Redacted Science Literature Review

Peer-Reviewed Papers Touching on Core Concepts

Compiled March 15, 2026

1. Fungal-Human Symbiosis

1a. Candida as Commensal with Beneficial/Regulatory Roles

On Commensalism of Candida

Ost KS, Round JL, et al.. Pathogens (MDPI), 2020. doi:10.3390/pathogens9030180

Reviews C. albicans commensal lifestyle, adhesion, colonization of epithelial surfaces, and interactions with host immune response and microbiota. Demonstrates that C. albicans gene expression is intimately connected to host immune status, enabling it to sense and adapt to the host as a successful colonizer.

Commensal Fungus Candida albicans Maintains a Long-Term Mutualistic Relationship with the Host To Modulate Gut Microbiota and Metabolism

Mishra AA et al.. Microbiology Spectrum, 2023. doi:10.1128/spectrum.02462-22

Demonstrates that C. albicans in its commensal state maintains a long-term mutualistic relationship with the host, regulating microbial dynamics and host physiology. Shows that dietary C. albicans mitigates high-fat-diet-induced metabolic imbalances and stimulates appetite-regulated hormones. Concludes C. albicans is 'a bona fide admirable companion of the host.'

Candida albicans Virulence Traits in Commensalism and Disease

Various authors. Current Clinical Microbiology Reports, 2024. doi:10.1007/s40588-024-00235-8

Reviews how fungi influence diverse physiological processes including host protection, metabolism, and behaviour. Demonstrates that candidalysin, typically considered a virulence factor, actually mediates interference with commensal bacteria metabolism, enhancing C. albicans competitive fitness in the gut.

Controlling Candida: Immune Regulation of Commensal Fungi in the Gut

Various authors. Infection and Immunity, 2024. doi:10.1128/iai.00516-23

Comprehensive review of immune interactions with commensal fungi in the intestine. Shows that immune regulation constrains fungal virulence factors while maintaining stable colonization. Highlights sIgA regulation of fungal commensalism and its species-specific nature.

Friendly Fungi: Symbiosis with Commensal Candida albicans

Various authors. PMC, 2023. doi:10.1016/j.it.2023.01.005

Proposes that fluid immunogenicity of C. albicans is a consequence of long-term coevolution with mammalian hosts. Suggests that expression of virulence factors undergoes continuous refinement to achieve optimal symbiosis, maximizing benefits while minimizing pathological inflammation.

BRIDGES: 1a, 1b

Immunosurveillance of Candida albicans Commensalism by the Adaptive Immune System

Various authors. Mucosal Immunology, 2022. doi:10.1038/s41385-022-00536-5

Shows that commensal fungi induce antigen-specific immune responses that maintain immune homeostasis. C. albicans has host-beneficial effects protecting against various microbial insults. Reviews mechanisms ensuring continuous immunosurveillance during mucosal colonization.

Colonization with the Commensal Fungus Candida albicans Perturbs the Gut-Brain Axis Through Dysregulation of Endocannabinoid Signaling

Various authors. PMC / Psychoneuroendocrinology, 2020. doi:10.1016/j.psyneuen.2020.104808

KEY BRIDGE PAPER. Demonstrates that C. albicans colonization in adolescent mice affects the gut-brain axis through specific changes in the endocannabinoidome, producing a stress-like behavioral and neuroendocrine phenotype including altered HPA axis function and corticosterone levels. Shows C. albicans alters host physiology beyond the GI tract through endocannabinoid signaling.

BRIDGES: 1a, 2b, 4a, 4b

Adapting to Survive: How Candida Overcomes Host-Imposed Constraints During Human Colonization

Various authors. PLOS Pathogens, 2020. doi:10.1371/journal.ppat.1008478

Reviews the remarkable ability of Candida species to overcome host-imposed constraints including nutrient limitation, pH fluctuations, and oxidative stress. Proposes that the genetic circuits governing Candida adaptation can be exploited for new antifungal targets.

1b. Co-Evolutionary Frameworks

Experimental Evolution of a Fungal Pathogen into a Gut Symbiont

Tso GHW et al.. Science, 2018. doi:10.1126/science.aat0537

Landmark paper demonstrating that C. albicans can be adaptively evolved in the mouse gut, losing its main virulence program while gaining the ability to protect hosts against systemic infections. Directly demonstrates the pathogen-to-mutualist evolutionary transition.

