Alzheimer's SAN DIEGO

DATE WITH A CURE
Michael Lobatz, MD

Medical Director, Neurosciences
Medical Director, Rehabilitation
Scripps Health

Senior Neurologist and Neuro-Rehabilitation Specialist,
The Neurology Center
Types of Dementia

• Mild Cognitive Impairment

• Alzheimer’s disease (60-80% of cases)

• Dementia with Lewy Body Disease or Parkinson’s Dementia (20% of cases)

• Frontotemporal Dementia (9% of cases)

• Vascular dementia (10% of cases)
First signs of Dementia

- Memory loss
- Poor judgment leading to bad decisions
- Loss of spontaneity and sense of initiative
- Taking longer to complete normal daily tasks
- Repeating questions
- Trouble handling money and paying bills
- Wandering and getting lost
- Losing things or misplacing them in odd places
- Mood or personality changes
- Increased anxiety and/or aggression
<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Approved For</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>donepezil</td>
<td>Aricept</td>
<td>All stages</td>
<td>Nausea, vomiting, loss of appetite and increased frequency of bowel movements.</td>
</tr>
<tr>
<td>galantamine</td>
<td>Razadyne</td>
<td>Mild to moderate</td>
<td>Nausea, vomiting, loss of appetite and increased frequency of bowel movements.</td>
</tr>
<tr>
<td>memantine</td>
<td>Namenda</td>
<td>Moderate to severe</td>
<td>Headache, constipation, confusion and dizziness.</td>
</tr>
<tr>
<td>rivastigmine</td>
<td>Exelon</td>
<td>Mild to moderate</td>
<td>Nausea, vomiting, loss of appetite and increased frequency of bowel movements.</td>
</tr>
<tr>
<td>memantine + donepezil</td>
<td>Namzaric</td>
<td>Moderate to severe</td>
<td>Nausea, vomiting, loss of appetite, increased frequency of bowel movements, headache, constipation, confusion and dizziness.</td>
</tr>
</tbody>
</table>
Recommended screening for cognitive impairment

Developed by:
Alzheimer’s Project
Clinical Roundtable
2016
Michael Jackson, PhD

Senior Vice President, Drug Discovery and Development

Conrad Prebys Center for Chemical Genomics, Sanford Burnham Prebys Medical Discovery Institute
How do you discover a drug?

Patients with rare genetic defects that cause very high cholesterol suffer heart attacks in their twenties.

How to stop cholesterol production?

Liver

HMG-CoA Reductase

HMG-CoA

Mevalonate

Cholesterol

Atorvastatin

Lipitor (Atorvastatin)
**Genetics of Alzheimer’s Disease**

**Genes Linked to Alzheimer’s**

- APP
- PS1
- PS2
- SORL1
- APOE
- PICALM
- ABCA7
- TREM2
- CR1
- CLU
- MS4A6A
- BIN1

**Pathway**

- Processing Amyloid precursor protein (APP)
- Accumulation of Amyloid beta (Aβ)
- Innate Immune and Inflammation
- Aggregation Tau (Tau)

**Pathology**

- Amyloid
- Immune activation
- Tangles

**Pathology Alzheimer’s Disease**
Interventions for Alzheimer’s Disease

Amyloid
Amyloid beta accumulation

Tangle
Neurofibrillary tangles
Neuronal cell death

Intervention to inhibit Aβ production and/or clearing it to reduce plaques

Intervention to inhibit formation of tau tangles & protect neurons from undue stress

Inflammation
Reactive microglia

Intervention to fight inflammation thus slow down or stop disease process
San Diego’s Neuroscience Research Community
Current C4C Targets/Pathways

Elena Pasquale (SBP)  
Robert Rissman (UCSD)

EphA4  
CRF-R1

Amyloid  
Amyloid beta accumulation

Tangle  
Neurofibrillary tangles  
Neuronal cell death

MAPT/Tau-RD

TDP-43

DISEASE PATHOLOGY

Inflammation  
Reactive microglia

CD33  
TREM2

Michael Jackson (SBP)  
Huaxi Xu (SBP)

Recently awarded $1.3M NIH grant

Shauna Yuan (UCSD)  
Don Cleveland (Ludwig)
Collection of
> 1 million drug like chemicals
Robotics to the rescue!
Smaller, faster, cheaper

Automation Compatible

Sanford Burnham Prebys
MEDICAL DISCOVERY INSTITUTE
Alzheimer’s “Disease in a dish”

3D human neural cell culture model of Alzheimer’s disease

(Tanzi and Kim Labs, Nature 2014)
James Brewer, MD, PhD

Director, Shiley-Marcos Alzheimer’s Disease Research Center
UC San Diego School of Medicine
Alzheimer’s Molecular Pathology

All genetic mutations that cause familial AD increase the production of \( \mathrm{A\beta}_{42} \).
Alzheimer’s Molecular Pathology
Amyloid Imaging
Amyloid Imaging Quantification
Main Pathological Components of Alzheimer’s Disease & Dementia

