

The Critical Scientific Challenges to Prevent Slow and Treat Alzheimer's Disease

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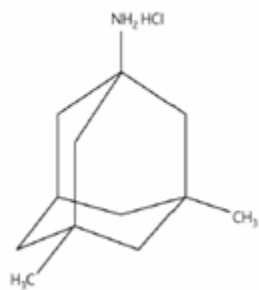
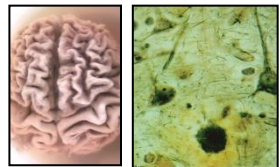
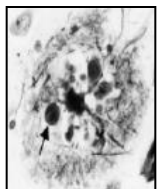


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Disclosure

- 2012 to present, service agreements, clinical trials and/or travel/meeting/lecture support
 - Eli Lilly, Kyowa Kirin, GE Healthcare, Biogen, Arena, Roche/Genentech, Eisai, Baxter
 - NIH, Alz Societies in Canada, Tau Consortium, New York Academy of Science, One Mind for Research, Fidelity Biosciences, Nutricia, Institute of Clinical and Economic Review MGH, CIHR
- 2009-2011, on leave from UBC and employed at Bristol-Myers Squibb Company in CT, USA
 - VP and Therapeutic Area Head, Neuroscience Global Clinical Research

Therapy for AD: Licensed Pharmacologic Therapies



Memantine
NMDA
Uncompetitive
Receptor
Antagonist

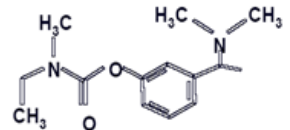


1906 1910 \gg 1974 1982 1997 2004 2010 2015 2020

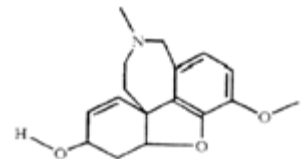


The
cholinergic
hypothesis

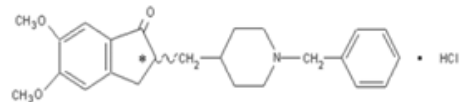
Acetylcholinesterase
inhibitors (AChEI),



