Dissolving the Plaque
Trehalose: A Novel Treatment

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Dissolving the Plaque: Trehalose - Dr. Jared M. Skowron, ND
Down & Amyloid

• Amyloid Precursor Proteins
• Increased in Down and Alzheimer and Autism

• Perturbs axonal pathfinding and circuit formation

Down & Amyloid

- Over-production of amyloid beta peptides plays the dominant role of dementia
- Adults with Down that reach the age of 40 have neuropathology to match Alzheimer diagnosis

Order of Disease

- Symptom Presentation
- Physiological creation of symptoms
- Homeostatis (inflammation)
- Etiological stressor
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Trisomy 21 → Neuroinflammation

- NFkB
- sAPPα
- MAPK-p38
- βAPP
- PPP-tau
- Aβ

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- Parietal lobe: Normal volume and altered microarchitecture of pyramidal cells
- Basal ganglia: Normal
- Temporal lobe: Reduced volume, reduced number of granule cells, and altered microarchitecture of pyramidal cells
- Hippocampal system: Altered microarchitecture of pyramidal cells
- Basal prosencephalon: Early cholinergic degeneration
- Amygdala: Normal
- Cerebellum: Hypoplasia and reduced number of granule cells
- Brainstem: Altered serotoninergic, noradrenergic, and cholinergic systems

Information acquisition → Information storage → Information processing → Information retrieval

Early onset Aβ in Down syndrome

Hippocampus

Midfrontal cortex

Intact neurons

4 months old – anti-Aβ1-16 immunostaining in free-floating formic acid pretreated 50 μm thick formalin-fixed sections.
The Callous On My Foot
Brain Plaques

• Plaque development is the result of prolonged inflammation
  – Worsens neurological function
• Trehalose is a potential treatment
  – Remove the plaques
  – Currently in Alzheimer’s research
Genes involved in the trehalose cycle and degrees of their up-regulation 10 – 20 minutes after moderate heat shock (37°C). Thickness of red, orange and pink arrows indicates the magnitude of up-regulation. Blue arrows indicate that these steps are unaltered over baseline.
Brain Plaques

- Down, Alzheimer, & Autism are linked with presence of amyloid material in the brain
  - sAPP-alpha
    - 60% severely autistic children
    - Immune dysfunction
    - Brain overgrowth – 90%
  - Amyloid-beta17-40 and Amyloid-beta17-42
    - Neurotoxic
    - Stimulates aggregation
    - Deposition of Alzheimer-type beta-amyloid plaques
    - Cause astrocyte proliferation – risk for plaques
Amyloid Material

• sAPP-alpha elevation
  – Response to brain injury
  – Glutamate toxicity
  – Excess IL-6 and NF-kB
  – Toxic exposure
  – Nutritional deficiencies
• Amyloid-beta17-40,17-42 elevation
  – Attracted to astrocytes
  – Attracted to lipofuscin
Amyloid Plaques

- Accumulation of amyloid material in childhood increases risk of amyloid plaque formation
- Down children probably have current amyloid plaque formation
- Beta-Amyloid plaques
  - Neuron cell death
  - Impairs synaptic transmission
  - Impairs neurotransmitter release
  - Enhances myelin lipid peroxidation
  - Enhances NMDA-induced excitotoxicity
  - Creates free radicals and pro-inflammatory cytokines
Treatment Goals

- Reduce aggregation of plaque-forming amyloid material
- Reduce neurotoxicity
- Reduce oxidative stress in the brain
- Prevent the formation of amyloid plaques
Trehalose

- Disaccharide composed of two glucose molecules linked through glycosidic bond
- Shown to be absorbed and cross BBB in mice
  - Stabilize protein structure as a molecular chaperone
  - Inhibits amyloid aggregation in vitro
  - Dissolves pre-formed amyloid aggregates
  - Protects neural cells from amyloid aggregates
  - Reduces neurotoxicity
  - Creates healthy mitochondrial function
mTOR-independent autophagy enhancer

• Bulk degradation of unwanted cellular material
  – Amyloid aggregates phagocytosis and lysosome destruction
• Trehalose upregulates autophagic removal of amyloid material
  – Beta-amyloid material shown to inhibit autophagy
  – Special affinity for proteins that are prone to aggregation
• Trehalose promotes organelle turnover
  – Protects from accumulation of dysfunctional mitochondria, acts as an anti-oxidant
  – Promote formation of healthy mitochondria
Trehalose Safety

• US FDA gives Trehalose a GRAS rating
  – Generally regarded as safe
• Safe in doses as high as 50g per day
• May lead to minor gastrointestinal upset
  – 15% lack Trehalase enzyme
Plasma insulin levels after consumption of beverages

- 5% Glucose
- 5% Trehalose
- Placebo

Time (minutes)

Trehalose Pilot Study

• Open-label, 45 days
• Before and after ATEC survey
  – Autism Treatment Evaluation Checklist
• 12 children enrolled
  – 5 dropped out due to GI distress
Trehalose Study Results

- **Language** - 10% improvement
  - Normal conversation, communication
  - More words per sentence
- **Sociability** - 14% improvement
  - Eye contact, cooperative
  - Command compliance, fewer tantrums
- **Cognition** - 12% improvement
  - Aware of others, curious of environment
- **General Health** - 12% improvement
  - Happier, less OCD, less agitated
  - Better toilet training
Inositol Treatment

• Scyllo-inositol
  – Another treatment to prevent plaque accumulation
  – Currently in Alzheimer research
• Also inhibits amyloid plaque growth
  – Binds pre-fibrillar aggregates
• Scyllo-inositol converted from myo-inositol with probiotics
• Found in purple yam, eggplant, artichoke, chicory, escarole, and endive
Scyllo-Inositol

Myo-Inositol

Summary

• Dissolve the Plaque
• Inflammation is cause of chronic disease
  – Scar/Plaque is the reaction of chronic inflammation
• Amyloid plaque reduces brain function and memory
• Prevent and Dissolve the Plaque
• Treatment Summary
  – Super Trehalose 3,000 mg
  – Inositol 3,000 mg
Research TGF

Research MIF

Research Ig

Research estrogen

Research ANA

Research Vitamin E

References

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References

References

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