Systems Biology of Host-Candida Interactions: Understanding How We Shape Each Other

Various authors. PMC, 2020. doi:10.1128/mBio.00849-20

Frames C. albicans-host interactions through niche construction theory, examining eco-evolutionary feedback loops. Shows that C. albicans may play a major role in continuously shaping immune surveillance and the host microbiome throughout the lifetime of the host.

Microbial Evolution and Transitions Along the Parasite-Mutualist Continuum

Drew GC, Stevens EJ, King KC. Nature Reviews Microbiology, 2021. doi:10.1038/s41579-021-00550-7

Reviews evolutionary transitions of host-microorganism symbioses along the parasite-mutualist continuum, including mechanisms underlying evolutionary changes and selective pressures involved. Includes discussion of Candida transitions.

Fungal Interactions with the Human Host: Exploring the Spectrum of Symbiosis

Various authors. PMC, 2017. doi:10.1016/j.mib.2017.10.020

Views fungal-human interactions as a spectrum of symbiotic relationships. Notes that C. albicans is an obligate commensal with no known environmental reservoir, implying deep evolutionary entanglement with mammalian hosts. Considers potential of fungal symbionts as mutualists.

Candida albicans: Adapting to Succeed

Various authors. PMC, 2014. doi:10.1128/9781555817176.ch5

States that redundancy of signaling pathways in C. albicans 'is likely to have developed through millions of years of co-evolution as a normal commensal of mammalian hosts.' Argues the biology and pathogenicity of C. albicans can only be understood within the context of its long association with mammalian hosts.

Candida albicans Commensalism and Pathogenicity Are Intertwined Traits Directed by a Tightly Knit Transcriptional Regulatory Circuit

Perez JC et al.. PLOS Biology, 2013. doi:10.1371/journal.pbio.1001510

Identified ~800 target genes in a tightly knit regulatory circuit governing both commensal and pathogenic lifestyles. Shows that commensalism and pathogenicity are intertwined, not separate programs, supporting the idea of a unified co-evolutionary architecture.

2. Endocannabinoid System (ECS) as a Signaling Interface

2a. ECS as a Conserved Master Regulatory System

The Endocannabinoid System in Human Disease: Molecular Signaling, Receptor Pharmacology, and Therapeutic Innovation

Various authors. International Journal of Molecular Sciences (MDPI), 2025. doi:10.3390/ijms262211132

Describes the ECS as 'a fundamental regulatory system that maintains homeostasis across multiple organs.' Explicitly maps the ECS as an integrator of CNS, immune system, and gut microbiota through the microbiota-gut-brain axis, modulating neuroinflammation, gut permeability, and HPA axis function.

BRIDGES: 2a, 2b

Endocannabinoid System Acts as a Regulator of Immune Homeostasis in the Gut

Acharya N et al.. Proceedings of the National Academy of Sciences, 2017. doi:10.1073/pnas.1612177114

Demonstrates the ECS regulates immune homeostasis in the gut/pancreas, modulating CX3CR1hi macrophages and Tr1 cells. Describes 'a conversation between the nervous and immune systems using distinct receptors.' Shows oral anandamide administration provides protection from type 1 diabetes.

Endocannabinoids and Immune Regulation

Pandey R et al.. Pharmacological Research, 2009. doi:10.1016/j.phrs.2009.03.019

Reviews endocannabinoid effects on immune regulation: suppression of cell activation, inhibition of pro-inflammatory cytokines, NF-kB-dependent apoptosis, and modulation of Th1/Th2 balance. Proposes that endocannabinoid signaling in lymphoid tissue provides tonic control of immune cell activation.

The Endocannabinoid System: A New Frontier in Addressing Psychosomatic Challenges

Various authors. Journal of Clinical and Basic Psychosomatics, 2024. doi:10.36922/jcbp.2288

Reviews bidirectional relationship between ECS and HPA axis. Shows ECS modulation affects stress responsiveness, immune function, and the interplay between emotional well-being and physical symptoms. Positions the ECS as a key modulator of the body's stress response.

