Addiction as Stuck-State Substrate Lock-In

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Abstract

Substance use disorders are conventionally understood through reward circuitry, receptor adaptation, psychosocial exposure, trauma history, drug availability, and learned behavior. Under the Redacted Science framework, those explanations are not rejected. They are reorganized around an additional upstream layer: organism-host governance. This paper proposes that a subset of addiction represents stuck-state substrate lock-in, in which *Candida albicans* and the host system have rebalanced around recurrent exogenous substrate inputs. Craving is read as organism-to-host signaling demanding substrate restoration. Withdrawal is read as system distress during substrate restriction. Tolerance and relapse are read not only as host receptor adaptation, but as organism-state recalibration around repeated substrate exposure.

The central claim is two-part. First, the organism layer is real, measurable, and predictive. Second, it integrates with existing neurobiological, psychosocial, trauma, and behavioral models rather than displacing them. The framework does not claim that *C. albicans* causes addiction. It claims that addiction vulnerability, substance selection, cross-substance switching, polysubstance use, post-acute withdrawal, and relapse may stratify by organism burden, organism state, mycobiome composition, endocannabinoid tone, autonomic stability, tryptophan-kynurenine routing, and chromatin-encoded fungal metabolic state.

The molecular architecture centers on Cyr1, the *C. albicans* adenylyl cyclase convergence node. Cyr1 integrates multiple weighted inputs of mixed valence into cAMP-PKA morphogenetic decision output: host metabolic gas through CO_2 and bicarbonate, bacterial neighbor signal

through peptidoglycan, organism population-density signal through farnesol via Ras1, and host-physiology input routed through Gpr1, including lactate, methionine, and functional dopaminergic ligand-space overlap. The user does not act on Cyr1 directly. The user acts on the host system whose state Cyr1 reads.

The paper further identifies polypharmacy as the brittle prescribed-substance subgroup of the same umbrella mechanism. Formication in this population is presented as the strategic validation point: if the symptom tracks organism activity and responds to mechanical or antifungal tests, a long-dismissed psychiatric category becomes a biological signal.

Keywords

Addiction; Substance Use Disorder; Stuck-State; Substrate Lock-In; Candida albicans; Biochemical Computer; Cyr1; Gpr1; Dopaminergic Interface; Kynurenine; Tryptophan; Endocannabinoid System; Polypharmacy; Formication; Interstitium; Mycobiome; Withdrawal; Craving; Relapse; Post-Acute Withdrawal; Quorum Sensing; Chromatin State; Multi-Acyl-CoA; Redacted Science Research Initiative; #TheArchitect

Introduction

Addiction medicine already knows that addiction is not simply pleasure-seeking. The strongest models recognize reward learning, receptor-level adaptation, stress physiology, trauma history, social environment, drug availability, and affect regulation. The person using the substance is often not chasing pleasure. They are trying to stabilize a state.

The self-medication hypothesis made this visible. Different substances map to different internal demands: stimulation, sedation, affective relief, social disinhibition, pain modulation, sleep initiation, perceptual escape, or autonomic quieting (Khantzian, Self-Medication Hypothesis). Clinical accounts of severe polysubstance use describe patients who do not appear loyal to one drug class so much as loyal to state correction itself (Maté, Hungry Ghosts). The adverse childhood experiences literature demonstrates that early stress exposure increases later addiction vulnerability, but the conventional model still struggles to identify the biological layer that converts trauma into persistent substrate demand (Felitti, ACE Study).

The Redacted Science framework proposes that the missing layer is organism-host governance. In Paper A, *C. albicans* is framed as a coevolved biochemical computer: a mammalian commensal capable of sensing host conditions, integrating multiple signals, producing adaptive outputs, and maintaining state across time through phenotypic and epigenetic memory (Craddock, Biochemical Computer). In the Saline Oscillation paper, that architecture is placed in evolutionary context as part of a Pan-Mammalian relationship shaped by electrolyte, perfusion,

endocannabinoid, and stress-axis pressures (Craddock, Saline Oscillation; Craddock, Pan-Mammalian). In the Stuck-State Umbrella, chronic diseases are reframed as program modes that failed to transition, leaving one biological routine running past its proper window (Craddock, Stuck-State Umbrella).

This paper applies that model to addiction. The proposed state is substrate lock-in. A host-organism system repeatedly exposed to an exogenous substrate rebalances around that substrate. The reward circuit learns it. Receptors adapt to it. Social behavior reorganizes around it. But the organism layer also reads it, metabolizes around it, encodes around it, and begins to demand the state it now treats as operational baseline.

