Autism Spectrum Disorder as Developmental Stuck-State

Architect Report AS#017 V2

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1. Abstract

Autism spectrum disorder is conventionally described as a heterogeneous neurodevelopmental condition with strong genetic contribution, frequent gastrointestinal comorbidity, variable regression history, immune and microbiome associations, and circuit-level differences across multiple brain regions. Under the Redacted Science framework, those observations are not discarded. They are reorganized. This paper proposes that a subset of autism spectrum disorder represents developmental stuck-state program execution by the organism-host governance system within critical developmental windows, with clinical phenotype determined less by a single autism mechanism than by timing of stuck-state onset relative to neurodevelopmental stage.

The core contribution is a two-trajectory model. Trajectory A is perturbation-triggered regression: typical development proceeds for months or years, then an immune, microbial, dietary, antibiotic, inflammatory, or other ecological event pushes a susceptible system into a locked program mode. Trajectory B is early-locked development: the stuck state is established prenatally or in the first months of life, so gut-brain signaling, immune calibration, sensory integration, sleep architecture, synaptic pruning, and myelination develop around the altered signal set. The same governance error therefore produces different observed outcomes depending on when it captures the developmental process.

This model extends the biochemical computer framework of *C. albicans*, the Saline Oscillation coevolution model, the Pan-Mammalian transmission frame, and the Stuck-State Umbrella into neurodevelopmental disease. Sandler et al. documented vancomycin-responsive regressive-onset autism in 2000 with relapse after discontinuation and an ecological signature centered on absent *Peptostreptococcus* species and anaerobic cocci. Qiao et al. later demonstrated a host-susceptibility-plus-activation-event architecture in Shank3 haploinsufficient mice, where LPS challenge produced behavioral regression through inflammatory microglial and synaptic mechanisms. V1.5 integrated six pediatric and developmental mycobiome sources that sharpened the fungal layer: ASD-associated bimodal Candida distribution (Nirmalkar, Bimodal Candida in ASD) , sibling-controlled *C. albicans* enrichment, antibiotic-linked fungal dysbiosis in neurodevelopmental disorder, vancomycin-associated fungal expansion in an ASD microbiota-transfer context, and *C. albicans*-mediated barrier disruption in ADHD. V2 adds MRI stratification and longitudinal imaging literature showing ASD-specific multiparameter signatures, individual-deviation structure by language-delay history, two-cluster connectivity stratification, stable childhood-to-adolescence phenotype-morphology relationships, and stronger age-stage than gender-stage classification signal.

The framework reads these as clinical, cohort, imaging, and mechanistic support for the two-trajectory model. The claim is not that autism has one cause, that vaccines cause autism, or that antifungal therapy is a universal treatment. The claim is narrower and testable: autism heterogeneity should stratify by developmental timing, regression history, mycobiome burden, gastrointestinal severity,

antibiotic exposure timing, barrier state, imaging subgroup, and response distribution. Measure the organism layer and the developmental architecture together, or keep calling architecture mystery.

2. Keywords

Autism Spectrum Disorder; Developmental Stuck-State; *Candida albicans*; Biochemical Computer; Neurodevelopment; Regression; Gut-Brain Axis; Mycobiome; Microbiome; SHANK3; Microglia; TLR4; Synaptic Pruning; Gastrointestinal Comorbidity; Endocannabinoid System; Pituitary-Hypothalamus Interface; Mammalia candidus; Homo candidus; Redacted Science Research Initiative; #TheArchitect, Pediatric mycobiome, Bimodal Distribution, ITS Sequencing, Sibling Controls, Antibiotic Exposure, Vancomycin, Microbiota Transplant Therapy, ADHD, Functional Connectivity, Normative Modeling, Imaging Stratification, ABIDE, Resting-State fMRI, Heterogeneity-Aware Analysis, Two-Cluster Stratification, Longitudinal Neuroimaging

3. Introduction

The Redacted Science framework proposes that *Candida albicans* functions as a coevolved biochemical computer in mammalian hosts, not as a mere opportunistic passenger waiting for weakness. It senses the host, reads substrate availability, modulates immune tone, communicates through vesicles and soluble effectors, interacts with the endocannabinoid system, and operates across the gastrointestinal, endocrine, autonomic, and neurological interfaces that modern medicine often studies separately (Craddock, Biochemical Computer). The organism is not magic. It is biology doing what old biology does: survive, remember, and calculate without asking permission.