- Tau
- Neurofibrillary Tangles
Imaging Tau (with $^{18}$F-MK6240)

- Excellent Target to Background
- Minimal “Off-target” binding
- May reveal subcategories of AD and improve AD diagnosis

“Stunning Tracer”
Imaging Neurodegeneration with volumetric MRI

Healthy Brain
Imaging Neurodegeneration with volumetric MRI

Alzheimer’s Brain
T2-FLAIR Signal (Lesion) Assessment
Longitudinal Structural Neuroimaging
Biomarkers - Brain Electrophysiology & disease progression

- P50 Click2-Click1; P300 Targets-Standards
- N400 (not shown) incongruous-congruous words
- FP Old-New Pictures;
- LPC Repetition effects New-Old
  - Blue Healthy control; Red Amnestic MCI
- Approximately 2 hour session
Shiley-Marcos Alzheimer’s Disease Research Center: Phenotyping Goals

• C, A, T, N, V, G Characterization
  – C- Cognitive (Neuropsych testing, Clinical Eval)
  – A- Amyloid (CSF Amyloid)
  – T- Tau (CSF Tau; Imaging Tau)
  – N- Neurodegeneration (MRI)
  – V- Vascular (MRI, Retina)
  – G- Genetics (Genome Wide)

• Plus CSF, Plasma, and Stem Cell Banking for future discovery

• Autopsy for confirmation and brain-tissue-based scientific discovery
Paul Aisen, MD
Director,
USC Alzheimer’s Therapeutic Research Institute
Traditional view:

*Alzheimer’s disease begins with the onset of dementia*

- **MCI due to AD**
  - MMSE 26–30
  - Mild subjective/objective memory loss
  - Normal function

- **Mild AD dementia**
  - MMSE 20–25
  - Forgetfulness
  - Repetitive questions
  - Daily function mildly impaired

- **Moderate AD dementia**
  - MMSE 10–19
  - Progression of cognitive deficits
  - Word-finding difficulties
  - Supervision required

- **Severe AD dementia**
  - MMSE 0–9
  - Agitation
  - Altered sleep patterns
  - Total dependence: dressing, feeding, bathing
Alzheimer’s Disease Continuum

- Cognitive performance, FDG-PET, tau PET, atrophy
- $a\beta$
- Clinical function

Clinical stage of disease:
- Normal
- Cognitively Normal
- MCI
- Dementia

Magnitude of change
Remove amyloid for a cure?
Michael Plopper, MD
Chief Medical Officer,
Sharp Behavioral Health Services
Myths of Clinical Trials

• “There are plenty of volunteers, I’m not needed.”
• “There’s no point if I don’t get the study drug.”
• “Trials involve too much time and effort.”
• “I don’t have insurance, so I can’t participate.”
• “I don’t want to lose my own doctors.”
• “If there was a clinical trial that could help me, my doctor would have told me about it.”
What to Expect

1. Prescreening
2. Sign informed consent
3. Evaluate for eligibility
4. Baseline visit if eligible
5. Randomized
6. Active participation and regular visits
7. Potential open label extension and follow up
Benefits of Participating in a Clinical Trial

- Contribute to a better understanding of health conditions
- Help find more effective diagnostic methods, treatments and potential cures
- Access to investigational medications and cutting edge treatments
- Expert medical care
- Take control of diagnosis
- Help others
- Offer hope for the future
Guerry Peavy, PhD

Neuropsychologist
Project Scientist,
UCSD Department of Neurosciences
Effects of Caregiver Stress on Cognition

- What is cognition?
- What do we know about stress?
- Why is caregiving so stressful?
- How does stress affect caregiver health and well-being?
- What is the future of care for Alzheimer’s?
What do we know about stress?

Why is caregiving so stressful?

• Age
• Number of mos /yrs of caregiving
• Number of caregiving hours
• Financial hardship
• Problem behaviors of care recipient
• Cumulative stressors
How does stress affect caregiver health and well-being?

- Thinking / Cognition
- Caring for self
- Responses to other stressful events
- Finding time / energy for socializing
- Sleep
- Mood / sense of well-being
- Physical health (e.g. cardiovascular disease)

What is the future of care for Alzheimer’s disease?
Got Questions?
stretch break
Q&A with the panel
Alzheimer's San Diego

DATE WITH A CURE
Helping families today, finding a cure for tomorrow

Alzheimer's San Diego

EDUCATION

SOCIAL WORK SUPPORT

SUPPORT AND DISCUSSION GROUPS

ALZ COMPANIONS RESPITE

EARLY STAGE SUPPORT

RESEARCH PARTNER

SOCIAL ACTIVITIES AND OUTINGS

MEMORY SCREENINGS

Free in-person support from local experts
alzsd.org | 858.492.4400