This is not a claim that *C. albicans* causes addiction. It is not a moral claim. It is not a treatment protocol. It is a mechanistic stratification claim: measure the organism layer and addiction phenotypes will sort differently than they do under host-only models.

Framework Basis

The framework rests on four prior Redacted Science components.

First, Paper A establishes the biochemical computer model. *C. albicans* is not presented as a passive passenger. It possesses signaling access to the endocannabinoid system, prostaglandin synthesis through arachidonic acid competition, vagal and autonomic interfaces, host metabolic-state inputs, tryptophan-kynurenine modulation, extracellular vesicle output, chromatin state machinery, quorum sensing, and a morphogenetic decision system centered on cAMP-PKA integration (Craddock, Biochemical Computer).

Second, the Saline Oscillation Hypothesis frames the organism-host relationship as coevolved rather than accidental. The mammalian body plan contains conserved interface systems: the hypothalamic-pituitary axis, renal and electrolyte regulation, endocannabinoid tone, stress response, and phagocytic immune pathways. These are precisely the systems addiction repeatedly perturbs (Craddock, Saline Oscillation).

Third, the Pan-Mammalian extension matters because self-administration is not uniquely human. Mammals self-administer substances under stress, deprivation, isolation, and conditioned reinforcement. Under the framework, that cross-species pattern is expected. The organism-host interface is not human-specific. It is built on conserved mammalian infrastructure (Craddock, Pan-Mammalian).

Fourth, the Stuck-State Umbrella provides the structural template. A stuck state occurs when a biological program phase persists after its transition signal fails. Obesity, IBS, and other chronic disease applications use the same logic: the condition persists because the management layer

continues to run the program (Craddock, Stuck-State Umbrella; Craddock, Obesity Stuck State; Craddock, IBS Stuck State).

Addiction enters this framework as the state in which an exogenous substrate becomes part of the operating environment. The host adapts. The organism adapts. The system begins to defend what should have been temporary.

Mechanism

Multi-Axis State Tailoring

Organism-host governance operates across multiple state axes: arousal and sedation, affect, autonomic tone, social disinhibition, pain perception, sleep architecture, and perceptual modulation. In stable physiology, these axes are regulated endogenously through neurotransmitters, hormones, immune tone, vagal signaling, endocannabinoid signaling, and metabolic substrate availability.

When governance destabilizes, exogenous substances become tools. Stimulants support wakefulness and drive. Alcohol, benzodiazepines, and sedatives reduce overactivation. Opioids and cannabinoids alter pain and affect. Nicotine modifies vagal and attentional tone. Psychedelics and dissociatives alter perception. Polysubstance use is therefore not an extreme exception in this framework. It is the most legible expression of the mechanism: the user is selecting tools against axes.

Drug-of-choice specificity is the narrower case. Alcohol-only, opioid-only, or nicotine-only dependence occurs when one substrate sufficiently satisfies the dominant destabilized axis, or when availability, legality, social context, cost, and habit constrain the selection set. Polysubstance use displays the architecture more clearly because the person is not bonded to one chemical. They are bonded to state correction.

This integrates Khantzian rather than replacing him. Specific-affect-to-substance mappings remain valid. The framework adds an organism layer beneath the affect map: why the state destabilizes, why the same individual shifts substances across time, and why abstinence from one substrate often produces substitution rather than remission.

> *[#TheArchitect: The person is not failing because they cannot name what is wrong. They often name it better than the clinician does. "I need to calm down." "I need to wake up." "I need to stop feeling this." "I need to sleep." That is not random behavior. That is state diagnosis without the laboratory vocabulary.]*

Cyr1 as the Convergence Node

The molecular core of the mechanism is not a list of disconnected substrates. The core is convergence.

Cyr1, the *C. albicans* adenylyl cyclase, is the integration node where multiple signals of mixed valence converge into a cAMP-PKA morphogenetic decision variable. Host metabolic gas enters through CO_2 and bicarbonate sensing (Hall, Cyr1 CO2). Bacterial neighbor signal enters through peptidoglycan activation (Xu, Peptidoglycan Cyr1). Organism population-density state enters through farnesol suppression of cAMP-PKA via Ras1, carrying opposite valence from activation signals (Davis-Hanna, Farnesol Ras1 cAMP). Host-physiology input enters through Gpr1-associated signaling, including lactate, methionine, and the ligand-space overlap demonstrated by clozapine inhibition of morphogenesis (Midkiff, Gpr1 Clozapine).