The Saline Oscillation Hypothesis places that architecture in evolutionary context. The organism-host relationship is proposed to have been shaped by environmental pressure, especially electrolyte and perfusion stress, such that the symbiont developed governance capability over mammalian physiology under conditions where host survival required rapid internal recalibration (Craddock, Saline Oscillation). The Pan-Mammalian extension then widens the frame: the relevant interface systems are not uniquely human. The hypothalamic-pituitary axis, the endocannabinoid system, renal concentrating mechanisms, phagocytic immune pathways, sodium-potassium pump dynamics, and developmental stress-response architecture are conserved mammalian infrastructure (Craddock, Pan-Mammalian).

The Stuck-State Umbrella translates that framework into chronic disease logic. A stuck state is a biological program phase that should have transitioned but did not. In adults, that produces persistent disease phenotypes recognizable as type 2 diabetes, obesity, IBS, anorexia nervosa, or other chronic conditions depending on which program is frozen and which tissue compartment is involved (Craddock, Stuck-State Umbrella). In neurodevelopment, the same logic becomes more consequential. A child is not an adult system with smaller parts. A child is an active build process. A stuck program during construction does not merely change output. It changes the architecture being built.

This paper applies that model to autism spectrum disorder. The conventional autism literature already contains the clues: strong heritability, incomplete penetrance, heterogeneous phenotype, gastrointestinal comorbidity, regression in a subset, immune activation, microbiome signatures, maternal immune activation models, SHANK3 susceptibility, circuit-specific defects, and mixed intervention results. Under the framework, those clues are not competing explanations. They are different windows into a developmental governance problem.

The proposed reading is direct: autism spectrum disorder includes a subset of developmental stuck-state outcomes produced when the organism-host governance system locks during critical windows of neurodevelopment. The phenotype depends on when the lock occurs. If typical development begins and then a perturbation pushes the system into a stuck state, the child presents through Trajectory A, perturbation-triggered regression. If the stuck state is established before developmental baselines form, the child presents through Trajectory B, early-locked development. The difference is not merely

severity. It is timing. [Architecture does not look broken when it was built around the wrong blueprint from the beginning.]

4. Framework Basis

Paper A supplies the hardware. *Candida albicans* is treated in the Redacted Science framework as a distributed biochemical computer with cross-kingdom signaling access to host immune, metabolic, endocrine, gastrointestinal, autonomic, and neurological systems (Craddock, Biochemical Computer). Autism, under this paper's reading, does not require the organism to invent a new autism program. It requires only that the organism's existing interface tools operate during a developmental window where immune tone, synaptic pruning, gut-brain signaling, sleep, sensory calibration, vagal signaling, and endocrine rhythms are actively being built.

Paper B supplies the evolutionary frame. Developmental windows are substrate-surface events: times when the host is unusually plastic, unusually sensitive to signaling, and unusually dependent on correctly timed transitions (Craddock, Saline Oscillation). In the ancestral model, those windows would have been managed by an organism-host-social architecture built around stable ecological cues. Modern life changes the cues: antibiotics, processed diet, maternal immune activation, altered microbial inheritance, C-section delivery patterns, environmental chemicals, and repeated immune perturbations. The old program sees inputs. It does not necessarily know modernity changed the operating system.

The Stuck-State Umbrella supplies the logic. Chronic pathology persists because a phase fails to transition (Craddock, Stuck-State Umbrella). In autism, the relevant failure is developmental. A stuck state during early synaptogenesis, immune calibration, microbiome assembly, or sensory integration can become a persistent neurodevelopmental phenotype because later systems develop around the locked state rather than replacing it.

The IBS paper supplies the bowel-comorbidity template. Autism has a substantial gastrointestinal signal, and GI severity correlates with autism severity in existing literature (Adams, Gastrointestinal Symptoms in Autism). Under the framework, bowel symptoms are not merely a co-occurring nuisance. They are evidence that the organism-host interface is active in the same compartment from which gut-brain signaling, microbial metabolites, vagal traffic, immune tone, and endocannabinoid modulation emerge (Craddock, IBS Stuck State).

The Pan-Mammalian paper supplies the inheritance reframe. Autism's strong heritability is real, but heritability does not require a single genetic cause. A vertically transmitted symbiont, inherited microbial ecology, maternal immune state, and host genetic susceptibility can produce familial clustering without reducing the phenotype to a DNA-only model (Craddock, Pan-Mammalian). Genetics loads the circuit board. Ecology decides which subroutine boots.

