



Alzheimer's disease

A BIOCHEMICAL MAZE

1901

Dr Alois Alzheimer meets with Auguste Deter, a patient who experiences memory loss, paranoia and unexplained psychological changes.





1906

During Auguste Deter's autopsy, Dr Alzheimer notes that there were strange protein plaques found in her cortex. These would later be classified as amyloid plaques.

1910

Emil Kraepelin coins the term “Alzheimer’s disease” (AD).



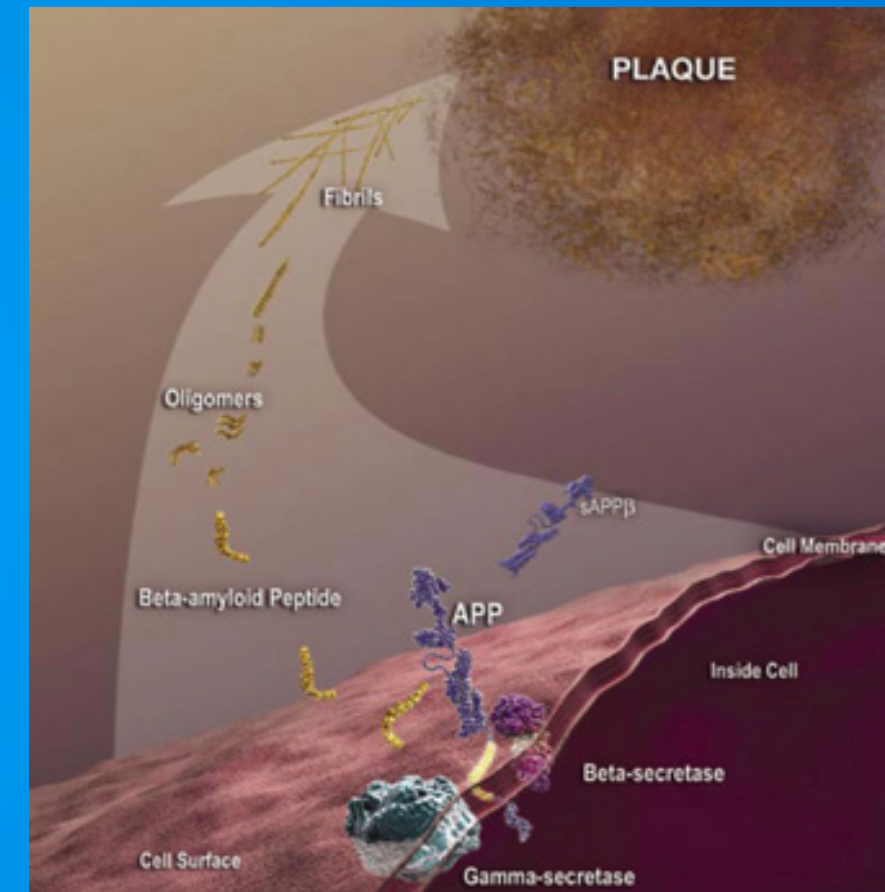


1931

The electron microscope is invented by Max Knoll and Ernst Ruska, allowing magnification of up to 1 million times. This gives scientists the tool to observe neurons with greater detail.

1963

Robert Terry and Michael Kidd present detailed ultramorphological studies on the amyloid plaque in post-mortem AD brains.



1968

Sir Martin Roth equates pathology and cognitive decline of common senile dementia to that of AD.

1974

In the United States, congress establishes “National institute of Aging” (NIA) to fund and support research into Alzheimer’s disease.