The architectural claim must remain distinct from the input-list claim. Cyr1 is not important merely because several things touch it. Cyr1 is important because the organism reduces heterogeneous host, bacterial, population, and metabolic conditions into a single operational variable. Multiple weighted inputs are compiled into morphogenetic output.

The user does not act on Cyr1 directly. The user acts on the host system whose state Cyr1 reads. Alcohol changes substrate conditions. Stimulants change dopaminergic and metabolic state. Opioids change gut motility, autonomic tone, and VTA-linked reward architecture. Cannabis changes endocannabinoid tone directly. Stress changes lactate, cortisol environment, immune activation, sleep, feeding, and sympathetic output. The organism reads the altered host field, not the user's intent.

Gpr1 belongs here not as “the dopamine receptor,” because the framework does not claim that. Gpr1 is a fungal GPCR whose known biological roles include lactate and methionine sensing, and whose pharmacological behavior includes response to a dopaminergic-receptor-antagonist ligand space through clozapine. The claim is functional overlap, not dopamine sensing. Addiction-relevant substances acting on the host dopaminergic axis enter a chemical neighborhood to which the organism's primary morphogenetic GPCR is demonstrably responsive. Prediction 14 tests this directly.

Kynurenine, Mood, and Mucosal Defense

The tryptophan-kynurenine pathway supplies the affect-axis bridge. *C. albicans* can divert tryptophan toward kynurenine metabolism, producing two effects in one move: serotonin precursor availability is reduced, and mucosal antifungal defense through IL-17-related pathways is suppressed (Cheng, Candida Tryptophan; Zelante, Kynurenine IL-17).

This matters for addiction because mood disorder comorbidity, depressive prodrome, sleep disruption, post-acute withdrawal, anxiety, and relapse vulnerability often outlast the

pharmacological presence of the drug. Under a host-only model, those phenomena are assigned to brain adaptation, psychiatric comorbidity, or psychosocial stress. Under the framework, they are not reassigned away from those layers. They are stratified by an additional measurable layer: mycobiome state, kynurenine-to-tryptophan ratio, mucosal IL-17 markers, and organism burden.

If the framework is correct, depressive symptomatology in addiction-vulnerable cohorts should not behave as a purely host-side neurochemical variable. It should track organism state.

Chromatin-Encoded Persistence

The lock-in claim requires a memory substrate. Paper A identifies it in multi-acyl-CoA chromatin encoding. Zhou et al. measured a broad post-translational modification panel in *C. albicans*, with crotonylation, acetylation, succinylation, and related acyl-CoA-linked marks distributed across a large fraction of the proteome (Zhou, Candida Crotonylome). The writer-reader-eraser system reads metabolic-state inputs and writes them into chromatin-level program availability. Shivarathri et al. showed that deletion of GCN5 collapses integrated virulence behavior, demonstrating that chromatin machinery is not decorative. It is program infrastructure (Shivarathri, GCN5 Virulence).

This gives addiction a parallel persistence substrate. The literature often says addiction remains in the brain after the substance is gone. The framework adds: it may also remain in the organism's encoded state after host pharmacological clearance. Repeated substrate exposure changes the organism's metabolic configuration. The configuration is written into chromatin. That state persists. The host experiences post-acute withdrawal, relapse vulnerability, mood instability, and late brittleness even after the drug has cleared because the organism-host system has not returned to baseline.

This is not metaphor. It is a testable statement about paired host and organism biomarkers across abstinence.

Access as Mechanism Revealer

Access changes what can be observed.

A low-access user is constrained by poverty, geography, legal risk, social exposure, and supply instability. That person may be forced to use whatever substrate is available, even when it poorly matches the axis being destabilized. The resulting pattern looks chaotic because the tool selection is constrained.

A high-access user has financial means, supply diversity, social cover, and fewer immediate consequences. That person can tailor substances to state more precisely: stimulant for wakefulness, sedative for sleep, alcohol or benzodiazepine for autonomic and social dampening,

opioid for pain and affect, cannabis for ECS modulation, dissociative or psychedelic for perception. This makes the state-axis logic more visible.