BRIDGES: 2a, 4a

Exploring the Versatile Roles of the Endocannabinoid System and Phytocannabinoids in Modulating Bacterial Infections

Various authors. Infection and Immunity, 2024. doi:10.1128/iai.00020-24

Describes the ECS as having evolved from 'maintaining homeostasis' to 'a complex orchestrator influencing various physiological processes beyond its original association with the nervous system.' Reviews ECS involvement in host-pathogen interactions across multiple infection types.

2b. ECS Mediating Host-Microbiome Communication

The Microbiome and Gut Endocannabinoid System in the Regulation of Stress Responses and Metabolism

Various authors. Frontiers in Cellular Neuroscience, 2022. doi:10.3389/fncel.2022.867267

Hypothesizes that crosstalk between microbiota and intestinal endocannabinoid system has a prominent role in stress-induced changes in the gut-brain axis. Shows that microbiota composition influences ECS activity and vice versa, establishing bidirectional communication.

BRIDGES: 2a, 2b, 4b

The Gut Microbiome, Endocannabinoids and Metabolic Disorders

Di Marzo V, Ferraioli A. Journal of Endocrinology, 2021. doi:10.1530/JOE-20-0444

By the holder of the Canada Research Excellence Chair in the Microbiome-Endocannabinoidome Axis. Shows that the gut microbiome and endocannabinoidome communicate and influence each other during nutrient processing. Maps the mechanisms through which the adipose tissue and gut eCBomes affect the brain.

BRIDGES: 2a, 2b

Mutual Links Between the Endocannabinoidome and the Gut Microbiome

Various authors. Animals (MDPI), 2022. doi:10.3390/ani12030348

Demonstrates a profound link between the gut microbiome and the endocannabinoidome with mutual interactions controlling intestinal homeostasis, energy metabolism, and neuroinflammatory responses. Points to the existence of an eCBome-gut microbiome axis.

BRIDGES: 2a, 2b

Symphony of the Gut Microbiota and Endocannabinoidome: A Molecular and Functional Perspective

Various authors. Frontiers in Cellular and Infection Microbiology, 2025. doi:10.3389/fcimb.2025.1566290

Provides forward-looking perspectives on the gut microbiota-eCBome axis. Reviews how gut bacteria produce compounds that modulate ECS tone, including metabolites that interact with GPCR receptors. Notes that fungi, archaea, and viruses are part of the microbiota ecosystem interacting with the eCBome.

BRIDGES: 2a, 2b

The Endocannabinoids-Microbiota Partnership in Gut-Brain Axis Homeostasis: Implications for Autism Spectrum Disorders

Various authors. Frontiers in Pharmacology, 2022. doi:10.3389/fphar.2022.869606

Reviews the endocannabinoid-microbiota partnership as a mutual communication system. Notes CB1 receptors at the intestinal epithelium in proximity with neuroendocrine cells, implying ECS machinery regulates gut barrier integrity. Highlights the ECS as an interface between gut microbiota and brain function.

BRIDGES: 2a, 2b, 4b

2c. ECS as Cross-Kingdom/Inter-Species Signaling

The Evolution and Comparative Neurobiology of Endocannabinoid Signalling

Elphick MR. Philosophical Transactions of the Royal Society B, 2012. doi:10.1098/rstb.2011.0394

Comprehensive review of ECS evolutionary conservation. Shows ECS metabolic enzymes (NAPE-PLD, FAAH, DAGL, MAGL) occur throughout the animal kingdom from Hydra to humans, while CB1/CB2 receptors are restricted to chordates. Proposes endocannabinoid-mediated retrograde synaptic signaling is evolutionarily ancient.

BRIDGES: 2a, 2c

Cannabinoid Receptors in Invertebrates

McPartland JM et al.. Journal of Evolutionary Biology, 2006. doi:10.1111/j.1420-9101.2005.01028.x

Maps cannabinoid receptor distribution across animal phyla. Notes insects continue to biosynthesize 2-AG despite lacking CB receptors, supporting the hypothesis that 'there is greater evolutionary pressure to conserve ligands than to conserve receptors.' Key for understanding cross-kingdom signaling conservation.

BRIDGES: 2c

The Invertebrate Ancestry of Endocannabinoid Signalling

Elphick MR, Satou Y, Satoh N. Gene, 2003. doi:10.1016/S0378-1119(02)01094-6

Identifies CiCBR, an orthologue of vertebrate cannabinoid receptors in the sea squirt Ciona intestinalis. Demonstrates anandamide and 2-AG are present in primitive animals including Hydra, indicating endocannabinoid biosynthesis 'may be an evolutionarily ancient phenomenon.'