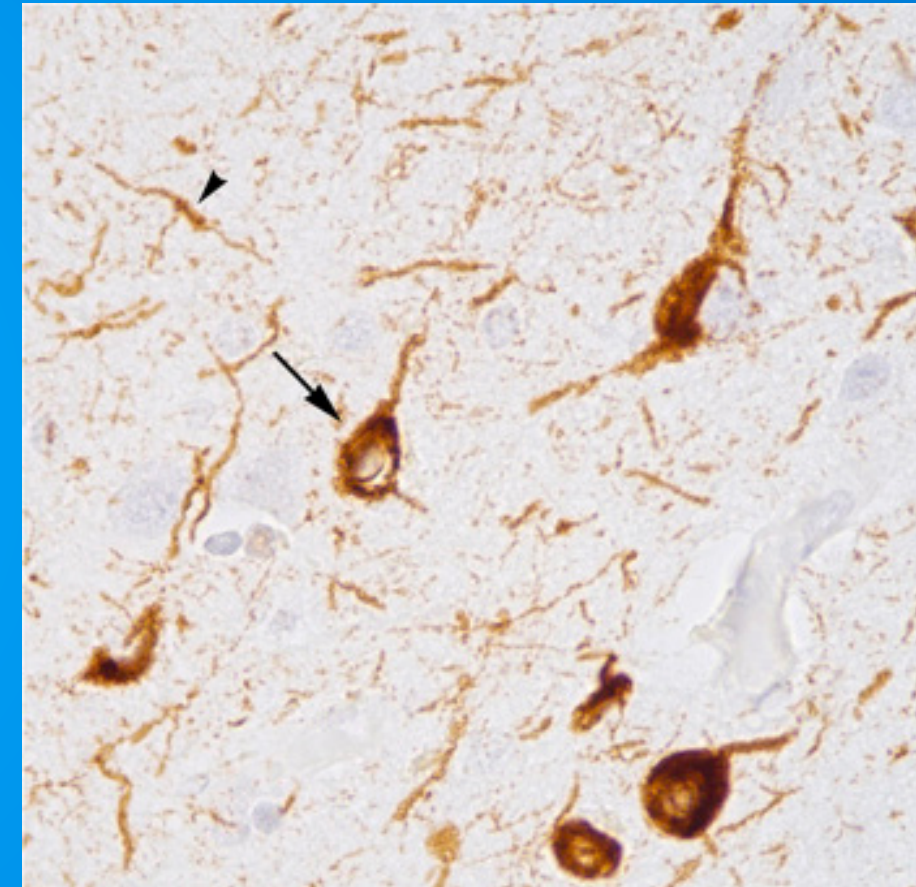
1975

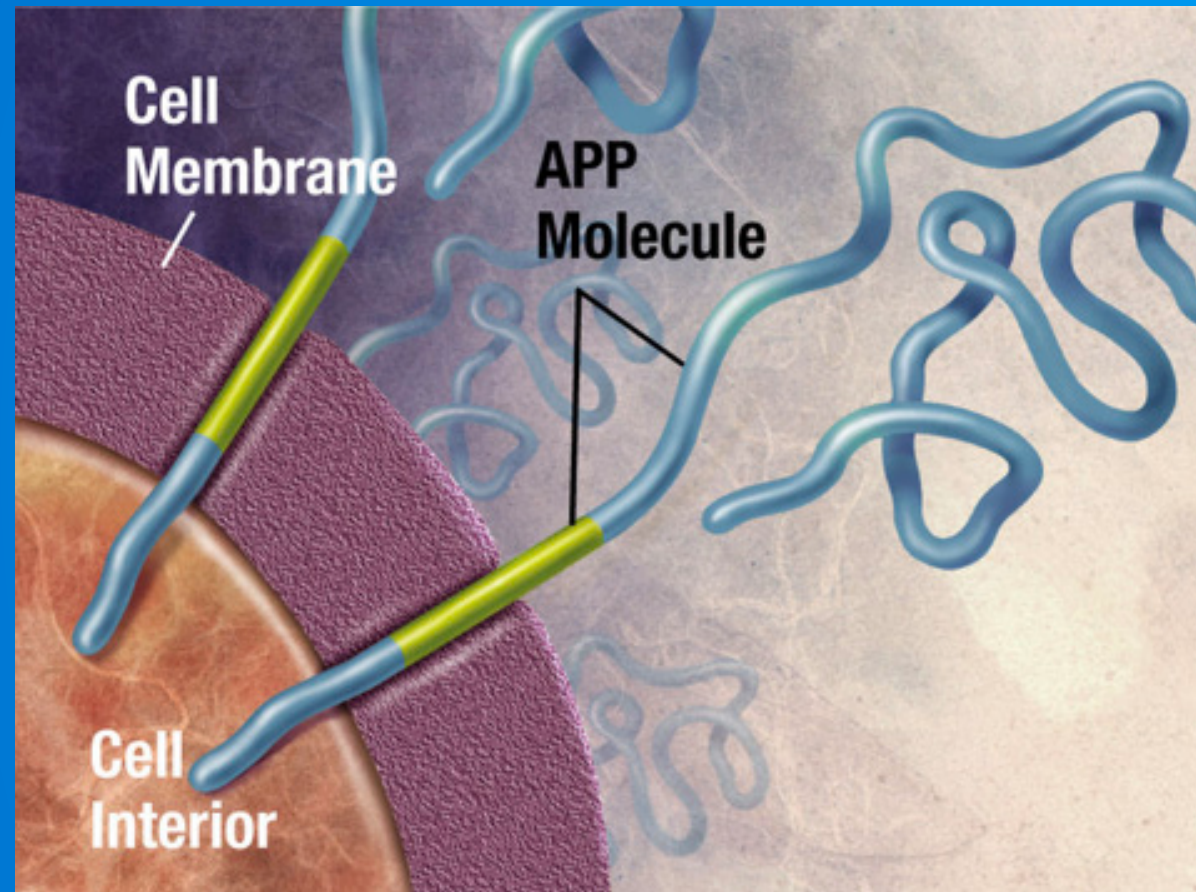
The mini-mental State Exam (MMSE) is developed to screen mental status. It is still used today by clinicians to help diagnose dementia and to help assess its progression and severity.

