ZAI Zimmerman Associates Inc.

AlzPED – Rigor, Reproducibility, Transparency

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Zimmerman Associates, Inc.
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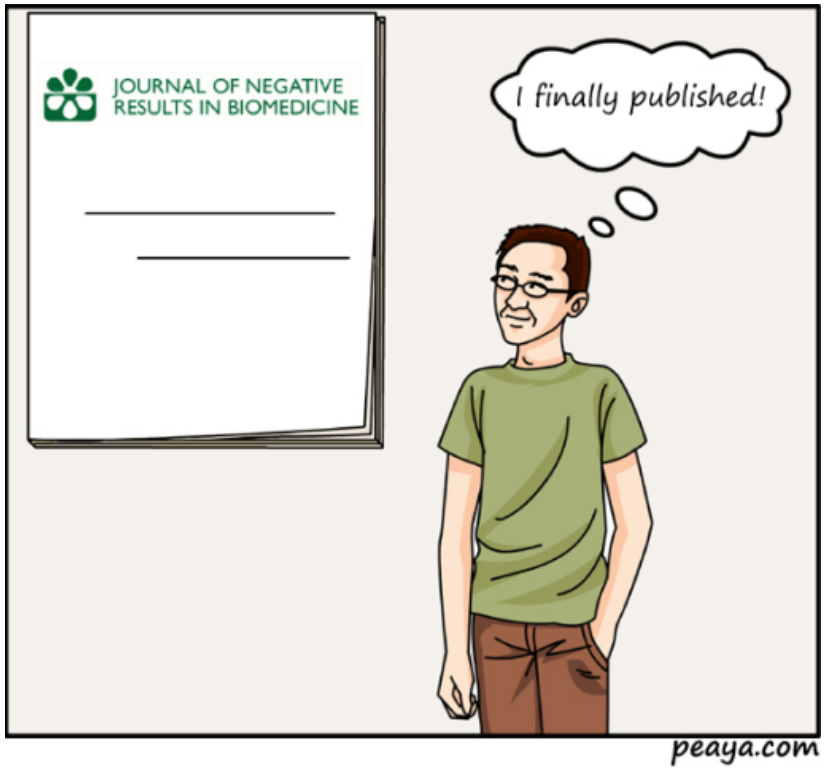
Alzheimer's Disease: Research and Impact

AlzPED Goals

- Provide relevant detailed information about:
  - animal models
  - **negative result studies**
  - related publications
  - therapy approaches
  - model availability
  - related clinical trials
  - outcome measures
  - outcome parameters