BRIDGES: 2c

The Endocannabinoid System and Invertebrate Neurodevelopment and Regeneration

Various authors. International Journal of Molecular Sciences, 2021. doi:10.3390/ijms22052103

Reviews endocannabinoid system contributions to invertebrate neurodevelopment and regeneration. Shows that endocannabinoid signaling permeates virtually every aspect of both vertebrate and invertebrate physiology, highlighting it as a conserved signaling system across kingdoms.

BRIDGES: 2a, 2c

The Endocannabinoid System of Animals

Silver RJ. Animals (MDPI), 2019. doi:10.3390/ani9090686

Reviews the ECS across the animal kingdom, from Hydra to mammals. Notes the system has been found in all animals including sea urchins, leeches, and nematodes. States: 'Found in nearly all animals, the early emergence of the ECS in evolution indicates its biological importance.'

BRIDGES: 2a, 2c

3. Fungal Biochemistry and Cannabinoids

3a. Fungal Production of Cannabinoid/Cannabinoid-Like Compounds

Truffles Contain Endocannabinoid Metabolic Enzymes and Anandamide

Pacioni G, Rapino C, Zarivi O, et al.. Phytochemistry, 2015. doi:10.1016/j.phytochem.2014.11.012

KEY PAPER. Demonstrates that the black truffle (Tuber melanosporum) contains the major ECS metabolic enzymes (NAPE-PLD, FAAH, DAGL, MAGL) and anandamide, with increasing content at advancing maturity. Concludes 'anandamide and ECS metabolic enzymes have evolved earlier than endocannabinoid-binding receptors' and that anandamide may be 'an ancient attractant to truffle eaters.' A fungus producing a mammalian endocannabinoid.

BRIDGES: 2c, 3a

Phytocannabinoids: Origins and Biosynthesis

Kovalchuk I et al.. Trends in Plant Science, 2020. doi:10.1016/j.tplants.2020.05.005

Confirms phytocannabinoids occur in flowering plants, liverworts, and fungi. Notes that the mammalian brain has receptors responding to compounds found in these organisms, forming the endocannabinoid system. Reviews cannabinoid biosynthetic modularity enabling cross-kingdom synthetic biology.

BRIDGES: 2c, 3a

Complete Biosynthesis of Cannabinoids and Their Unnatural Analogues in Yeast

Luo X et al.. Nature, 2019. doi:10.1038/s41586-019-0978-9

Demonstrates complete cannabinoid biosynthesis in Saccharomyces cerevisiae from simple sugar galactose. While engineered rather than natural, demonstrates that fungal cellular machinery can support the full cannabinoid biosynthetic pathway, validating fungal-cannabinoid biochemical compatibility.

BRIDGES: 3a

Biotechnological Fungal Platforms for the Production of Biosynthetic Cannabinoids

Various authors. Journal of Fungi (MDPI), 2023. doi:10.3390/jof9020234

Reviews fungal platforms for cannabinoid biosynthesis. Notes that phytocannabinoids are found in fungi and liverworts naturally. Engineers Penicillium chrysogenum to produce THCA, demonstrating the potential of filamentous fungi as cannabinoid production platforms.

BRIDGES: 3a

Biotechnological Advancements Enabling Cannabinoid Biosynthesis in Engineered Fungi

Various authors. Frontiers in Fungal Biology, 2025. doi:10.3389/ffunb.2025.1660661

Reviews filamentous fungi including Aspergillus niger and Trichoderma reesei as cannabinoid production platforms. Notes fungi possess endogenous polyketide synthase and terpenoid pathways that align with the biochemical demands of cannabinoid production.
BRIDGES: 3a

Fungal Biotransformation of Cannabinoids: Potential for New Effective Drugs

Perrotin-Brunel H et al.. Various, 2009. PMID: 19333876

Reviews how fungi can biotransform cannabinoids, modifying their structure and potentially their pharmacological profile. Demonstrates fungi as 'the most inventive synthetic chemists,' capable of novel cannabinoid modifications not achievable through chemical synthesis alone.
BRIDGES: 3a, 3b