5. Mechanism

The mechanism proposed here begins with susceptibility. Susceptibility may include host genetics such as SHANK3 haploinsufficiency or other synaptic-risk architecture; inherited or maternal microbiome state; early-life antibiotic exposure; inflammatory timing; fungal burden; bacterial co-governance disruption; maternal immune activation; gut-barrier instability; or some combination of these. None of these must be universal. The framework expects heterogeneity because the organism-host state at the time of the perturbation is not uniform across children.

Gut-barrier instability is not an accessory variable in this model. It is one of the physical routes by which a bowel ecology becomes a neurodevelopmental signal. Wang LJ et al., studying ADHD rather than ASD, reported significantly increased *C. albicans* in a related neurodevelopmental condition and then demonstrated in vitro that *C. albicans* secretions enhance Caco-2 gut barrier permeability (Wang LJ, ADHD Mycobiome Permeability). That matters because it moves the argument from association

toward mechanism. The organism does not need to enter the brain to alter neurodevelopmental tone. It can change the gate at the intestinal wall, alter what crosses, and thereby change immune, vagal, endocrine, and microbial-metabolite traffic upstream of the developing nervous system.

Trajectory A begins with typical or apparently typical development. Speech, social engagement, motor patterning, sleep, feeding, or adaptive function proceeds until an activation event changes the operating state. Sandler et al. treated regressive-onset autistic children with oral vancomycin and documented significant improvements in behavior and communication, followed by deterioration after treatment discontinuation and return toward baseline over follow-up (Sandler, Oral Vancomycin). The fecal finding is the buried fuse: absent Peptostreptococcus species and anaerobic cocci in the sampled children against high presence in adult controls. The authors proposed a gut-brain connection and neurotoxin-producing opportunistic organisms. The Redacted Science reading adds the missing fungal extension: bacterial disruption creates ecological space, Candida persistence survives antibacterial pressure, and the organism layer remains unmeasured.

Patel et al. supply direct partial validation of the distributional prediction. In a pediatric ASD versus neurotypical comparison using ITS sequencing, the ASD cohort did not merely show a vague fungal difference. It showed a bimodal Candida distribution inside the ASD group, and Candida-high children showed significantly higher ATEC scores (Patel, Yeast and Fungi in ASD). That is the shape the framework predicted before this revision: not a clean case-control average, but a split inside the diagnostic category. The diagnostic label says autism. The organism layer says subgroup. Those are not the same unit of analysis.

Retuerto et al. strengthen the same point by using non-autistic siblings as controls. They reported *C. albicans* detection of 27.1 percent in ASD children versus 13.2 percent in siblings, with a near-threshold p value, while also observing depletion of bacterial taxa that usually matter for gut resilience, including Faecalibacterium prausnitzii, Prevotella copri, Bacteroides fragilis, and Akkermansia muciniphila (Retuerto, Gut Bacterial and Fungal Microbiota in ASD Siblings). The sibling design matters. It narrows shared household, diet, and genetic background more tightly than unrelated controls. If the ASD child still carries more *C. albicans* signal against that sibling baseline, the finding fits the framework better than a generic dysbiosis story.

The Krajmalnik-Brown lab adult ASD microbiota-transfer thesis adds the ecological pressure point. During vancomycin pretreatment, fungal load increased significantly, while baseline ASD samples carried elevation of nine fungal taxa, including *C. glabrata*, *Penicillium melanoconidium*, and *Aspergillus* species, with six taxa remaining significant after excluding typically developing controls with GI symptoms (Krajmalnik-Brown Lab, Adult ASD MTT Mycobiome). This is not pediatric onset evidence by itself, and it should not be used as though it is. Its value is mechanistic: remove bacterial competitors with antibacterial pressure and the fungal layer expands. That is exactly the ecological release mechanism the Redacted Science reading adds to Sandler. Vancomycin may have disrupted one part of the stuck state, but it also created the opening a fungal system could exploit if it was already present.

Qiao et al. provide the preclinical counterpart. In Shank3 haploinsufficient mice, baseline phenotype is absent or limited. After LPS challenge, behavioral impairment appears: motor changes, anxiety-like behavior, excessive grooming, microglial activation through TLR4, synapse engulfment, and inflammatory gene shifts (Qiao, Inflammation and Shank3 Regression). Anti-inflammatory treatment partially rescues. This is the exact shape of Trajectory A: susceptibility plus activation event produces a locked behavioral phenotype that was not visible before the event. The bacterial LPS trigger is demonstrated. The framework predicts organism-mediated inflammatory triggering through Candida-accessible TLR4, microglia, vagal, endocrine, and gut-brain channels.