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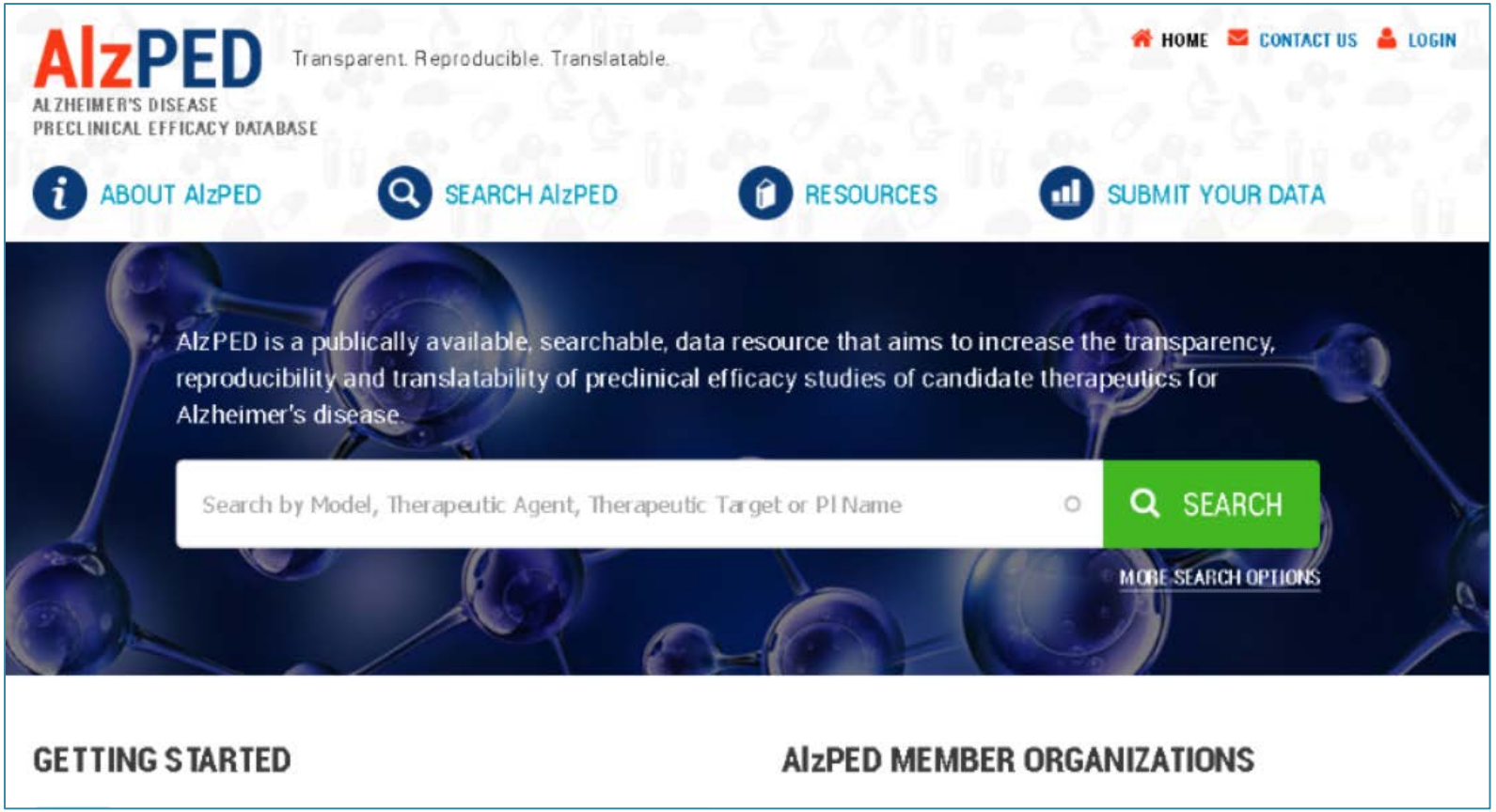
AlzPED Home Page



http://alzped.nihlibrary.com/

Full Text Search

Full Text Search

Title

Title

PI Full Name

PI Name

Pubmed ID

Primary Reference (PubMed ID)

SEARCH RESET

Filter by therapeutic agent:

- Ibuprofen (12)
- Memantine (10)
- beta amyloid peptide 1-42 (9)
- CHF5074 (9)
- Rosiglitazone (8)

...

Filter by therapeutic target:

- Multi Target (51)
- beta amyloid peptide (42)
- Gamma secretase (31)

Search Results

Displaying 1 - 15 of 279

Download to CSV: All Results | Selected Results

APID	Title	Year	PI Name	Therapeutic Agent(s)
4510715	Beneficial Effects of the Beta-Secretase Inhibitor GRL-8234 in 5XFAD Alzheimer's Transgenic Mice Lessen During Disease Progression	2015	Masuo Ohno	• GRL-8234
4560715	Combined Treatment with a BACE Inhibitor and Anti-Abeta Antibody Gantenerumab Enhances Amyloid Reduction in APP London Mice	2014	Bernd Bohrmann	• RO5508887 • Gantenerumab
4610714	Zileuton restores memory impairments and reverses amyloid and tau pathology in aged Alzheimer's disease mice	2014	Domenico Pratico	• Zileuton
4810714	A Neuroprotective Brain-penetrating Endopeptidase Fusion Protein Ameliorates Alzheimer Disease Pathology and Restores Neurogenesis	2014	Brian Spenser	• ASN12(neprilysin+brain target peptide)
4860714	7,8-dihydroxyflavone prevents synaptic loss and memory deficits in a mouse model of Alzheimer's disease	2014	Keqiang Ye	• 7;8-dihydroxyflavone (7;8-DHF)