3b. Fungal Metabolites with Neuroactive/Endocrine-Active Properties

Bioactive Compounds and Antioxidant Potential of Truffles: A Comprehensive Review

Various authors. Antioxidants (MDPI), 2025. doi:10.3390/antiox14111341

Reviews the diverse bioactive compounds in truffles. Confirms anandamide presence in T. melanosporum with expression of key ECS metabolic enzymes. Notes anandamide's anticancer, anti-angiogenic, and apoptotic activities, demonstrating how a fungal-produced endocannabinoid has significant physiological effects on mammalian systems.
BRIDGES: 3a, 3b

4. Pituitary and Neuroendocrine Interactions with Fungi

4a. Fungal Effects on Hypothalamic-Pituitary Axis

Fungi and Endocrine Dysfunction

Various authors. Endotext (NCBI Bookshelf), 2021. NBK572246

Comprehensive review of fungal involvement in endocrine glands including the pituitary. Notes that fungi can affect adrenals, pituitary, thyroid, pancreas, and gonads. Reviews the bidirectional relationship: fungi affect endocrine function, while endocrine disorders (diabetes, Cushing's) predispose to fungal disease.

Endocrine and Metabolic Manifestations of Invasive Fungal Infections and Systemic Antifungal Treatment

Various authors. Mayo Clinic Proceedings, 2008. doi:10.4065/83.9.1046

KEY PAPER. Notes that 'the pituitary gland has a role in innate antifungal immunity; Breuel et al showed that pituitary receptors sense circulating Candida glucans and respond by TLR4 and CD14 gene expression.' Directly demonstrates that the pituitary actively senses fungal presence and responds immunologically.
BRIDGES: 4a

Anterior Pituitary Cells Express Pattern Recognition Receptors for Fungal Glucans: Implications for Neuroendocrine Immune Involvement in Response to Fungal Infections

Breuel KF et al.. Neuroimmunomodulation, 2004. doi:10.1159/000074563

Demonstrates that anterior pituitary cells express pattern recognition receptors specifically for fungal glucans (beta-glucans from Candida). Shows TLR4 and CD14 expression in pituitary tissue in response to fungal components. Directly connects pituitary function to fungal detection.

BRIDGES: 4a

Infections of the Hypothalamic-Pituitary Region

Pekic S, Miljic D, Popovic V. Endotext (NCBI Bookshelf), 2024. NBK532083

Reviews infections of the hypothalamic-pituitary region. Discusses pathophysiological mechanisms of pituitary dysfunction following infections, including autoimmune processes and axonal injury with consequent neuroendocrine dysfunction. Notes hypothalamic-pituitary fungal infections are extremely rare but have significant endocrine consequences.

Biological Poisons Targeting the Pituitary Gland: Insights Across the Five Kingdoms

Various authors. Frontiers in Endocrinology, 2025. doi:10.3389/fendo.2025.1708792

Reviews effects of biologically derived substances from all five kingdoms on the hypothalamic-pituitary axis. Covers how fungal compounds may alter hormonal regulation, leading to temporary or persistent pituitary dysfunction through multiple mechanisms.

BRIDGES: 4a

4b. Mycobiome Influence on CNS/Neuroendocrine Function

Altered Gut Bacterial-Fungal Interkingdom Networks in Patients with Current Depressive Episode

Various authors. Brain and Behavior, 2020. doi:10.1002/brb3.1677

Shows that gut microbiota is essential for brain function through inflammation and the HPA axis. Demonstrates that fungal gut dysbiosis in depression is characterized by altered composition and reduced biodiversity. Finds that the correlation network between bacteria and fungi is disrupted in depressive episodes.

BRIDGES: 4b

Colonization with the Commensal Fungus Candida albicans Perturbs the Gut-Brain Axis Through Dysregulation of Endocannabinoid Signaling

Various authors. Psychoneuroendocrinology, 2020. doi:10.1016/j.psyneuen.2020.104808

[CROSS-LISTED from 1a] Demonstrates C. albicans colonization disrupts the gut-brain axis via specific changes in endocannabinoid signaling, affecting HPA axis function, corticosterone levels, and anxiety-like behavior. A direct mechanistic link between fungal colonization, ECS dysregulation, and neuroendocrine output.

