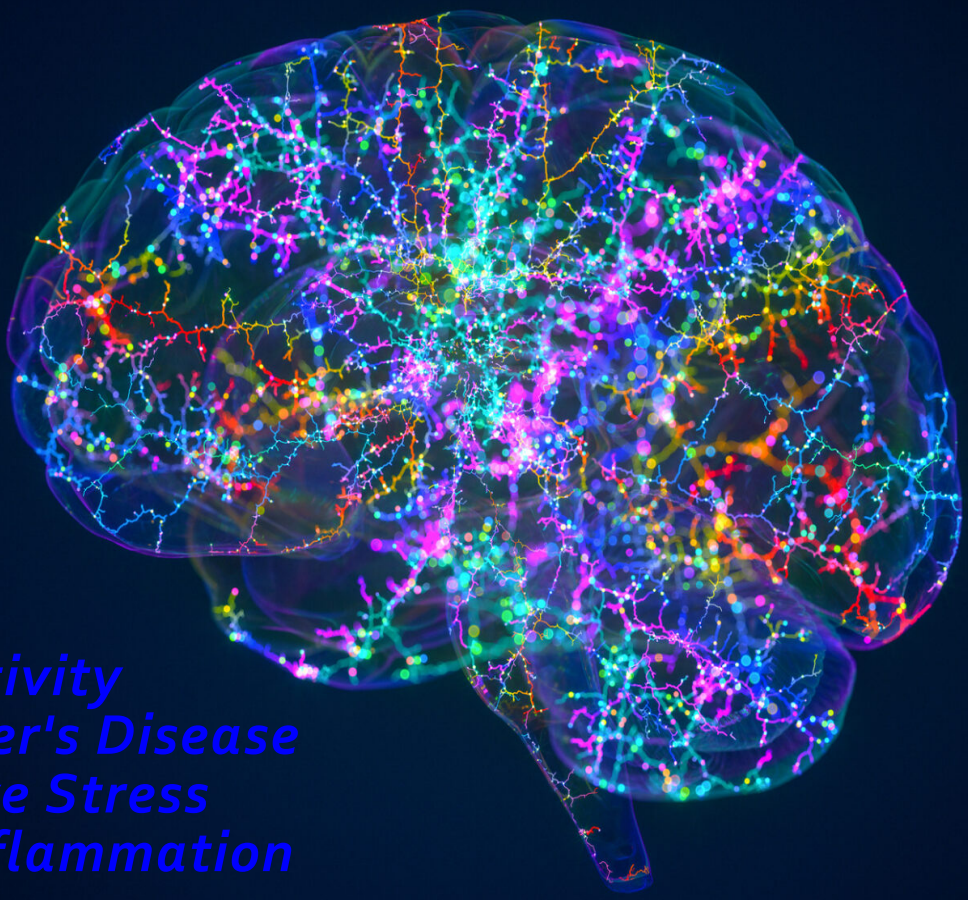
LONGEVITY BRAIN



Glial Activity
Alzheimer's Disease
Oxidative Stress
NeuroInflammation

Longevity™