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The selective positive allosteric M1 muscarinic receptor modulator PQCA attenuates learning and memory deficits in the Tg2576 Alzheimer's disease mouse model

BIBLIOGRAPHIC | THERAPEUTIC AGENT | ANIMAL MODEL | EXPERIMENTAL

Bibliographic

Published: Published

Year of Publication: 2015

Contact PI Name: Vanita Puri

Contact PI Affiliation:
Merck Research Laboratories, West Point, Pennsylvania, USA

Co-Authors: Xiaohai Wang, Joshua D. Vardigan, Scott D. Kuduk, Jason M. Uslaner

Primary Reference (PubMED ID): 25800972

Funding Source:
Not Reported

Study Goal and Principal Findings:
The purpose of this study was to characterize the effects of the M1 muscarinic receptor pos
PQCA in a mouse model of Alzheimer's disease. Tg2576 transgenic mice that have elevated
novel object recognition task to characterize recognition memory as a function of age and tr
effects of PQCA were compared to the acetyl-cholinesterase inhibitor donepezil, the standar
disease. In addition, the effect of co-administering PQCA and donepezil was evaluated. Aged
a deficit in recognition memory that was significantly attenuated by PQCA. The positive cont
the deficit. Furthermore, doses of PQCA and donepezil that were inactive on their own were f
memory when given together. These studies suggest that M1 muscarinic receptor positive a
ameliorate memory deficits in disease relevant models of Alzheimer's disease. These data, c
findings demonstrating PQCA improves scopolamine-induced cognitive deficits in both roden
suggest that M1 positive allosteric modulators have therapeutic potential for the treatment

Therapeutic Agent

Therapeutic Information:

Therapy Type: Small Molecule
Therapeutic Agent: PQCA
PubMed | ClinicalTrials | Patents
Therapeutic Target: M1 muscarinic receptor
Open Targets | Pharos

Therapy Type: Small Molecule
Therapeutic Agent: Donepezil
PubChem | DrugBank | PubMed | ClinicalTrials | Patents
Therapeutic Target: Acetylcholinesterase
Open Targets | Pharos

Therapeutic Notes:
For structure and other information of PQCA see the following:
 http://www.medkoo.com/products/39978

Animal Model

Model Information:

Species: Mouse
Model Type: APP
Model Name: Tg2576 ALZFORUM
Strain/Genetic Background: C57BL/6

Species: Mouse
Model Type: non transgenic
Strain/Genetic Background: C57BL/6

Experimental Design

Is the following information reported in the study?:

✗ Power/Sample Size Calculation	✗ Randomized into Groups
✗ Blinded for Treatment	✗ Blinded for Outcome Measures
✗ Pharmacokinetic Measures	✗ Pharmacodynamic Measures
✗ Toxicology Measures	✗ ADME Measures
✗ Biomarkers	✓ Dose
✓ Formulation	✓ Route of Delivery
✗ Duration of Treatment	✓ Frequency of Administration
✓ Age of Animal at the Beginning of Treatment	✓ Age of Animal at the End of Treatment
✓ Gender	✗ Study Balanced for Gender
✗ Number of Premature Deaths	✗ Number of Excluded Animals
✓ Statistical Plan	✓ Conflict of Interest
✗ Inclusion/Exclusion Criteria Included	

Outcomes

Outcomes:

Outcome Measured	Outcome Parameters
Behavioral	• Novel Object Recognition Test (NORT)