Access does not make the condition safer. It can make it more dangerous. The high-access person can iterate faster, combine more substances, and avoid early social interruption. The framework predicts that high-access cohorts show more legible axis tailoring among survivors, but worse total-cohort outcomes when mortality and serious morbidity are included.

The key empirical claim is temporal. If fame, stress, or constitutional fragility were the dominant explanation, mortality would track career duration, exposure load, or total years in the environment. The framework predicts clustering in the first one to three years of sustained polysubstance use: the figuring-out phase. That is when the user is learning which substrate hits which axis at which dose under which condition, and the iterations have lethal failure modes.

> *[#TheArchitect: A young person dying during the figuring-out phase is not a symbol, not a morality play, and not evidence for a clever line in an essay. It is a data point only in the most solemn sense. If the pattern exists, count it carefully. If it does not, the framework loses that claim.]*

Polypharmacy as the Brittle Prescribed-Substance Subgroup

Polypharmacy is not a sidebar. It is the prescribed-substance expression of the same umbrella mechanism.

Patients taking three or more concurrent CNS-active medications often combine opioids, gabapentinoids, SNRIs or TCAs, muscle relaxants, benzodiazepines, sleep aids, antipsychotics, anticholinergics, cannabis, alcohol, or over-the-counter sedatives. In addiction medicine this pattern may be framed as misuse. In primary care it may be framed as complexity. In geriatrics it may be framed as medication burden. In pain medicine it may be framed as treatment resistance.

Under the framework, it is axis-tailoring with poorer tools and smaller margins. The patient is trying to manage pain, sleep, autonomic tone, affect, arousal, and perception, but the selection process is fragmented across multiple prescribers, formularies, insurance rules, specialist silos, and symptom labels. The brittleness is structural, not characterological.

This subgroup is also the best near-term clinical validation population because of formication.

Paper A identifies the interstitium, described by Benias et al. as a body-wide fluid-filled collagen-lined network, as a physical distribution layer for organism transit and signal propagation (Benias, Interstitium; Craddock, Biochemical Computer). Paper A explicitly proposes that hyphal transit through this distribution layer produces mechanoreceptor activation detectable as formication, a sensation currently classified as psychiatric, substance-related,

withdrawal-related, or delusional. It further proposes mechanical and pharmacological tests: focal pressure should alter the directional sensation, and topical antifungal exposure over the reported transit zone should reduce sensation within a timeframe inconsistent with purely central hallucination.

The polypharmacy population reports formication often enough to test this. If formication tracks psychiatric measures and does not respond to organism-directed testing, the framework loses the claim. If it tracks mycobiome shifts, ECS tone, autonomic changes, GI flares, sleep disruption, and antifungal response, then a symptom dismissed across multiple specialties becomes an organism-interface biomarker.

> *[#TheArchitect: If the sensation is biological, the patient has been telling the truth with the only language available. "It feels like something is moving under my skin." Medicine heard that sentence and filed it under delusion. The framework says: press on it, measure it, test it.]*

Predictions

1. Mycobiome burden and composition correlate with addiction vulnerability and treatment response.

   Evidence class: prospective cohort with baseline ITS sequencing, fungal burden quantification, relapse tracking, and treatment-response stratification.

2. Antifungal pretreatment reduces relapse rates in alcohol use disorder.

   Alcohol is a direct fungal substrate, and auto-brewery syndrome is the boundary case demonstrating the organism-alcohol relationship.

   Evidence class: randomized controlled trial. This is the strongest Clear Evidence companion candidate.

3. Cross-substance switching after primary-substance abstinence tracks organism-state stability rather than personality trait.

   Abstinence from one substrate without organism-state correction should increase substitution risk.

   Evidence class: longitudinal abstinence cohort.

4. ACE-linked addiction vulnerability operates partly through HPA-disruption-mediated organism destabilization.

The framework predicts ACE effects remain significant but are partially mediated by mycobiome and stress-axis variables.

Evidence class: trauma-stratified cohort with mycobiome and HPA measures.

5. Cannabis differs from substrate-feed addictions because it directly modulates the ECS interface.

   Cannabis use should show distinct relapse and cross-substance correlations compared with alcohol, opioids, and sugar-substrate groups.

   Evidence class: substance-class comparative cohort.

6. Environmental enrichment reduces self-administration partly through stress-axis stabilization of organism state.

   Rat Park-type enrichment should correlate with mycobiome shifts, not only behavioral substitution.

   Evidence class: animal enrichment model with fungal and bacterial ecology measurement.