LAB-SOLUTIONS
Where Health Gets Perfected

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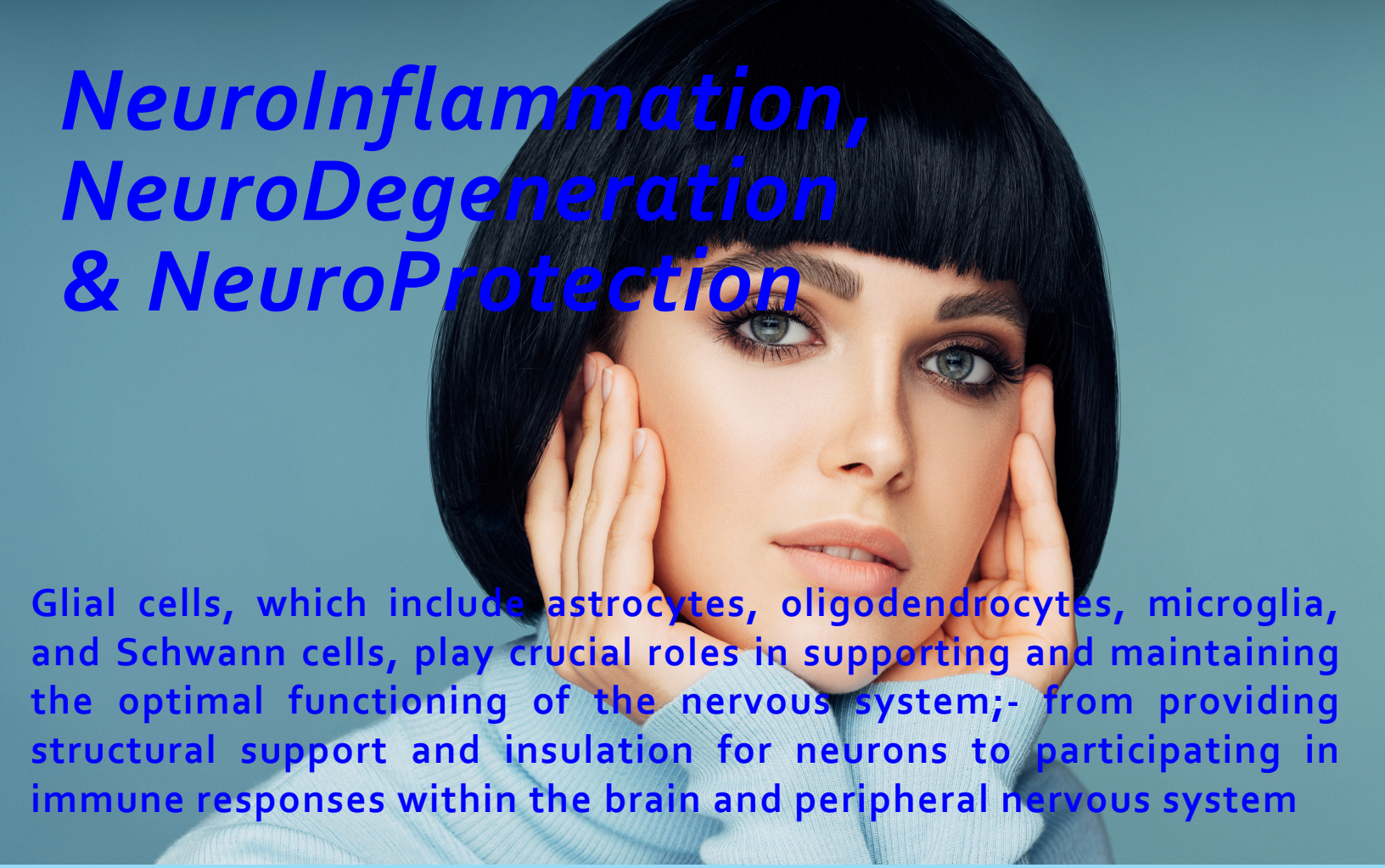