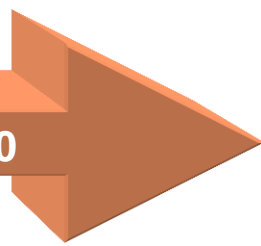
rivastigmine



galantamine

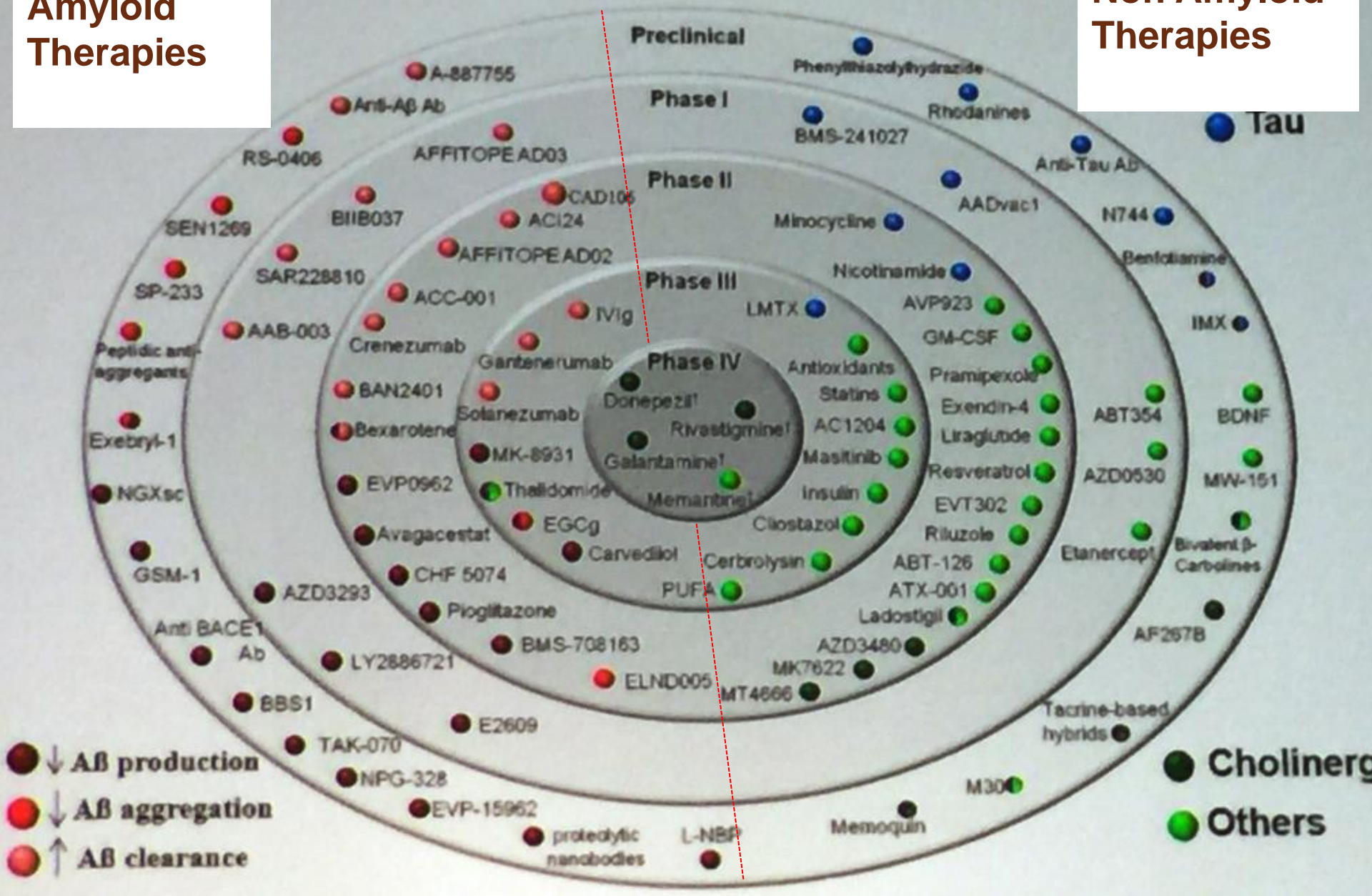


donepezil

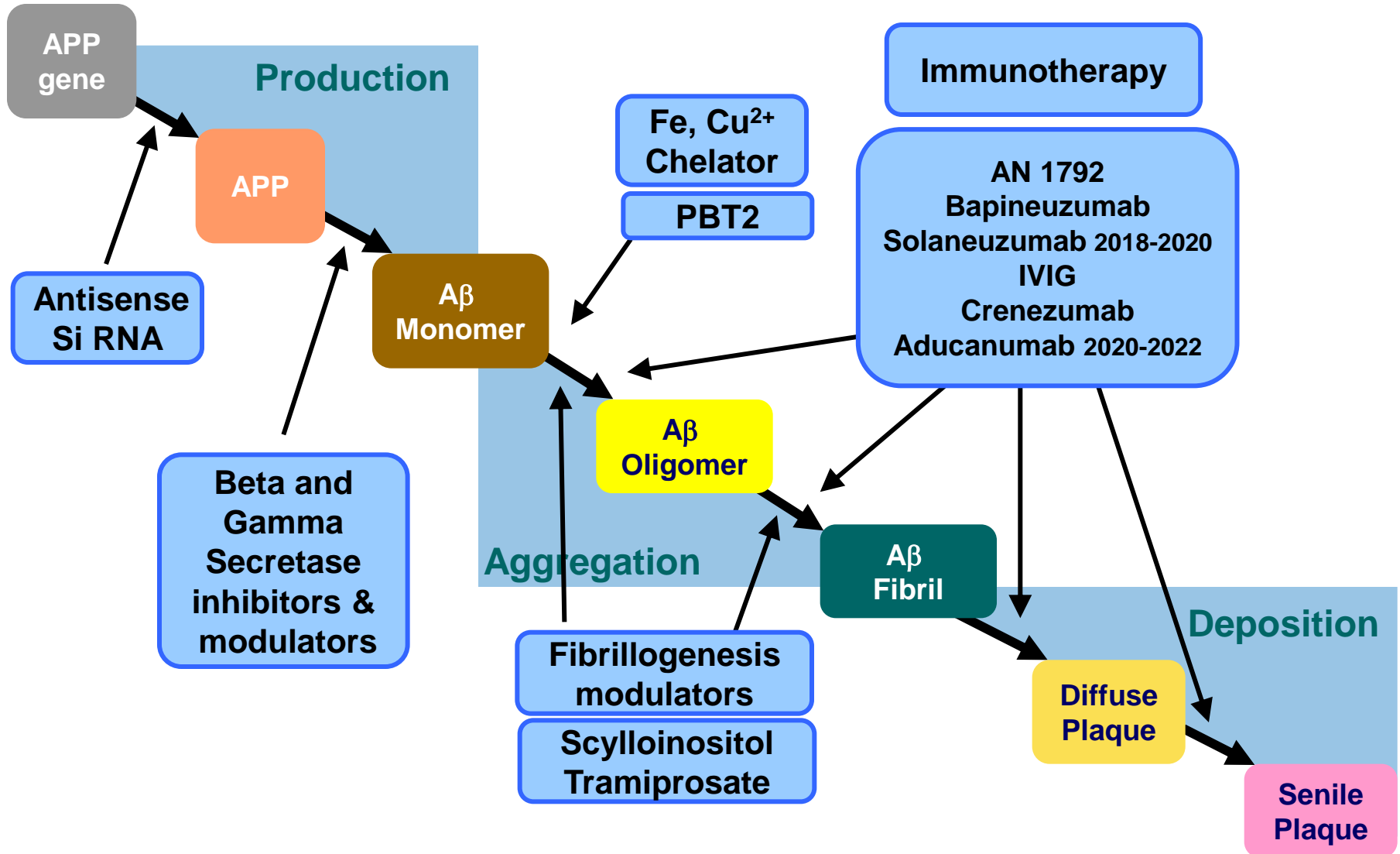


Amyloid Therapies

Non Amyloid Therapies



Experimental Approaches to Amyloid Lowering

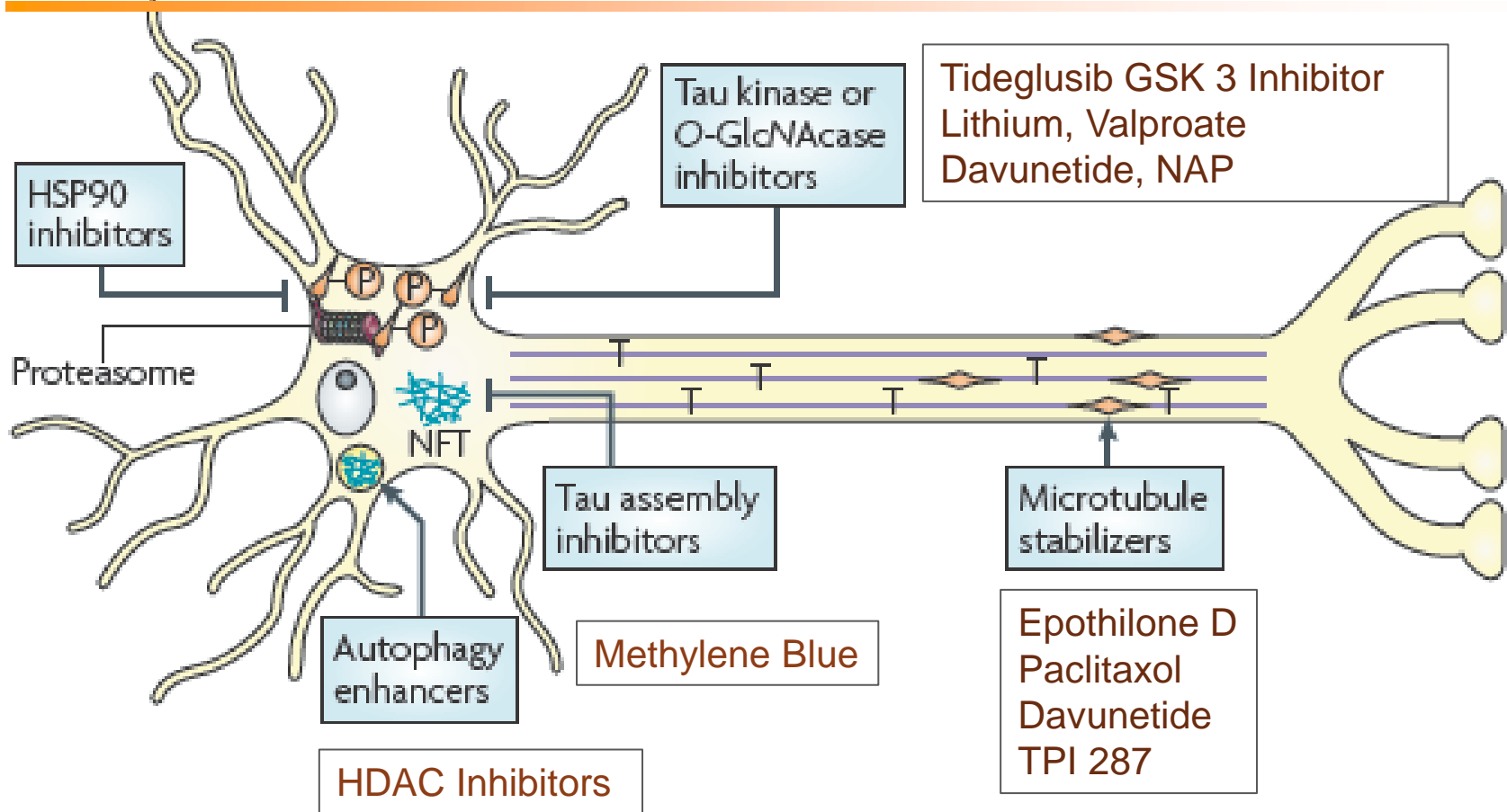


Scorecard for Amyloid Immunotherapy for AD 2014

	Status of Completed Trials	Results	Positive Findings on Subanalyses
Bapineuzumab ¹ N-terminus Soluble/Fibrillar	Phase 3 studies (x2) Mild to Mod AD	Negative trials Terminated program	E4 carriers + Effects PIB PET + Effects p-tau
Solaneuzumab ² Mid domaine Soluble/Sink	Phase 3 studies (x2) Mild to Mod AD	Negative trials Currently mild AD and prevention of AD in DIAN	mild AD on 2ndary outcomes Delayed start
Gammagard IVIG ³ Polyclonal	Phase 2-3 (x1) Mild to Mod AD	Negative trial n/a	E4 carriers + cognitive effects ↓ Aβ 42 Mod AD benefit
Crenezumab Oligomers	Phase 1 Phase 2 trials (x2)	Negative trials Current Ph 2 API trial in PS 1 FAD	Mild AD slower decline
AN 1792 Active vaccination	Phase 1-2	Terminated	Effective removal of aggregated amyloid No correlative clinical benefit

1. Salloway SS et al *N Engl J Med* 2014; 2. Doody R et al *N Engl J Med* 2014
3. Relkin N *J Clin Immunol* 2014 4. Ostrowitzki et al *Arch Neurol* 2012