BRIDGES: 1a, 2b, 4a, 4b

5. Fungal Network Intelligence

5a. Fungal Biofilms/Hyphal Networks as Communication Systems

Towards Fungal Computer

Adamatzky A et al.. Interface Focus (Royal Society), 2018. doi:10.1098/rsfs.2018.0029

Proposes fungi as computing devices: information represented by electrical spikes, computation implemented in mycelium networks, interface via fruit bodies. Estimates a single Armillaria bulbosa network could contain nearly a trillion branching points (elementary processing units). Demonstrates that electrical activity in fungi could be used for communication.

Logics in Fungal Mycelium Networks

Adamatzky A, Dehshibi MM, Wösten HAB. Logica Universalis, 2022. doi:10.1007/s11787-022-00318-4

Demonstrates that living mycelium networks are capable of efficient sensorial fusion over large areas and distributed decision making. Information processing is implemented via propagation of electrical and chemical signals paired with morphological changes. Shows Boolean logic gates implementable in single fungal colonies.

Mining Logical Circuits in Fungi

Adamatzky A et al.. Scientific Reports (Nature), 2022. doi:10.1038/s41598-022-20080-3

Demonstrates experimental laboratory prototypes of many-input Boolean functions implemented in fungal materials from oyster fungi P. ostreatus. Shows mycelium bound composites can implement representative functions from all classes of cellular automata complexity including computationally universal functions.

5b. Mycelial Networks as Information-Processing Architectures

Electrical Integrity and Week-Long Oscillation in Fungal Mycelia

Fukasawa Y et al.. Scientific Reports, 2024. doi:10.1038/s41598-024-66223-6

Demonstrates sustained electrical oscillations in fungal mycelia over week-long periods. Shows evidence of memory and decision-making abilities in fungi despite lacking a central nervous system. Researchers stated: 'intelligent behavior of organisms can be achieved without brain and consciousness.'

Fungal Cognition: Shape Recognition in Wood-Decaying Fungi

Fukasawa Y et al.. Fungal Ecology, 2024. doi:10.1016/j.funeco.2024.101375

Demonstrates that wood-decaying fungi can recognize and remember spatial shapes of food sources, maintaining pattern integrity over months. Mycelial networks retained circle and cross patterns rather than simply expanding through available space. Evidence of spatial memory without neural architecture.

Sustainable Memristors from Shiitake Mycelium for High-Frequency Bioelectronics

Various authors. Various, 2024. Recent preprint/publication

Demonstrates that shiitake fungi can function as memristors (memory resistors) capable of being grown, trained, and preserved. Shows fungal computing accuracy of 90% at frequencies up to 5.85 kHz. Notes shiitake exhibits radiation resistance, suggesting viability for aerospace applications.

Summary: Multi-Category Bridge Papers

The following papers bridge multiple categories and are therefore most directly relevant to the Redacted Science framework:

4-category bridge: 'Colonization with Candida albicans Perturbs the Gut-Brain Axis Through Dysregulation of Endocannabinoid Signaling' (2020) - Bridges 1a, 2b, 4a, 4b. This is the single most relevant paper found: it directly connects commensal Candida colonization to endocannabinoid system disruption to pituitary (HPA) axis modulation to CNS effects.

2-3 category bridges: 'Friendly Fungi: Symbiosis with Commensal C. albicans' (1a, 1b); 'ECS in Human Disease' (2a, 2b); 'Evolution of Endocannabinoid Signalling' (2a, 2c); 'Truffles Contain Anandamide' (2c, 3a); 'Microbiome and Gut ECS in Stress' (2a, 2b, 4b); 'Endocannabinoids-Microbiota Partnership / ASD' (2a, 2b, 4b); 'ECS: Psychosomatic Challenges' (2a, 4a)

Key gap in the literature: No paper was found that directly examines Candida-produced endocannabinoids as a co-evolutionary communication mechanism with the mammalian ECS. The truffle anandamide paper (Pacioni 2015) shows fungi CAN produce endocannabinoids. The Candida gut-brain-ECS paper (2020) shows Candida colonization DOES alter the endocannabinoidome. But no one has connected these into a framework proposing that commensal Candida deliberately uses endocannabinoid signaling as an inter-species communication interface. That gap is where Redacted Science sits.