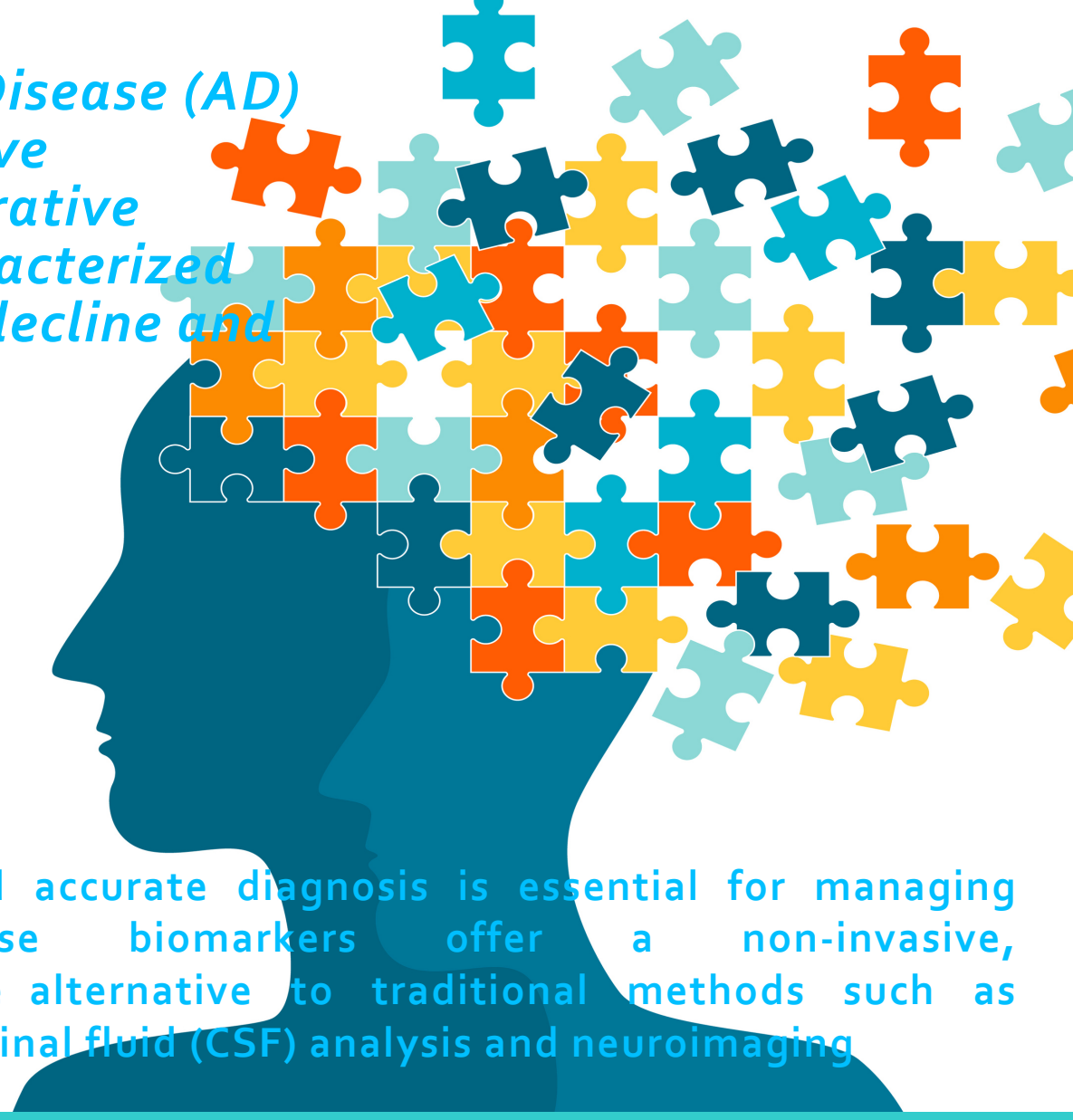
NeuroInflammation, NeuroDegeneration & NeuroProtection

Glial cells, which include astrocytes, oligodendrocytes, microglia, and Schwann cells, play crucial roles in supporting and maintaining the optimal functioning of the nervous system;- from providing structural support and insulation for neurons to participating in immune responses within the brain and peripheral nervous system

Longevity Brain Glial Blood Test

1. Alpha-Synuclein
2. Amyloid Beta (Aβ) Peptides 42/40
3. Brain-Derived Neurotrophic Factor (BDNF)
4. C-Reactive Protein (CRP)
5. Glial Fibrillary Acidic Protein (GFAP)
6. Interleukin-1β (IL-1β)
7. Interleukin-6 (IL-6)
8. Interleukin-10 (IL-10)
9. Interferon-gamma (IFN-γ)
10. Matrix Metalloproteinase 8 (MMP8)
11. Neurofilament Light Chain (NfL)
12. Phosphorylated Tau 181 (p-T181)
13. Soluble Triggering Receptor Expressed on Myeloid cells 2 (sTREM2)
14. S100 Calcium-Binding Protein B (S100B)
15. Total Tau Proteins (t-tau)
16. Tumor Necrosis Factor-alpha (TNF-α)
17. YKL-40 (Chitinase 3-like-1)

Alzheimer's Disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and memory loss



Early and accurate diagnosis is essential for managing AD. These biomarkers offer a non-invasive, accessible alternative to traditional methods such as cerebrospinal fluid (CSF) analysis and neuroimaging