Treatments Directed at Tau

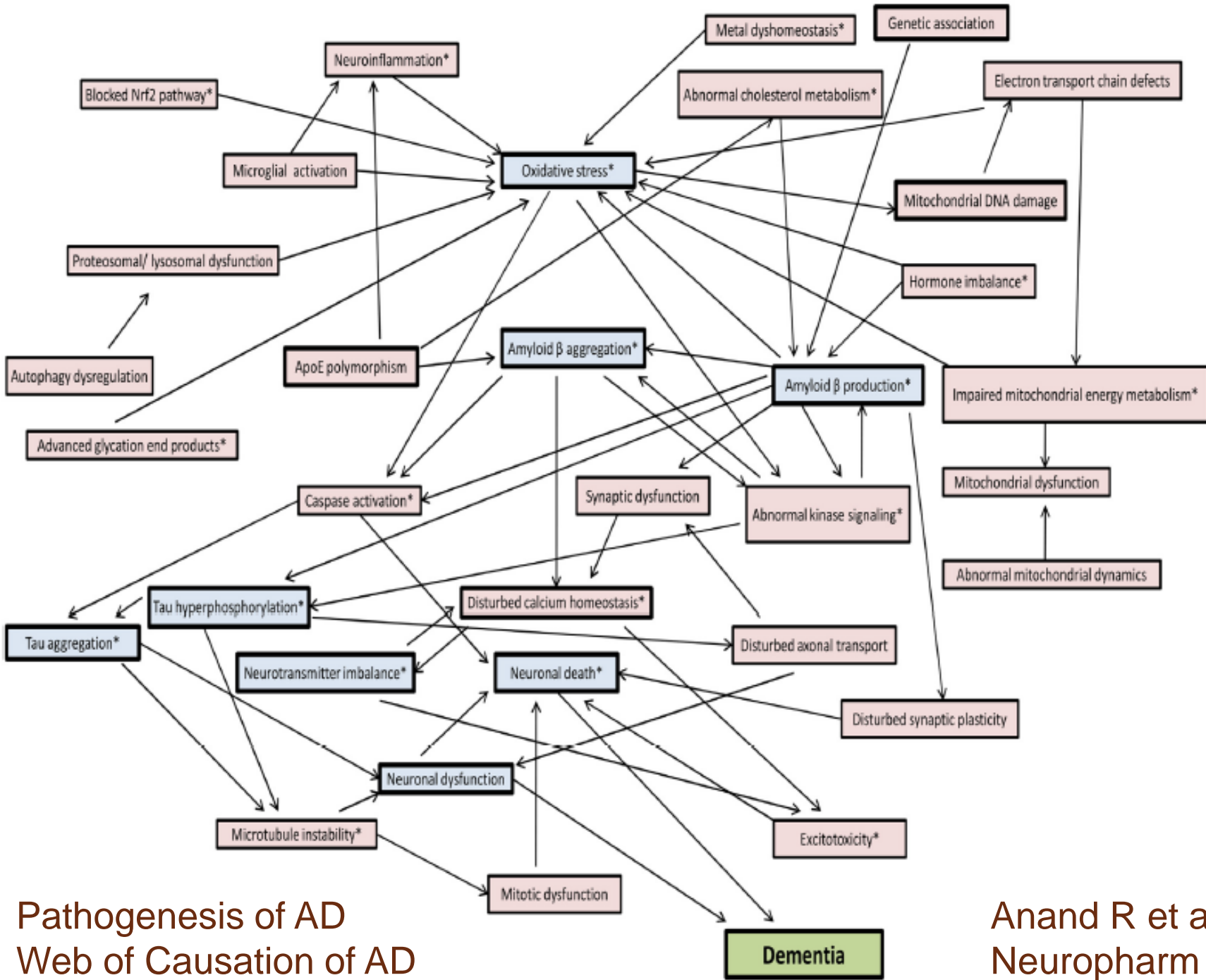


Immunotherapy directed at tau;

Antisense Oligonucleotides

AAD Vac 1, C2N8E12, BMS 986168

Tau Mutations



Pathogenesis of AD
Web of Causation of AD

Anand R et al
Neuropharm 2014

Summary

- **No new therapies approved in 12 years.....unmet needs in**
 - **Treating symptoms, cognitive and behavioral**
 - **Prevention of disease**
 - **Rx that can sustain benefits over the disease course**
- **Deep investment made by industry and academe in amyloid rx**
 - **Expected readouts in 2018-2022, negative trials to date**
 - **No well formed “plan B”**
- **Unique opportunity for academic networks to innovate and lead**
 - **Broaden targets and compound selections**
 - **Focus on achieving**
 - **POC including clinical evidence**
 - **advancing novel design and methods (GAP, CPAD)**
 - **biomarkers and outcomes**

Priority Efforts for Consideration

Focus for our Meeting

- **Public health interventions directed at prevention**
- **Advancing systems of care; workforce, delivery, societal change**
 - **Dementia friendly communities**
 - **National plan**
- **Mobilizing technologies**
- **Setting a broad agenda**
- **Consideration of a CAHS formal assessment**

What Opportunities and Challenges Stand Out in the Canadian Environment?

Opportunities

- Recognition of the national significance of AD and dementia
 - Dementia Friends
 - National research strategies CCNA, CLSA, C5R
- Single payer system
- Systems of care
- Some provincial plans

Challenges

- Health as a provincial jurisdiction
- Speed of mobilization and adoption of research to practice