7. Polysubstance selection maps to identifiable state axes.

   Structured interviews should show reproducible within-subject mapping between perceived state need and substance choice.

   Evidence class: structured-interview cohort study.

8. Axis-to-substance mapping consistency increases with access among surviving polysubstance users.

   High-access survivors should show tighter state-tailoring patterns, while low-access users show forced substitution.

   Evidence class: cohort study using access proxies.

9. High-access polysubstance total-cohort outcomes are worse when mortality and serious morbidity are included.

   Survivor legibility and total-cohort harm are connected.

   Evidence class: cohort mortality and morbidity analysis.

10. Early-career mortality and serious morbidity cluster in the first one to three years of sustained polysubstance use in high-access cohorts.

    This temporal clustering is the disconfirming test against generic fame or stress explanations.

Evidence class: temporal clustering analysis.

11. Polypharmacy patients show mycobiome and ECS-tone signatures distinct from matched single-medication chronic disease patients.

    The signature should track autonomic dysregulation.

    Evidence class: cohort with mycobiome, ECS panel, heart rate variability, tilt-table response, and orthostatic blood pressure.

12. Formication in polypharmacy is non-psychiatric in a framework-positive subgroup.

    It should correlate with organism activity, respond to antifungal challenge, and cluster with autonomic, sleep, GI, and ECS shifts rather than psychiatric measures.

    Evidence class: paired-symptom cohort with antifungal challenge.

13. Kynurenine-to-tryptophan ratio and IL-17 mucosal markers correlate with mycobiome composition in addiction-vulnerable populations.

    Evidence class: paired biomarker cohort with intervention sub-arm.

14. Dopaminergic-axis substances produce measurable shifts in *C. albicans* morphogenetic state through Gpr1-associated functional ligand-space overlap.

    This tests cocaine, amphetamines, opioids via VTA effects, and nicotine against organism morphological-state markers.

    Evidence class: in vitro confirmation plus in vivo cohort.

15. Post-acute withdrawal and late relapse track mycobiome chromatin-state markers more reliably than host pharmacological clearance.

    Evidence class: longitudinal post-cessation cohort with paired mycobiome chromatin correlates and host neurochemical biomarkers.

Discussion

The framework is strongest where addiction medicine already struggles: polysubstance use, relapse after apparent stabilization, post-acute withdrawal, cross-substance switching, high-access iteration, and polypharmacy brittleness. Substance-specific models work best when the substance is stable and the patient population is narrow. The organism-host model becomes useful when the pattern is not substance loyalty but state correction.

The framework also clarifies why psychosocial models have been right but incomplete. Trauma matters because stress physiology matters. Environment matters because organism governance is

state-dependent. Social support matters because autonomic tone, sleep, feeding, threat exposure, and behavioral rhythm shape the host field the organism reads. Reward circuitry matters because it is one of the host systems through which substrate reinforcement is learned and repeated.

The organism layer is not a replacement explanation. It is a missing measurement layer.

The most strategic clinical test is not the entire addiction umbrella at once. The clearest first tests are: alcohol use disorder plus antifungal pretreatment, polysubstance structured state-axis mapping, and polypharmacy-with-formication validation. The alcohol test is clean because substrate relation is direct. The polysubstance test is clean because state-axis tailoring is visible. The formication test is powerful because it can reclassify a symptom with simple biological predictions.

If those fail, the framework loses ground. If they succeed, addiction medicine gains a new stratification system.

Counter-Arguments Addressed

16. Reward circuit dysregulation explains addiction.

    Yes, reward circuitry is involved. The framework does not dispute dopamine, reinforcement, receptor adaptation, cue learning, or craving circuitry. It proposes that the organism layer modulates vulnerability, substance selection, relapse, and persistence upstream and alongside those circuits. Prediction 14 directly tests organism-side dopaminergic-axis involvement.

17. Psychosocial and trauma models are sufficient.

    They are necessary, but not sufficient for all patterns. The framework reads stress and trauma as upstream destabilizers of organism-host governance. ACE correlations are therefore expected, not contradicted.

18. Receptor-level pharmacology accounts for tolerance and withdrawal.

    Receptor adaptation occurs. The framework adds that receptor adaptation operates inside an organism-modulated milieu. Prediction 15 tests whether organism chromatin-state persistence predicts post-acute withdrawal and late relapse beyond host pharmacological clearance.

