiota on host adiposity are modulated by the short-chain fatty-acid binding G protein-coupled receptor, Gpr41. *Proc Natl Acad Sci USA* 105(43):16767–16772.

Stevenson LG, et al. (2007) Rhomboid protease AarA mediates quorum-sensing in *Providencia stuartii* by activating TatA of the twin-arginine translocase. *Proc Natl Acad Sci USA* 104(3):1003–1008.

Vijay-Kumar M, et al. (2010) Metabolic syndrome and altered gut microbiota in mice lacking Toll-like receptor 5. *Science* 328(5975):228–231.

Webb JS, Givskov M, Kjelleberg S (2003) Bacterial biofilms: Prokaryotic adventures in multicellularity. *Curr Opin Microbiol* 6(6):578–585.

Nested Ecosystems. Dunbar HE, Wilson AC, Ferguson NR, Moran NA (2007) Aphid thermal tolerance is governed by a point mutation in bacterial symbionts. *PLoS Biol* 5(5):e96.

Gonzalez A, et al. (2011) Our microbial selves: What ecology can teach us. *EMBO Rep* 12(8):775–784.

Hartmann M, et al. (2012) Significant and persistent impact of timber harvesting on soil microbial communities in Northern coniferous forests. *ISME J* 6(12):2199–2218.

Knight TM, Chase JM (2005) Ecological succession: Out of the ash. *Curr Biol* 15(22):R926–R927.

Oliver KM, Russell JA, Moran NA, Hunter MS (2003) Facultative bacterial symbionts in aphids confer resistance to parasitic wasps. *Proc Natl Acad Sci USA* 100(4):1803–1807.

Table S1. Examples of signals and receptors used in bacteria to animal communication

Bacterial signal	Animal receptor/enzyme
AI-3 (quorum signal) (1)	Epidermal growth-factor receptor (EGFr)
Homoserine lactone(quorum signal) (2–4)	?
Acetate(5)	?
Butyrate (6, 7)	G protein-coupled receptors (GPR41 and GPR43)
Bile-acid derivatives (8)	G protein-coupled bile acid receptor 1 (Gpbar1)
Polysaccharide A (PSA) (9)	?
Trimethylamine (TMA) (10)	Macrophage scavenger receptor
?	GABA _A and GABA _B (11)
Tripeptides (12)	Angiotensin converting enzyme (ACE)
Invasion (13)	Integrin
Peptidoglycan (PGN) (14–16)	NOD1
Lipopolysaccharide (LPS) (17)	Toll-like receptor 4 (TLR4)
Indole (18)	Toll-like receptor 3/9 (TLR3/9)
<i>N</i> -formyl peptides (19)	Formyl peptide receptors
Several other ligands (20)	Other TLRs, NLRs, RLRs, lectins, etc.

- Gallio M, Sturgill G, Rather P, Kylsten P (2002) A conserved mechanism for extracellular signaling in eukaryotes and prokaryotes. *Proc Natl Acad Sci USA* 99(19):12208–12213.
- Ritchie AJ, et al. (2005) The *Pseudomonas aeruginosa* quorum-sensing molecule *N*-3-(oxododecanoyl)-L-homoserine lactone inhibits T-cell differentiation and cytokine production by a mechanism involving an early step in T-cell activation. *Infect Immun* 73(3):1648–1655.
- Smith RS, Harris SG, Phipps R, Iglewski B (2002) The *Pseudomonas aeruginosa* quorum-sensing molecule *N*-3-(oxododecanoyl)homoserine lactone contributes to virulence and induces inflammation in vivo. *J Bacteriol* 184(4):1132–1139.
- Williams SC, et al. (2004) *Pseudomonas aeruginosa* autoinducer enters and functions in mammalian cells. *J Bacteriol* 186(8):2281–2287.
- Fukuda S, et al. (2011) Bifidobacteria can protect from enteropathogenic infection through production of acetate. *Nature* 469(7331):543–547.
- Brown AJ, et al. (2003) The Orphan G protein-coupled receptors GPR41 and GPR43 are activated by propionate and other short chain carboxylic acids. *J Biol Chem* 278(13):11312–11319.
- Kimura I, et al. (2011) Short-chain fatty acids and ketones directly regulate sympathetic nervous system via G protein-coupled receptor 41 (GPR41). *Proc Natl Acad Sci USA* 108(19):8030–8035.
- Swann JR, et al. (2011) Systemic gut microbial modulation of bile acid metabolism in host tissue compartments. *Proc Natl Acad Sci USA* 108(Suppl 1):4523–4530.
- Round JL, et al. (2011) The Toll-like receptor 2 pathway establishes colonization by a commensal of the human microbiota. *Science* 332(6032):974–977.
- Wang Z, et al. (2011) Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature* 472(7341):57–63.
- Bravo JA, et al. (2011) Ingestion of *Lactobacillus* strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proc Natl Acad Sci USA* 108(38):16050–16055.
- Tuomilehto J, et al. (2004) Effect of ingesting sour milk fermented using *Lactobacillus helveticus* bacteria producing tripeptides on blood pressure in subjects with mild hypertension. *J Hum Hypertens* 18(11):795–802.
- Wong KW, Isberg RR (2005) Emerging views on integrin signaling via Rac1 during invasion-promoted bacterial uptake. *Curr Opin Microbiol* 8(1):4–9.
- Eberl G (2010) A new vision of immunity: Homeostasis of the superorganism. *Mucosal Immunol* 3(5):450–460.
- Koropatnick TA, et al. (2004) Microbial factor-mediated development in a host-bacterial mutualism. *Science* 306(5699):1186–1188.
- Altura MA, Stabb E, Goldman W, Apicella M, McFall-Ngai MJ (2011) Attenuation of host NO production by MAMPs potentiates development of the host in the squid-vibrio symbiosis. *Cell Microbiol* 13(4):527–537.
- Ortega-Cava CF, et al. (2003) Strategic compartmentalization of Toll-like receptor 4 in the mouse gut. *J Immunol* 170(8):3977–3985.
- Bansal T, Alaniz RC, Wood TK, Jayaraman A (2010) The bacterial signal indole increases epithelial-cell tight-junction resistance and attenuates indicators of inflammation. *Proc Natl Acad Sci USA* 107(1):228–233.
- Wentworth CC, Jones RM, Kwon YM, Nusrat A, Neish AS (2010) Commensal-epithelial signaling mediated via formyl peptide receptors. *Am J Pathol* 177(6):2782–2790.
- Carvalho FA, Aitken JD, Vijay-Kumar M, Gewirtz AT (2012) Toll-like receptor-gut microbiota interactions: Perturb at your own risk! *Annu Rev Physiol* 74:177–198.