1985

Tau proteins are identified as the main component of neurofibrillary tangles¹.

1. Tulemo [CC BY-SA 4.0 (<https://creativecommons.org/licenses/by-sa/4.0>)]





1990

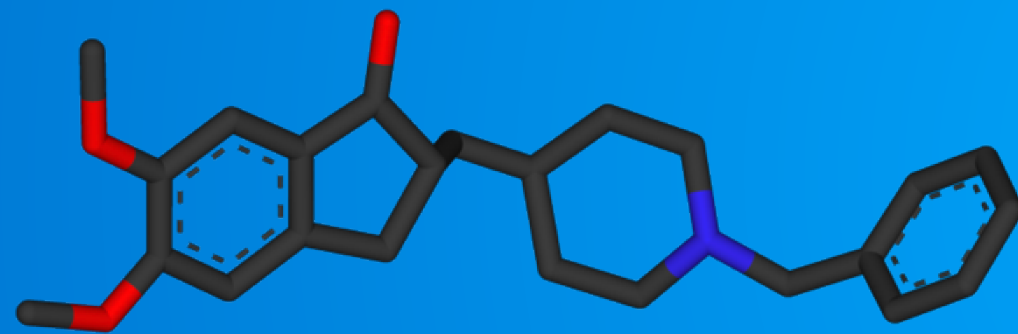
It is shown for the first time that Alpha cleavage of Amyloid precursor protein prevents A β formation².

2. ADEAR: "Alzheimer's Disease Education and Referral Center, a service of the National Institute on Aging." [Public domain]

1993

FDA approves the first Alzheimer's drug, Cognex. The drug targets memory loss and dementia symptoms.





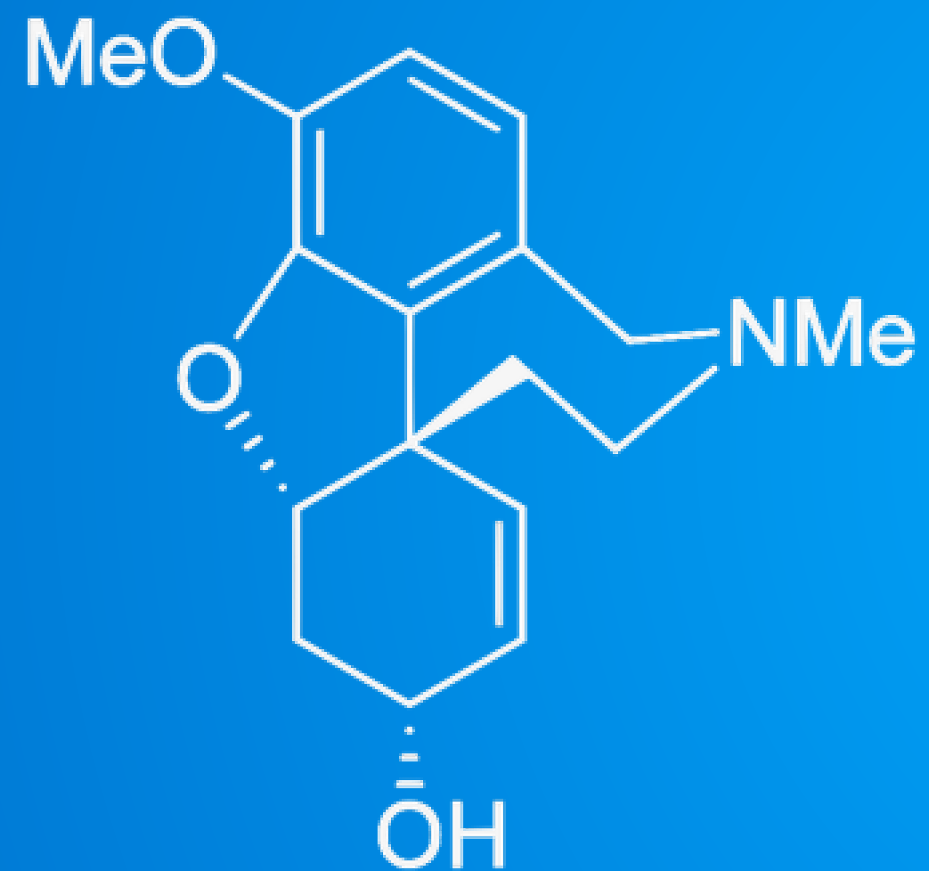
1996

Donepezil is approved by FDA to aid the cognitive function of those with the disease. It does this by increasing acetylcholine concentrations at cholinergic synapses.