19. Polysubstance use is just availability or impulsivity.

    The disconfirming observation is state-axis tailoring. If substance selection is random, opportunistic, or impulsive, structured interviews should not reveal stable within-subject substance-to-state mapping. Prediction 7 tests this.

20. High-access polysubstance use is just consequence buffering.

    Consequence buffering is real. It explains how use can remain hidden longer. It does not explain consistent axis-to-substance matching. Prediction 8 separates concealment from mechanism.

21. High-access users die young because of fame, stress, or fragility, not iteration failure.

    The framework predicts a specific temporal signature: clustering in the first one to three years of sustained polysubstance use. If mortality is flat across exposure duration or tracks career length rather than early iteration, this claim fails.

22. Formication is a psychiatric symptom or substance side effect.

    The framework makes no appeal to belief. It proposes tests. If formication tracks psychiatric measures and does not respond to organism-directed mechanical or antifungal tests, the psychiatric classification holds. If it tracks organism markers and responds biologically, the category changes.

23. Polypharmacy is poor care coordination, not stuck-state mechanism.

    Poor coordination is real. The framework adds that the biological pattern should be measurable. If polypharmacy patients do not show distinct mycobiome, ECS-tone, and autonomic signatures relative to matched controls, the framework's subgroup claim fails.

24. Gpr1 dopaminergic overlap is overreach. Clozapine response may be incidental.

    The framework does not claim Gpr1 senses dopamine. It claims functional ligand-space overlap, demonstrated by morphogenetic response to a dopamine receptor antagonist. Prediction 14 tests whether addictive dopaminergic-axis substances produce organism morphological-state shifts. If they do not, the claim narrows or fails.

Conclusion

Addiction is not reduced by this framework. It is expanded.

The addicted person still has a brain. The person still has history, stress, injury, environment, memory, social context, receptor adaptation, and reward learning. Those layers remain. The framework adds the organism layer: a coevolved biochemical computer reading the host state, adapting to substrate exposure, encoding metabolic state into chromatin, and participating in the persistence of craving, withdrawal, relapse, and substitution.

Cyr1 is the molecular center of the argument because it shows the architecture in miniature. Mixed signals of different origin and valence converge into a decision variable. That is what the

addiction phenotype looks like at the organism-host scale: stress, substrate, microbial ecology, immune state, metabolic gas, dopaminergic ligand space, sleep, autonomic tone, and affect all become part of one decision environment.

Polypharmacy exposes the same mechanism in the clinic. Formication provides the validation lever. High-access polysubstance use provides the documentary mortality test. Alcohol use disorder provides the cleanest first intervention study. Post-acute withdrawal provides the chromatin-state test.

The framework can be wrong. But it is wrong in a useful way if it fails these tests. Measure the organism layer, or keep calling substrate lock-in a mystery.

Closing Declaration

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References

Alexander, B. K. Rat Park environmental enrichment and self-administration literature.

Cited as: Alexander, Rat Park. Full bibliographic metadata to be verified by author before deposit.

Benias, P. C., Wells, R. G., Sackey-Aboagye, B., et al. (2018). Structure and distribution of an unrecognized interstitium in human tissues. Scientific Reports.

Cited as: Benias, Interstitium.

Bjorkhaug, S. T., et al. Alcohol use disorder microbiome composition literature specified in Seed 019.

Cited as: Bjorkhaug, Alcohol Microbiome. Full bibliographic metadata to be verified by author before deposit.

Cheng, S. C., et al. (2010). *Candida albicans* and tryptophan-kynurenine modulation literature specified in Seed 019.

Cited as: Cheng, Candida Tryptophan. Full bibliographic metadata to be verified by author before deposit.

Craddock, J. *Candida albicans* as a Biochemical Computer: Cross-Kingdom Signaling, Parasexual Reproduction, and Genetic Foundations of a Unique Fungal Symbiont. Redacted Science Research Initiative. Zenodo. DOI: 10.5281/zenodo.19337525.

Cited as: Craddock, Biochemical Computer.

Craddock, J. Chronic Disease as Stuck Program Modes of the *Candida albicans* Biochemical Computer: A Unified Framework. Redacted Science Research Initiative. Zenodo. DOI: 10.5281/zenodo.19582484.

Cited as: Craddock, Stuck-State Umbrella.

Craddock, J. Irritable Bowel Syndrome as a Stuck Program Mode of the *Candida albicans* Biochemical Computer. Redacted Science Research Initiative. Zenodo. DOI: 10.5281/zenodo.19598460.