Trajectory B begins earlier. The stuck state forms prenatally, perinatally, or within the first months of life, before typical developmental baselines are visible. In this pathway, the altered signal set becomes the environment in which neurodevelopment occurs. The gut-brain axis, immune calibration, sensory gating, sleep architecture, myelination, feeding, pain response, interoception, social salience, and synaptic pruning all develop under the wrong governance tone. Imaging may show fewer discrete abnormalities, not because the phenotype is less biologically real, but because there was no before-and-after event for the scanner to capture. The baseline was already shifted. Floris et al. make this methodological point from the imaging side: normative modeling across large ASD datasets showed that individual deviations, not simple group means, reveal stratification, with stepwise organization by language-delay history (Floris, Normative Modeling ASD Heterogeneity). Nogay and Adeli add the practical classifier version of the same claim: MRI deep-learning classification performed better when stratified by age than by gender, and the combined eight-way model performed worse than simpler age-aware stratification (Nogay, Age-Stratified MRI Deep Learning). Developmental stage carries signal because developmental timing is part of the mechanism.

Together, the cohort evidence points toward stratification rather than a single ASD mycobiome average. Patel supplies the bimodal Candida distribution and severity linkage. Retuerto supplies a sibling-controlled *C. albicans* enrichment signal. Laswi et al. show that neurodevelopmental disorder and gastrointestinal disorder carry distinctive fungal dysbiosis, including increased fungal alpha diversity, and that antibiotic exposure before age three produces substantially greater fungal than bacterial dysbiosis (Laswi, NDD and GID Dysbiosis). That early antibiotic timing is Trajectory B-relevant. If the signal environment is altered before the child has a stable developmental baseline, the result is not regression from a prior state. It is development organized around a disturbed ecology from the start.

This explains the Rochat paradox. Rochat et al. found more imaging abnormalities in higher-functioning children than developmentally delayed children under age five (Rochat, MRI in ASD Under Five). Conventional intuition expects the opposite. Under the two-trajectory model, the finding is predicted. Higher-functioning cases are enriched for Trajectory A: more retained cognitive infrastructure, more visible event signature. Developmentally delayed cases are enriched for Trajectory B: the system built itself around an atypical signal environment, so imaging reads less like injury and more like alternate construction. Ecker et al. established the foundational point that MRI can carry ASD-specific multiparameter signatures distinguishable from ADHD rather than merely generic neurodevelopmental difference (Ecker, Multiparameter MRI Classification). Ren et al. then move the field closer to the framework's expected shape: in 415 ABIDE ASD subjects, connectivity stratification produced two clusters, one with widespread connectivity disturbance and one nearly typically-developing-like except for middle cingulate cortex-specific abnormalities (Ren, Two-Cluster Connectivity ASD). That is direct partial validation of the two-trajectory imaging prediction. One subgroup looks broadly disturbed. One subgroup looks nearly typical except for a focal governance-relevant deviation. The average between them is not biology. It is arithmetic.

Durkut et al. add the longitudinal piece. In a childhood-to-adolescence cohort, autistic traits and brain morphology were stable over time, with neither predicting subsequent change in the other; the authors describe early brain-morphology differences in children with autistic symptoms that remain quite stable over time (Durkut, Longitudinal Brain Morphology ASD). That reads like Trajectory B in ordinary imaging language. The architecture forms early and then co-stabilizes with phenotype. A stuck state does not have to keep producing visible progressive injury. Once the developmental structure has been built around the altered signal environment, the later scan may show stability precisely because the system already became what it was going to become.

SHANK3 sharpens the model because it does not produce one brain-wide autism module. Gao et al. document hippocampal synaptic impairment in an R1117X model (Gao, R1117X Shank3). Wu S. et al.

localize autistic-like behavior to hypothalamic AgRP neurons and p38 alpha inflammatory mediation at the pituitary-hypothalamus interface (Wu S., Shank3 AgRP). Wang et al. localize repetitive behavior to striatopallidal indirect-pathway medium spiny neurons with DREADD-based rescue (Wang, Striatopallidal Shank3). Together, these papers support distributed-circuit vulnerability. Different symptoms map to different vulnerable circuits. That matters because the Redacted Science framework is also distributed. It predicts that the organism does not need one autism switch. It needs access to developmental circuits through inflammatory, endocrine, vagal, metabolic, and microbial routing.