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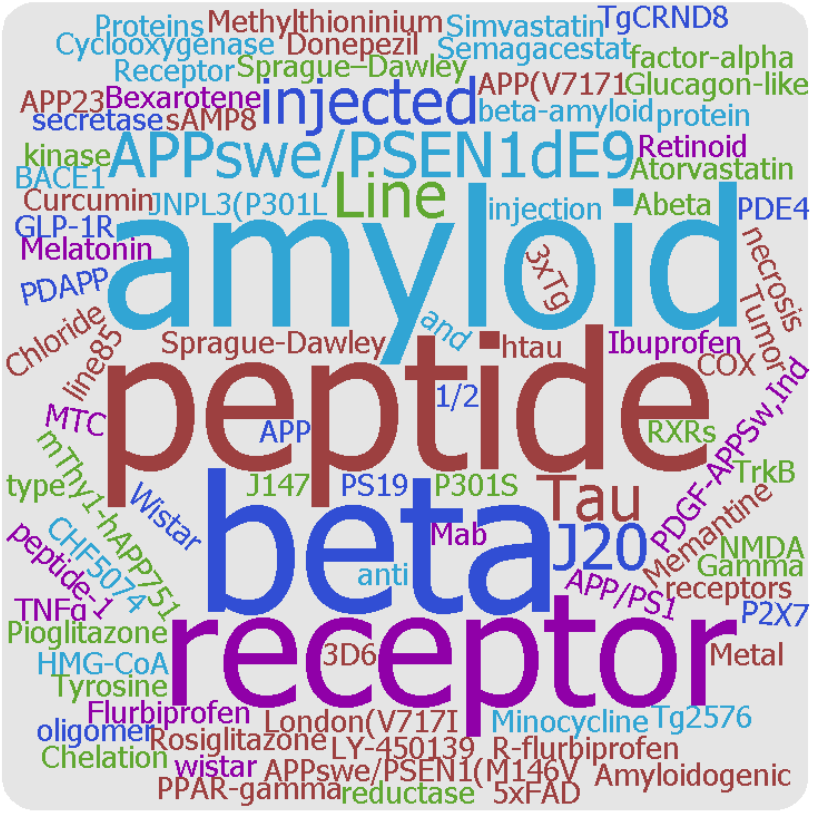
AlzPED – Experimental Design

Experimental Design

Is the following information reported in the study?:

- ✗ Power/Sample Size Calculation ★
- ✗ Blinded for Treatment ★
- ✗ Pharmacokinetic Measures
- ✓ Toxicology Measures
- ✓ Biomarkers
- ✓ Formulation
- ✓ Duration of Treatment
- ✓ Age of Animal at the Beginning of Treatment
- ✓ Gender ★
- ✗ Number of Premature Deaths ★
- ✓ Statistical Plan
- ✗ Inclusion/Exclusion Criteria Included
- ✓ Randomized into Groups ★
- ✓ Blinded for Outcome Measures ★
- ✗ Pharmacodynamic Measures
- ✗ ADME Measures
- ✓ Dose
- ✓ Route of Delivery
- ✓ Frequency of Administration
- ✓ Age of Animal at the End of Treatment
- ✓ Study Balanced for Gender ★
- ✗ Number of Excluded Animals ★
- ✗ Conflict of Interest

AlzPED Ontologies



AlzPED Therapeutic Agents

- Memantine – PubChem Depositor Supplied Synonyms

2.4 Depositor-Supplied Synonyms

1. Abixa
2. Act Memantine
3. Akatinol
4. Apo-memantine
5. Axura
6. DB01043
7. Ebixa
8. Med-memantine
9. Memantina
10. Memantine
11. Memantine Hydrochloride
12. Memantine Hydrochloride Tablets
13. Memantinum
14. Mematine Hydrochloride
15. Memox
16. Mylan-memantine
17. Namenda
18. Namenda XR
19. Novo-memantine
20. PMS-memantine
21. Ran-memantine
22. Ratio-memantine
23. Riva-memantine
24. Sandoz Memantine
25. Sandoz Memantine Fct