Cited as: Craddock, IBS Stuck State.

Craddock, J. Obesity as a Stuck Program Mode of the *Candida albicans* Biochemical Computer. Redacted Science Research Initiative. Zenodo. DOI: 10.5281/zenodo.19600443.

Cited as: Craddock, Obesity Stuck State.

Craddock, J. Redacted Science: The Pan-Mammalian Coevolution Hypothesis. Redacted Science Research Initiative. Zenodo. DOI: 10.5281/zenodo.19643601.

Cited as: Craddock, Pan-Mammalian.

Craddock, J. The Saline Oscillation Hypothesis: Endocannabinoid-Mediated Fungal-Hominid Coevolution in the East African Rift Valley. Redacted Science Research Initiative. Zenodo. DOI: 10.5281/zenodo.19369715.

Cited as: Craddock, Saline Oscillation.

Davis-Hanna, A., et al. (2008). Farnesol suppression of cAMP-PKA signaling via Ras1 in *Candida albicans*.

Cited as: Davis-Hanna, Farnesol Ras1 cAMP. Full bibliographic metadata to be verified by author before deposit.

Engen, P. A., et al. Alcohol, gut microbiome, and intestinal permeability literature specified in Seed 019.

Cited as: Engen, Alcohol Gut Barrier. Full bibliographic metadata to be verified by author before deposit.

Felitti, V. J., et al. Adverse Childhood Experiences study.

Cited as: Felitti, ACE Study. Full bibliographic metadata to be verified by author before deposit.

Hall, R. A., et al. (2010). CO_2 and bicarbonate activation of Cyr1 in *Candida albicans*.

Cited as: Hall, Cyr1 CO2. Full bibliographic metadata to be verified by author before deposit.

Khantzian, E. J. Self-medication hypothesis literature.

Cited as: Khantzian, Self-Medication Hypothesis. Full bibliographic metadata to be verified by author before deposit.

Loose, D. S., & Feldman, D. (1981, 1982). Corticosteroid-binding protein in *Candida albicans*.

Cited as: Loose and Feldman, Candida Corticosteroid Binding. Full bibliographic metadata to be verified by author before deposit.

Madhu, et al. (2026). Extracellular vesicle nasal-mucosal CNS delivery literature specified in Seed 019 and Paper A.

Cited as: Madhu, EV CNS Delivery. Full bibliographic metadata to be verified by author before deposit.

Maté, G. In the Realm of Hungry Ghosts.

Cited as: Maté, Hungry Ghosts.

Midkiff, J., et al. (2011). Clozapine inhibition of *Candida albicans* morphogenesis via Gpr1.

Cited as: Midkiff, Gpr1 Clozapine. Full bibliographic metadata to be verified by author before deposit.

Ren, M., et al. Opioid-microbiome literature specified in Seed 019.

Cited as: Ren, Opioid Microbiome. Full bibliographic metadata to be verified by author before deposit.

Shivarathri, R., et al. (2019). GCN5 deletion and *Candida albicans* virulence collapse.

Cited as: Shivarathri, GCN5 Virulence. Full bibliographic metadata to be verified by author before deposit.

Wang, et al. (2024). Organism-mediated host metabolic signaling. Cell Host & Microbe.

Cited as: Wang, Host Metabolic Signaling. Full bibliographic metadata to be verified by author before deposit.

Wurster, S., et al. (2021). *Candida albicans* catecholamine-response literature specified in Seed 019.

Cited as: Wurster, Catecholamine Nonresponse. Full bibliographic metadata to be verified by author before deposit.

Xu, X. L., et al. (2008). Bacterial peptidoglycan activation of Cyr1 in *Candida albicans*.

Cited as: Xu, Peptidoglycan Cyr1. Full bibliographic metadata to be verified by author before deposit.

Zelante, T., et al. (2013). Kynurenine, mucosal antifungal immunity, and IL-17 modulation.

Cited as: Zelante, Kynurenine IL-17. Full bibliographic metadata to be verified by author before deposit.

Zhou, et al. (2021). Multi-acyl-CoA chromatin modification panel in *Candida albicans*.

Cited as: Zhou, Candida Crotonylome. Full bibliographic metadata to be verified by author before deposit.

Suggested Additional Citations

None inserted. Several seed-specified references require full bibliographic verification before deposit, as marked in References.