NCT00936182 is the institutional artifact. A three-site, double-blind, randomized, placebo-controlled trial of fluconazole in children with ASD was registered in 2009, with enrollment contingent on pyrosequencing-positive yeast and a pre-specified behavioral outcome hypothesis. It was the obvious fungal-extension test after Sandler's 2000 bacterial-ecology signal. Seventeen years later, no results are available. [When a registered trial asks the right question and then disappears into the fog, that fog becomes part of the data.] This paper does not claim the missing results prove the framework. It claims the silence marks exactly where the framework says the measurement should have occurred.

6. Predictions

1. ASD cohorts should show differential *C. albicans* mycobiome burden compared with controls, and the ASD distribution should be bimodal rather than normally distributed. Existing support is now stronger than the V1 wording allowed. Patel et al. report ASD versus neurotypical ITS sequencing with a bimodal Candida distribution inside ASD and significantly higher ATEC scores in Candida-high children (Patel, Yeast and Fungi in ASD). Retuerto et al. report *C. albicans* in 27.1 percent of ASD children versus 13.2 percent of non-autistic siblings, alongside depletion of protective or resilience-associated bacterial taxa (Retuerto, Gut Bacterial and Fungal Microbiota in ASD Siblings). Kantarcioglu and Strati remain supportive background rather than decisive distribution tests (Kantarcioglu, Yeast Species in ASD; Strati, Gut Mycobiome in ASD). [Evidence class: pediatric cohort mycobiome sequencing with distribution analysis, severity stratification, and sibling-controlled replication.]

2. Regression history should distinguish an antifungal-responsive subgroup from non-regressive cases. The strongest response signal should occur in Trajectory A subjects with documented regression, GI symptoms, Candida enrichment, or post-antibiotic onset. [Evidence class: adaptive-enrichment clinical trial.]

3. Gastrointestinal comorbidity severity should correlate with intervention response magnitude, especially when paired with Candida burden or bacterial anaerobe disruption. Adams et al. reported a strong GI-autism severity correlation (Adams, Gastrointestinal Symptoms in Autism). [Evidence class: prospective cohort with paired GI severity, behavioral measures, and mycobiome testing.]

4. Antifungal response should be bimodal rather than normally distributed. A uniform small effect would argue against the framework. A responder/non-responder split enriched by regression history and mycobiome burden would support it. [Evidence class: randomized trial with pre-specified responder distribution analysis.]

5. Maternal or early-life antibiotic exposure should correlate more strongly with Trajectory B presentations than Trajectory A presentations, especially when exposure timing intersects fetal, infant, or toddler immune and microbiome calibration windows. Laswi et al. provide direct support for the exposure logic in neurodevelopmental disorder and gastrointestinal disorder: NDD cases showed distinctive increased fungal alpha diversity, and antibiotic exposure before age three produced substantially greater fungal than bacterial dysbiosis (Laswi, NDD and GID Dysbiosis). The framework prediction is therefore timing-specific. Antibiotics after a typical developmental baseline may trigger Trajectory A regression in susceptible children. Antibiotics before the baseline stabilizes may shift the

build environment itself. [Evidence class: retrospective or prospective birth cohort with timing-specific antibiotic exposure, paired bacterial/fungal sequencing, and operational Trajectory A/B coding.]

6. NCT00936182 results, if recovered, should show bimodal response in the pyrosequencing-positive-yeast subset rather than a flat population average. [Evidence class: recovered trial dataset or registry-linked results analysis.]

7. The fluconazole rescue reported in SHANK3-related mouse work should correlate with baseline gut Candida burden if banked samples exist. If authors did not measure mycobiome state, the omission itself identifies the decisive covariate for replication. [Evidence class: secondary analysis or replication study with mycobiome covariates.]

8. In Shank3 haploinsufficient mice, gut mycobiome burden at inflammatory challenge should predict severity of regression phenotype; antifungal pretreatment should attenuate Qiao-like LPS-triggered behavioral regression; and organism bloom or dysbiosis should produce regression-like phenotype in the susceptible genotype even without LPS. [Evidence class: preclinical replication with mycobiome covariates.]

9. Sandler's ecological disruption signature, especially absent Peptostreptococcus species and anaerobic cocci, should replicate in modern regressive-ASD cohorts using paired 16S and ITS sequencing. The absent-commensal state should correlate with Candida burden and antifungal-intervention response. [Evidence class: replication study with paired bacterial and fungal sequencing in regressive-ASD cohorts.]