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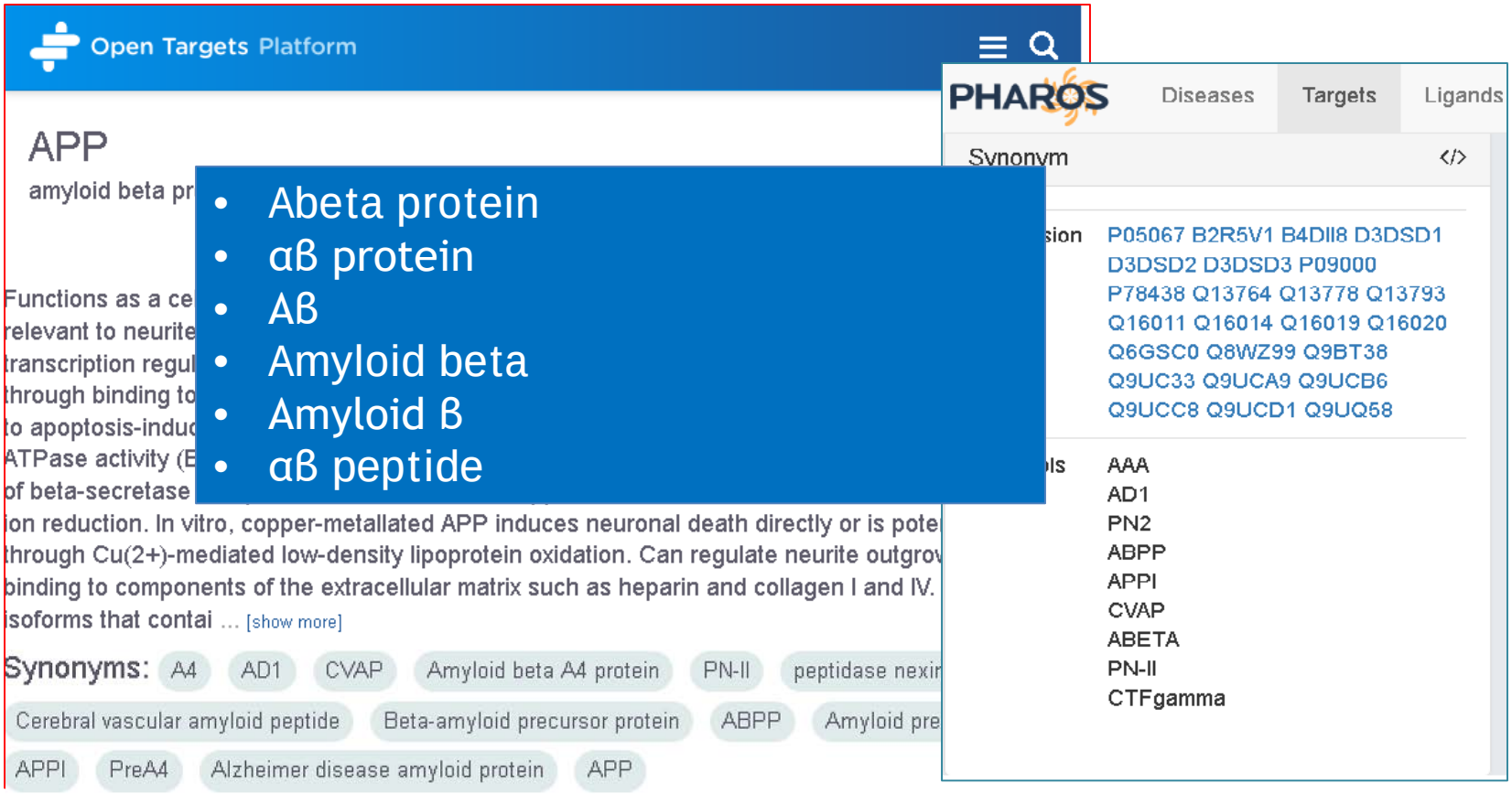
AlzPED Therapeutic Targets



