Preclinical Research
The Information Professionals Role in Inspiring Preclinical Efficacy and Improved Outcomes

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Project Manager – AlzPED
Zimmerman Associates, Inc.
Mid-Atlantic Atlantic Chapter - Medical Library Association
October 19, 2015
Alzheimer’s Disease

Healthy Brain  Severe Alzheimer’s
Efficacy in Preclinical AD Research

Accelerating drug discovery for Alzheimer’s disease: best practices for preclinical animal studies

Diana W Shineman, Gurqbal S Bas, Jennifer L Bizon, Carol A Colton, Barry D Greenberg, Beth A Hollister, John Linzecum, Gabrielle G Leblanc, Linda (Bobb) H Lee, Feng Luo, Dave Morgan, Ma Moore, Lorenzo M Refolo, David R Ridde III, Kimberly Scourto-Levie, Patrick Sweeney, Juha Yrjanheikki and Howard M Fillit
AlzPED Goals

- Provide relevant detailed information about:
  - animal models
  - negative result studies
  - related publications
  - therapy approaches
  - model availability
  - related clinical trials
NIH Principles and Guidelines

April 8th 2015 NIH Announced:
Principles and Guidelines for Reporting Preclinical Research

About NIH

Principles and Guidelines for Reporting Preclinical Research

The signatories represent journals that publish preclinical biological research — an area of research that encompasses both exploratory studies...
Roles for Information Professionals

- Library Science
- Project Management
- Information Science

Library Science

Information Science

Project Management
AlzPED Home Page

Introduction

AlzPED provides distilled scientific model, target and agent data as well as other aspects of experimental design in AD preclinical efficacy studies for easy assessment, and to improve rigor in scientific reporting.

http://alzped.nihlibrary.com/
### AlzPED Search Results

#### Search Results

<table>
<thead>
<tr>
<th>APID</th>
<th>Title</th>
<th>Year</th>
<th>PI Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>5219609</td>
<td>Intracellular oxidative DNA damage in the development of neocortical tauopathy in a mouse model of Alzheimer's disease</td>
<td>2009</td>
<td>Vandy Ballew</td>
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<tr>
<td>5459805</td>
<td>Antioxidant agents decrease reactive lipid peroxidation and oxidative stress in a mouse model of Alzheimer's disease</td>
<td>2009</td>
<td>Sheila Hendricks</td>
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<td>5018952</td>
<td>Alzheimer-like high cerebellar excitotoxicity and synaptic dysfunction in a mouse model of Alzheimer's disease</td>
<td>2013</td>
<td>Susana Estructo</td>
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<td>6019056</td>
<td>Effects of dexamethasone administration on brain and systemic toxicity in the 5xFAD mouse model of Alzheimer’s disease</td>
<td>2009</td>
<td>Hongmei Ding</td>
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<tr>
<td>5100301</td>
<td>Intracerebroventricular injection of V94205S inhibits Aβ-42 and improves cognitive function in Alzheimer’s disease transgenic mice</td>
<td>2008</td>
<td>Frank K. Landis</td>
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<tr>
<td>5859815</td>
<td>A single nucleotide polymorphism at chromosome 8p11.21 is associated with Alzheimer’s disease</td>
<td>2010</td>
<td>Hiroshi Fukumoto</td>
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<tr>
<td>5569811</td>
<td>The second generation anti-Aβ immunotherapy C0911 reduces amyloid accumulation in APP transgenic mice while minimizing potential side effects</td>
<td>2011</td>
<td>Christof Voehringer</td>
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<tr>
<td>5719812</td>
<td>Inhibition of neuroinflammation reduces amyloid and tau pathology in Alzheimer’s transgenic mouse</td>
<td>2013</td>
<td>Miriam Ramirez</td>
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<tr>
<td>5569810</td>
<td>Incretines modulate cognitive disease progression in an Alzheimer’s mouse model</td>
<td>2010</td>
<td>Peter F. Seiden</td>
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</tbody>
</table>

#### Filter by therapeutic target:
- Amyloid-beta (40)
- Tau protein (40)
- Cholinergic System (2)
- Neuropeptides (2)
- ApoE (1)
- Aβ-p42 (1)

#### Filter by therapy type:
- Small Molecule (2)
- Biologic (14)
- Small molecule antagonist (1)
- Anti-Aβ (6)

#### Filter by model type (genes):
- APP (10)
- APP-PD (6)
- Aβ (1)
- Wnt (5)
Nicotinamide restores cognition in Alzheimer’s disease transgenic mice via a mechanism involving sirtuin inhibition and selective reduction of Thr231-phosphorylation.
Experimental Design

Is the following information reported in the study?

- ✔ Power Calculation
- ✔ Blinded for Treatment
- ✔ Pharmacokinetic Measures
- ✔ Toxicology Measures
- ✔ Use of Biomarkers
- ✔ Formula
- ✔ Duration of Treatment
- ✔ Age at the beginning of Treatment
- ✔ Gender
- × Randomized into Groups
- × Blinded for Outcome Measures
- ✔ Pharmacodynamic Measures
- × ADMET Measures
- ✔ Dosage
- ✔ Route of Delivery
- ✔ Frequency of Delivery
- ✔ Age at the end of treatment
- × Study Balanced for Gender
AlzPED – Individual Record (3 of 3)

### Outcomes

**Study Goal and Principal Findings:**

Here the authors evaluated the efficacy of nicotinamide, a competitive inhibitor of the sirtuin class III NAD+ dependent HDACs, in 3xTg-AD mice, and found that it restored cognitive deficits associated with pathology. In addition, nicotinamide treatment was found to selectively reduce hyperphosphorylated species of tau associated with microtubule depolymerization and implicated in AD. In addition, treatment also up-regulated presenilin 1 associated with increased microtubule stabilization and upregulated p25, which is linked to improved learning and memory. These experimental findings suggest that oral nicotinamide may represent a safe treatment for AD and other tauopathies, and that the co-administration of tau and NRD may regulate tau stability.

#### Outcomes:

<table>
<thead>
<tr>
<th>Outcome Measured</th>
<th>Specific Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemical</td>
<td>beta amyloid peptide</td>
</tr>
<tr>
<td>Electrophysiology</td>
<td>Synaptic density</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Amyloid beta plaque load</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Synaptophysin</td>
</tr>
</tbody>
</table>

**Is the following information reported in the study?**

- [x] Number of premature deaths
- [x] Number of excluded animals
- ✔ Statistical Test
- ✔ Statistical Significance (P-value)
AlzPED – Preclinical Roles for Librarians

Inspire Reporting

Teach Resources

Engage Progress
AlzPED Team

- Dr. Lorenz Refolo
- Dr. Suzana Petanceska
- Mr. James King
- Ms. MaShana Davis
- Ms. Lonelyss Charles
- Mr. Sanjay Patel
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"Your Partner in Research"