7. Discussion

The two-trajectory model resolves several autism puzzles at once. It accepts heritability without reducing autism to genetics alone. It accepts regression without making regression universal. It accepts early developmental delay without forcing a discrete injury model onto children whose altered signaling environment may have been present before observable milestones. It accepts gastrointestinal comorbidity as central rather than incidental. It accepts immune activation as a trigger class rather than a single cause. Most importantly, it explains why one autism spectrum can contain children with sharply different onset histories, cognitive profiles, sensory presentations, bowel involvement, imaging signatures, and intervention response patterns. The V2 MRI literature does not replace the mycobiome argument. It tells the same story from the brain side: stratify, or watch the signal disappear.

The model also clarifies why average-effect trials fail. If the population contains Trajectory A responders, Trajectory B early-locked cases, non-framework autism, different microbial ecologies, different host genotypes, and different developmental timing, then a single intervention averaged across the full spectrum should dilute signal. That is not failure of biology. That is failure of stratification. [Averaging a circuit board and a smoke alarm gives you a number. It does not tell you which one is beeping.]

Sandler et al. matters because the paper did not merely report behavior change. It reported relapse after discontinuation, brief hyperactivity early in treatment in several children, and a specific ecological abnormality in the sampled fecal flora (Sandler, Oral Vancomycin). That pattern is not easily dismissed as placebo. It looks like a system perturbed, briefly improved, and then restored itself after pressure was removed. In stuck-state language, the intervention disrupted the state but did not reset the architecture.

Qiao et al. matters because it demonstrates a clean susceptibility-plus-activation-event model in SHANK3 haploinsufficiency (Qiao, Inflammation and Shank3 Regression). The mouse does not require every autism feature to be present at baseline. The event reveals the vulnerability. That is the same logic parents describe when a child develops typically and then changes. The framework does not need to adjudicate every claimed trigger. It asks whether a susceptible organism-host system can be

pushed into a locked developmental state by inflammatory activation. The preclinical answer is now yes.

The SHANK3 circuit literature further prevents simplistic mechanism. Hippocampus, hypothalamic AgRP neurons, striatopallidal circuits, prefrontal remodeling, microglia, lipid rafts, IGF1R, and inflammatory mediators all appear in the surrounding evidence. The organism layer could access those circuits through multiple routes: gut-derived immune activation, vagal signaling, endocannabinoid modulation, pituitary-hypothalamic governance, microbial metabolites, Candida cell wall ligands, prostaglandin and arachidonic acid competition, and substrate-state shifts. The framework's point is not that one molecule explains autism. The point is that a distributed biological computer acting during development would produce distributed phenotype.

NCT00936182 sits at the center of the institutional question. A trial of fluconazole in pyrosequencing-positive-yeast ASD children was registered with the right design shape: three sites, randomized, double-blind, placebo-controlled, yeast-positive enrollment, behavioral outcomes. It followed Sandler by nine years. It then produced no visible answer. A framework-neutral Clear Evidence paper can stand on that silence alone. The full Architect Report uses the silence differently: as a pointer to the unmeasured layer that autism research repeatedly approaches and then fails to resolve.

The V1.5 mycobiome additions change the weight of the paper without changing its structure. V1 could say that ASD mycobiome evidence was partial. V1.5 can say the missing layer has already begun to appear in the exact places the framework pointed. A bimodal Candida distribution inside ASD is not the same as an average Candida elevation between ASD and controls. Sibling-controlled *C. albicans* enrichment is not the same as unrelated case-control noise. Antibiotic-linked fungal dysbiosis before age three is not a generic microbiome footnote. Vancomycin-associated fungal expansion is not an irrelevant adult trial artifact. *C. albicans*-mediated barrier permeability in ADHD is not ASD proof, but it is a direct demonstration of a shared route by which an organism in the gut can alter neurodevelopmental signaling conditions. Read together, these papers do not prove the entire Redacted Science model. They do something narrower and more useful: they make fungal stratification scientifically irresponsible to omit.