AlzPED Animal Models

Model Name	Synonyms	Description
mThy1-hAPP751 (TASD41)	Line 41 hAPPSL hAPP-SL AβPP751 mThy1-hAβPP751 Swe Lon (line 41) APP751SL hAPPlon/swe line 41 APP41	Strain Name: mThy1-hAβPP751 Swe Lon Genetic Background: C57BL/6 x DBA
APP751SL/PS1KI	APP(SL)PS1KI APPxPS1-Ki APPSL/PS1KI APP(SL)/PS1(KI) APP/PS1KI	Strain Name: N/A Genetic Background: The PS1KI line was established in 129SV and backcrossed >7 times to C57BL/6 background. The PS1KI were bred with APPSL mice on a C57BL background (two rounds) to obtain a homozygote PS1KI and heterozygote APP.

AlzPED – Outcomes Example

Outcomes

Outcomes:

Outcome Measured	Outcome Parameters
Behavioral	• Morris Water Maze
Histopathology	• beta amyloid load • Activated Microglia • Activated Astrocytes
Biochemical	• Brain-beta amyloid peptide 40 • Brain-beta amyloid peptide 42 • APP • APP Metabolites • TNF alpha • Brain Interleukin-1 beta (IL-1beta)
Immunochemistry	• Monocyte Chemoattractant Protein-1 (MCP-1)

AlzPED – Early Feedback

We wanted feedback on:

- The organization of information
- The navigation of the tool
- The Search capabilities of the tool
- The value of the content
- Would this help them to make research decisions

Beta test – Critic

- "Glossary of terms would be really helpful. That might placate some of these issues. Perhaps employ an "Consider Using these Terms"
- "Findability – Sample searches: "3xTg" = 18 hits; "3xTg-AD" = 10 hits; "3xTgAD" = 1 hit; "triple transgenic" = 6 hits; "APPxPS1xTau" = 17 hits"
- "Variability in results is problematic"
- "No internal controlled vocabulary to pick up synonyms; users will become frustrated as a result because it will not be usable."

Beta test – Critic

- “Information is a little tricky to be discoverable by a general researcher. For instance, if they’re utilizing a specific term or abbreviation (ex. ABP), only one result will come up. However, if they typed in Amyloid beta Peptides, they’ll have 92 results.”
- “Searchers may want to filter results according to the Quality Measures in the Experimental Design section.”
- “Curious about the ease of making edits and what that process is. Not knowing that might make me reluctant to add data to the repository.”

Beta test – Positive comments

- "Very helpful in allowing investigators to take a quick look to see what is out there, see what work could be done in-house, and assess what work could be done more quickly. It allows the investigator the ability to assess more accurately what resources need to be brought to the investigation in terms of time and budget."
- "Love what you are doing; providing the ability to drill down to the disease; assist translational research; highlight key elements. Disconcerting how my own publication rated in the assessment. I had some of that information and did not include it in the publication."

Beta test – Positive comments

- "It will change the culture when people have to enter their own studies, and they know they have to address all of these issues [Experiment Design]."
- "This offers one less step of searching which is nice for someone reviewing studies in the discipline or collecting information."
- "A great site for preclinical models as long as scientists populate it. It is easy to navigate, has a lot of functionality and is easy to upload data. The search function was fantastic."

Summary Point

- There needs to be more Rigor and Reproducibility in Alzheimer's disease laboratory research.
- AlzPED can help bring these needed changes.
- A standardize Ontology will also likely help improve discovery of information and comparisons between studies.
- Feedback has been encouraging and many advocate adding unpublished studies to the database.

AlzPED Team

- Dr. Lorenz Refolo
- Dr. Suzana Petanceska
- Dr. Zane Martin
- Ms. Cindy Sheffield
- Ms. Katarina Mancevska

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