Longevity Alzheimer's Disease Blood Test

1. Amyloid Beta (Aβ) Peptides 42/40
2. Malondialdehyde (MDA)
3. Neurofilament Light Chain (NfL)
4. Phosphorylated Tau (p-T181)
5. Total Tau Proteins (t-tau)

Longevity Alzheimer's Disease DNA Test

1. APOE4 (Apolipoprotein E4) Allele Testing

Oxidative Stress: The spark that lights the fire of aging and disease

Oxidative stress occurs when there's an imbalance between the production of reactive oxygen species (ROS) and the body's ability to detoxify these reactive intermediates or repair the resulting damage

Longevity Oxidative Stress Blood Test

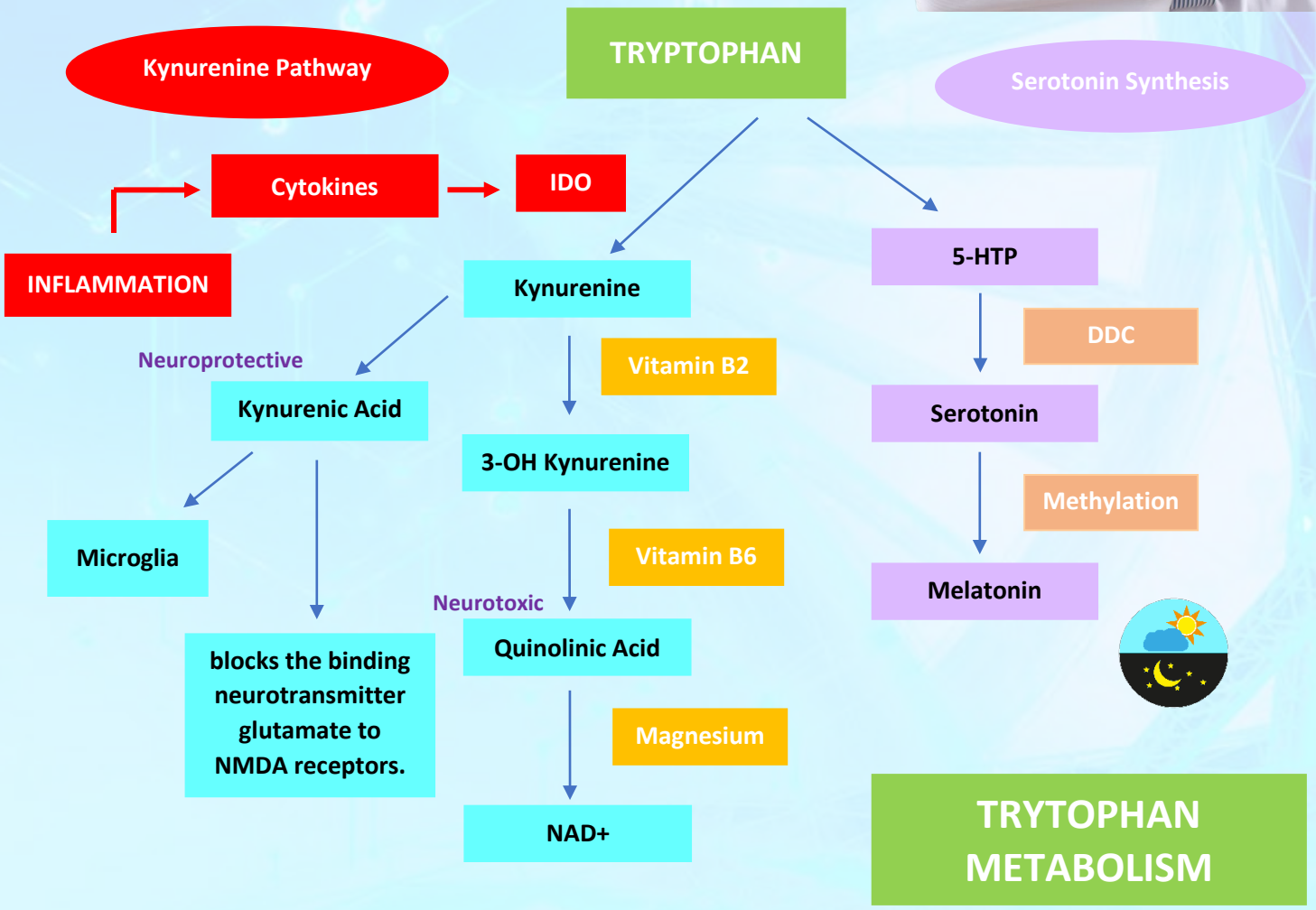
1. GSH/GSSG
2. 8-Isoprostane
3. Malondialdehyde (MDA)
4. NAD/NADH
5. inducible Nitric Oxide Synthase (iNOS)
6. Reactive Oxygen Species (ROS)
7. Peroxidases
8. Superoxide Dismutases (SODs)
9. Advanced Oxidation Protein Products (AOPP)
10. Total Antioxidant Capacity (TAC)
11. Protein Carbonyls, 8-Hydroxy-2-deoxyguanosine (8-OHdG)