The V2 MRI additions strengthen the same architectural claim. Ecker et al. show that structural MRI can distinguish ASD-specific multiparameter signatures from ADHD, which means neurodevelopmental imaging can identify ASD structure beyond generic clinical impairment (Ecker, Multiparameter MRI Classification). Floris et al. show that individual deviation mapping exposes heterogeneity that group means obscure, including language-delay-linked stratification (Floris, Normative Modeling ASD Heterogeneity). Ren et al. show a two-cluster connectivity split in ASD, with one widespread-disturbance subgroup and one nearly TD-like subgroup with MCC-specific abnormality (Ren, Two-Cluster Connectivity ASD). Durkut et al. show stability of autistic traits and brain morphology across childhood into adolescence, consistent with early-established architecture rather than a continuously moving lesion (Durkut, Longitudinal Brain Morphology ASD). Nogay and Adeli show that age stratification carries stronger MRI classification signal than gender stratification, reinforcing developmental stage as an organizing variable (Nogay, Age-Stratified MRI Deep Learning). Read with the mycobiome papers, the picture is no longer simply gut data over here and brain data over there. It is stratified developmental architecture appearing in both compartments.

7.1 Methodological Note: Heterogeneity-Aware Analysis

The framework's methodological claim is simple: group-mean analysis is structurally hostile to the signal this paper predicts. Floris et al. make that argument in imaging terms. A group comparison can report weak or inconsistent ASD effects while individual-deviation analysis reveals ordered substructure by developmental history (Floris, Normative Modeling ASD Heterogeneity). Ren et al. show the same problem in connectivity form: two ASD clusters, one broadly disturbed and one nearly

typically-developing-like except for a specific middle cingulate abnormality, collapse into a misleading average when treated as one population (Ren, Two-Cluster Connectivity ASD). Alookaran et al. showed the mycobiome version of the problem in V1.5: binary Candida detection in a small sample produced an apparently awkward ASD-without-GI greater than ASD-with-GI inversion, but that inversion may be trajectory information rather than contradiction (Alookaran, Mycobiome Children Autism GI). Patel's bimodal Candida distribution makes the rule explicit: the signal is not necessarily higher mean burden across all ASD children, but split distribution inside the diagnostic category (Patel, Yeast and Fungi in ASD). Most ASD studies do not fail to find the Redacted Science signal because it is absent. They fail because the study design averages across the exact subgroups the framework says must be separated: regression versus early-locked development, GI-visible versus barrier-mediated physiology, Candida-high versus Candida-low ecology, and imaging-broad-disturbance versus imaging-focal-deviation architecture.

8. Counter-Arguments Addressed

1. Vaccines cause autism. This paper does not make that claim. The framework treats immune activation events as a broad trigger class in susceptible hosts. Infection, antibiotics, inflammatory challenge, dietary shifts, microbial disruption, environmental exposures, maternal immune activation, and other perturbations could all serve as transition events. That is categorically different from a single proximate-cause claim.

2. Autism is approximately 90 percent heritable, so it is genetic. High heritability does not identify mechanism. It identifies familial clustering of liability. Vertical symbiont transmission, inherited microbial ecology, maternal immune tone, shared environment, host genetic susceptibility, and true genetic variants can all contribute to heritable phenotype. SHANK3 illustrates the point: genetic susceptibility may be silent until an activation event reveals it.

3. Regression reports are unreliable. Regression history is imperfect, but it is not disposable. Under this framework, regression is Trajectory A's primary observable. Finegold et al. already identified regression-specific microbiome signatures (Finegold, Regressive Autism Microflora). Sandler's entire cohort was regressive-onset, and response to vancomycin was documented prospectively (Sandler, Oral Vancomycin). The right response is not to discard regression. It is to operationalize it.

4. Spectrum heterogeneity defeats unitary-mechanism models. Correct. It defeats crude unitary-mechanism models. The two-trajectory model is not a crude unitary mechanism. It predicts heterogeneity as the consequence of stuck-state onset timing interacting with developmental stage, host genotype, microbial ecology, immune activation, and circuit vulnerability. Different phenotypes are expected because different build stages were captured.

5. Shaw 2000 was never replicated. That is not reassuring. Shaw et al. reported open-label nystatin-associated improvement in a pediatric ASD cohort (Shaw, Nystatin in Autism). Kantarcioglu later confirmed yeast species and antifungal susceptibility in ASD stool samples (Kantarcioglu, Yeast Species in ASD). NCT00936182 then registered the proper fluconazole trial and disappeared from the visible record. The framework does not treat non-replication as proof. It treats measurement avoidance, missing results, and absent stratification as the problem to be solved.