Bio-GPS

Biomarker Guided Patient Selection

The KYNURENINE PATHWAY

Addressing NeuroInflammation, Brain Fatigue And Long Covid Syndrome



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The Kynurenine Pathway (KP) of tryptophan metabolism plays a crucial role in the balance between neuroprotection and neurotoxicity. Dysregulation of this pathway has been associated with several neurodegenerative and neuropsychiatric disorders, largely due to the potential role of KP metabolites in mediating neuroinflammation.

1) **Initiation of the Pathway:** The metabolism of tryptophan via the kynurenine pathway begins with its conversion into kynurenine. This step is catalyzed by two primary enzymes: indoleamine 2,3-dioxygenase (IDO) and tryptophan 2,3-dioxygenase (TDO). Both enzymes can be induced by pro-inflammatory stimuli, especially IDO, which is upregulated by pro-inflammatory cytokines like interferon-gamma (IFN-γ).
2) **Neuroactive Metabolites:**
    a) **Kynurenic Acid (KYNA):** Produced in astrocytes, KYNA acts as an antagonist at NMDA and α7 nicotinic acetylcholine receptors. It has neuroprotective effects but, in elevated concentrations, might also contribute to cognitive dysfunctions.
    b) **Quinolinic Acid (QUIN):** This is synthesized in microglia and acts as an NMDA receptor agonist. Elevated levels can lead to excitotoxicity, which is damaging to neurons and is associated with several neurodegenerative conditions.
3) **Neuroinflammation:** An imbalance favoring the production of QUIN over KYNA can contribute to neuroinflammation. QUIN's agonistic action on NMDA receptors can lead to excitotoxic neuronal death. Moreover, QUIN can generate reactive oxygen species (ROS) and exacerbate inflammation. Chronic inflammation can upregulate IDO, leading to a sustained increase in kynurenine metabolites, which further skews the balance towards neurotoxic effects.
4) **Role in Neurodegenerative Diseases:** Dysregulation of the kynurenine pathway is observed in various neurodegenerative conditions, including:
    a) **Alzheimer's Disease (AD):** Elevated levels of QUIN and reduced KYNA levels have been reported in the brains of AD patients. QUIN can promote amyloid-beta aggregation, a hallmark of AD pathology.
    b) **Parkinson's Disease (PD):** KP dysregulation is suggested to be involved in the dopaminergic neuronal loss characteristic of PD.
    c) **Huntington's Disease (HD):** Elevated QUIN levels have been observed in the brains of HD patients and are believed to contribute to the striatal neurodegeneration seen in HD.
5) **Neuropsychiatric Implications:** Changes in the KP have also been associated with neuropsychiatric disorders like depression, schizophrenia, and bipolar disorder. The balance between KYNA and QUIN can influence neurotransmission, synaptic plasticity, and neural integrity, potentially leading to mood and cognitive disturbances.

Kynurenine Pathway, NeuroInflammation & Long Covid-19 Syndrome

The Kynurenine Pathway of tryptophan metabolism is intricately linked with the immune response, inflammation, and neurological function; hallmarks of long-haul Covid

Longevity Brain Kynurenine Pathway NeuroInflammation Blood Test

Tryptophan Metabolites

1) Tryptophan
2) Kynurenine
3) Tryptophan/Kynurenine Ratio
4) Quinolinic Acid

Inflammatory & Cytokines

5) C-Reactive Protein (CRP)
6) Interleukin-1β
7) Interleukin-6
8) Interleukin-10
9) Tumor Necrosis Factor-alpha

REDOX & Oxidative Stress

10) GSH/GSSG
11) Malondialdehyde (MDA)
12) NAD^+/NADH
13) Reactive Oxygen Species (ROS)

Coagulation

14) D-Dimer
15) Ferritin

Methylation

16) Homocysteine
17) Vitamin B9 (Folate)
18) Vitamin B12
19) Active Vitamin B12

Co-Factors

20) Magnesium
21) Vitamin B12
22) Vitamin B6
23) Vitamin D 25-OH
24) Zinc

Additional Inflammation Markers

25) Creatine Kinase (CK)
26) Complement 3 (C_3)
27) Complement 4 (C_4)
28) Covid-19 Spike Antibodies
29) Immunoglobulin A (IgA)
30) Immunoglobulin G (IgG)
31) Immunoglobulin M (IgM)
32) Lactate Dehydrogenase (LDH)

Pathways To Alzheimer's Disease (AD)

Alzheimer's disease (AD) is a complex neurodegenerative disorder with multiple interrelated pathways leading to its pathogenesis. While the primary pathways revolve around amyloid-beta (Aβ) accumulation, tau protein hyperphosphorylation, and neuroinflammation, several other mechanisms and factors contribute to the development and progression of the disease.

1. Amyloid Beta (Aβ) Pathway

Aβ Production and Aggregation: Arising from the cleavage of the amyloid precursor protein (APP) by β-secretase and γ-secretase, Aβ peptides aggregate to form plaques that are toxic to neurons.

2. Tau Pathology

Hyperphosphorylation and Tangle Formation: Tau proteins stabilize microtubules in neurons. In AD, tau becomes hyperphosphorylated, losing its ability to bind to microtubules and forming neurofibrillary tangles that contribute to neuronal dysfunction and death.

3. Neuroinflammation

Chronic Inflammatory Response: Activated microglia and astrocytes release pro-inflammatory cytokines, chemokines, and reactive oxygen species (ROS), exacerbating neuronal damage and contributing to a cycle of chronic neuroinflammation.

4. Oxidative Stress

Reactive Oxygen Species (ROS): Accumulation of ROS leads to oxidative damage to DNA, proteins, and lipids, disrupting cellular function and contributing to neurodegeneration.

5. Cholesterol Metabolism

ApoE4 and Cholesterol: The ε4 allele of the apolipoprotein E (APOE) gene is a strong genetic risk factor for AD. ApoE4 affects cholesterol transport and has been implicated in Aβ aggregation and clearance.

6. Mitochondrial Dysfunction

Energy Metabolism and ROS Production: Impaired mitochondrial function leads to decreased energy production and increased ROS, contributing to neuronal damage and apoptosis.

7. Insulin Resistance and Glucose Metabolism

Brain Insulin Resistance: Altered insulin signaling in the brain affects glucose metabolism, contributing to tau phosphorylation and Aβ accumulation. AD has been referred to as "type 3 diabetes" by some researchers due to these disruptions in insulin signaling.

8. Cellular Calcium Dysregulation

Calcium Ion Imbalance: Abnormalities in calcium homeostasis within neurons trigger pathways leading to cell death, and are implicated in both Aβ and tau pathologies.

9. Vascular Dysfunction

Blood-Brain Barrier Breakdown: Vascular factors, including hypertension and atherosclerosis, lead to blood-brain barrier dysfunction, contributing to AD pathology by affecting Aβ clearance and promoting inflammation.

10. Genetic Factors

Genetic Mutations: Beyond APOE ε4, mutations in the APP, PSEN1, and PSEN2 genes are associated with early-onset AD, affecting Aβ production and aggregation.

11. Environmental and Lifestyle Factors

Diet, Exercise, and Cognitive Engagement: These factors modulate the risk of AD through various mechanisms, including inflammation, oxidative stress, and vascular health.