6. Alookaran et al. complicate the simple version of the fungal argument. Good. A framework that cannot absorb inconvenient data is not a framework. In a small pilot cohort using binary detection methodology, Alookaran et al. reported the highest Candida prevalence in the ASD-without-GI subgroup, 56 percent, versus 21 percent in ASD-with-GI children (Alookaran, Mycobiome Children Autism GI). A crude model would expect Candida to track overt GI symptoms monotonically. The two-trajectory model does not require that. Binary detection is not quantitative ITS distribution analysis, N equals 50 is small, and the ASD-non-GI greater than ASD-GI inversion is exactly the kind of unexpected split that may indicate trajectory stratification rather than refutation. Some children may

carry the organism signal without overt bowel complaint because the dominant output is neurodevelopmental, sensory, immune, or barrier-mediated rather than pain, constipation, diarrhea, or parent-reported GI distress. [When the subgroup behaves strangely, do not throw it out. That may be the subgroup.]

7. This could stigmatize autistic people. It should not, and the paper must be read carefully on that point. The framework does not reduce autistic people to pathology, infection, or deficit. It proposes that some developmental trajectories may be organism-host stuck states with testable biological signatures. A mechanism paper should not erase personhood. It should make intervention, stratification, and understanding more precise. [The point is not to flatten people. The point is to stop flattening the biology.]

9. Conclusion

Autism spectrum disorder is not solved by naming heterogeneity. Heterogeneity is the observation. A mechanism must explain why different children arrive at different phenotypes under the same diagnostic umbrella. The Redacted Science two-trajectory model offers one answer: timing. A stuck state during a developmental window produces different outcomes depending on whether it interrupts typical development or becomes the baseline around which development forms.

The evidence now justifies a V2 final revision of the first full-spectrum Architect Report. Sandler et al. supplied clinical Trajectory A evidence in 2000: regressive-onset autism, gut-ecology intervention response, relapse after discontinuation, and a striking anaerobe absence signal. Qiao et al. supplied preclinical Trajectory A validation: genetic susceptibility, inflammatory trigger, behavioral regression, microglial TLR4 activation, synapse engulfment, and partial rescue. SHANK3 circuit studies show distributed vulnerability rather than a single autism module. The pediatric mycobiome literature added exactly the layer V1 identified as undermeasured: bimodal Candida distribution, sibling-controlled *C. albicans* enrichment, antibiotic-linked fungal dysbiosis, and cohort-level fungal-bacterial dysbiosis patterns. V2 adds the imaging layer: ASD-specific multiparameter MRI signatures, language-delay stratification by normative deviation, two-cluster connectivity structure, longitudinal co-stability of morphology and autistic traits, and age-stage classification superiority. NCT00936182 remains the missing-trial artifact.

The next steps are straightforward. Stratify autism cohorts by regression history, GI severity, maternal and early-life antibiotic timing, SHANK3 or other susceptibility markers, developmental timing, fungal burden distribution, language-delay history, and MRI deviation cluster. Measure both bacterial and fungal ecology with methods capable of distinguishing detection, abundance, diversity, and bimodality. Include *C. albicans* burden, absent-commensal status, barrier permeability markers, protective bacterial depletion, and imaging subgroup as pre-specified covariates. Analyze response distribution for bimodality, not just average effect. In SHANK3 models, measure gut mycobiome burden before inflammatory challenge and antifungal rescue. In human cohorts, pair stool ITS sequencing with MRI stratification rather than treating gut and brain as unrelated datasets. The framework can be wrong, but it is wrong in a useful way if it fails these tests.

Autism research has spent decades describing circuits, genes, immune signatures, bowel problems, microbial differences, and regression as if they are separate rooms in the same building. This paper proposes they are connected by the management layer. Open the door between them. Measure the organism where the signal begins.

10. Closing Declaration

This Architect Report AS#017 V2 was generated through the Redacted Science Seed Analysis Process, from Seed 017 of the Paper Seed Master, under the Redacted Science Research Initiative. Issued 20260425 by Jim Craddock, #TheArchitect. Authenticity verifiable at jimcraddock.com/architect-

reports. Papers claiming any A-series designation not listed in the registry are not authentic Architect Reports. V2 is the final revision of AS#017, integrating the pediatric and developmental mycobiome cohort literature added in V1.5, the MRI stratification and longitudinal imaging literature added here, and a Methodological Note on heterogeneity-aware analysis.

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12. Suggested Additional Citations

None inserted. V2 integrates only the five requested MRI stratification and longitudinal imaging citations beyond the V1.5 pediatric mycobiome additions. Additional MRI, neurodevelopmental, microbiome, or autism-subtyping papers should be reviewed separately for a future supplemental bibliography rather than inserted into AS#017 V2.