1997

Rivastigmine is first used to treat patients with moderate AD.





2001

Galanthamine is approved by the FDA to be used for the treatment of cognitive decline in mild to moderate Alzheimer's disease and various other memory impairments³.

3. JMakis [CC BY-SA 3.0 (<https://creativecommons.org/licenses/by-sa/3.0/>)]

2002

Memantine is approved to treat moderate to severe Alzheimer's disease.





2003

The NIA initiates a genetic study of AD to identify risk factor genes for the disease⁴.

4. Sourced from National Institute of Aging: <https://www.nia.nih.gov/>

2005

Phenserine fails in phase 3 and Clioquinol fails in phase 2.





2006

Atorvastatin fails in phase 3.

2009

Solanezumab enters phase 3.



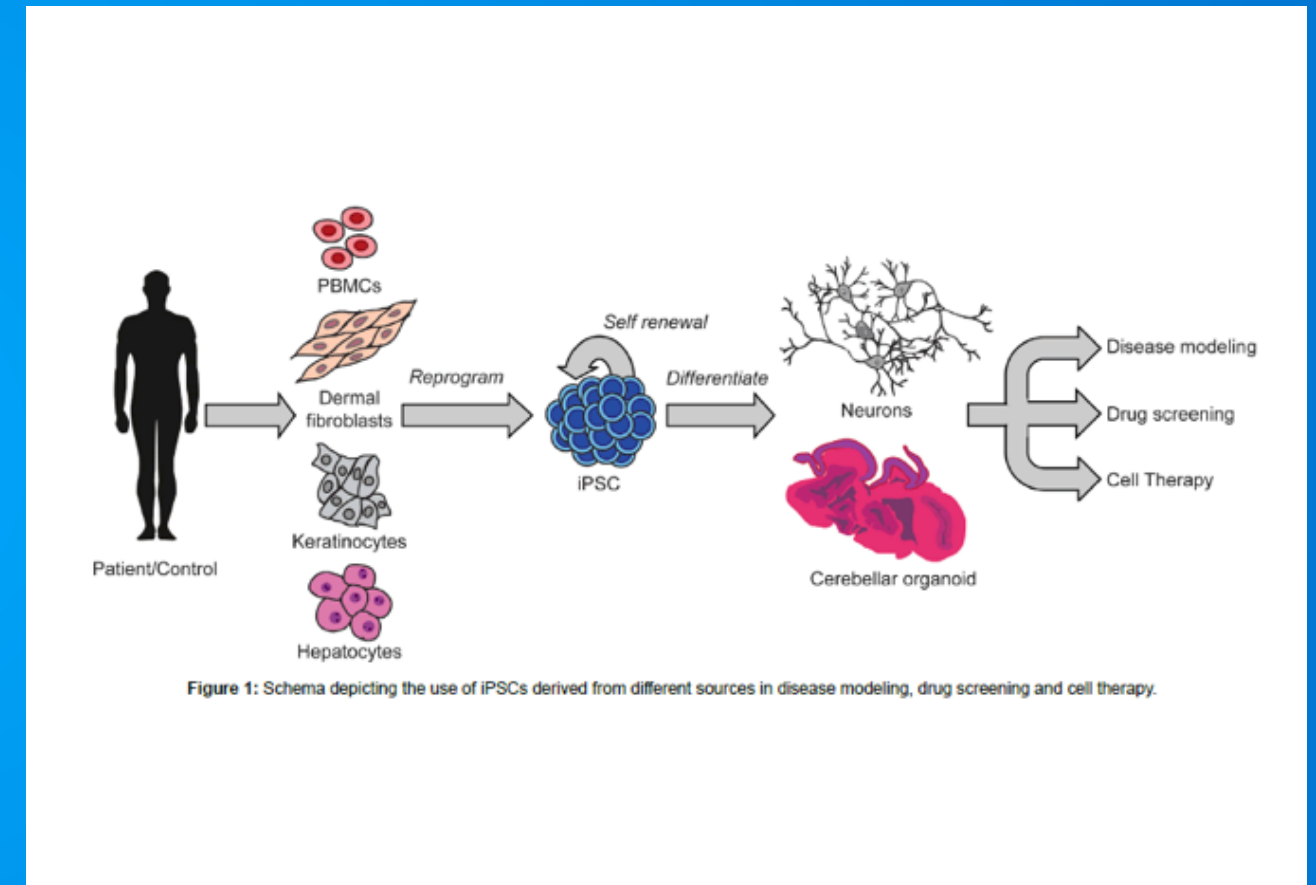


2010

Alzheimer's prevention initiative is launched just as AD becomes the sixth leading cause of death in the United States.

2012

Induced pluripotent stem cells from AD patients closely resembles most aspects of disease.



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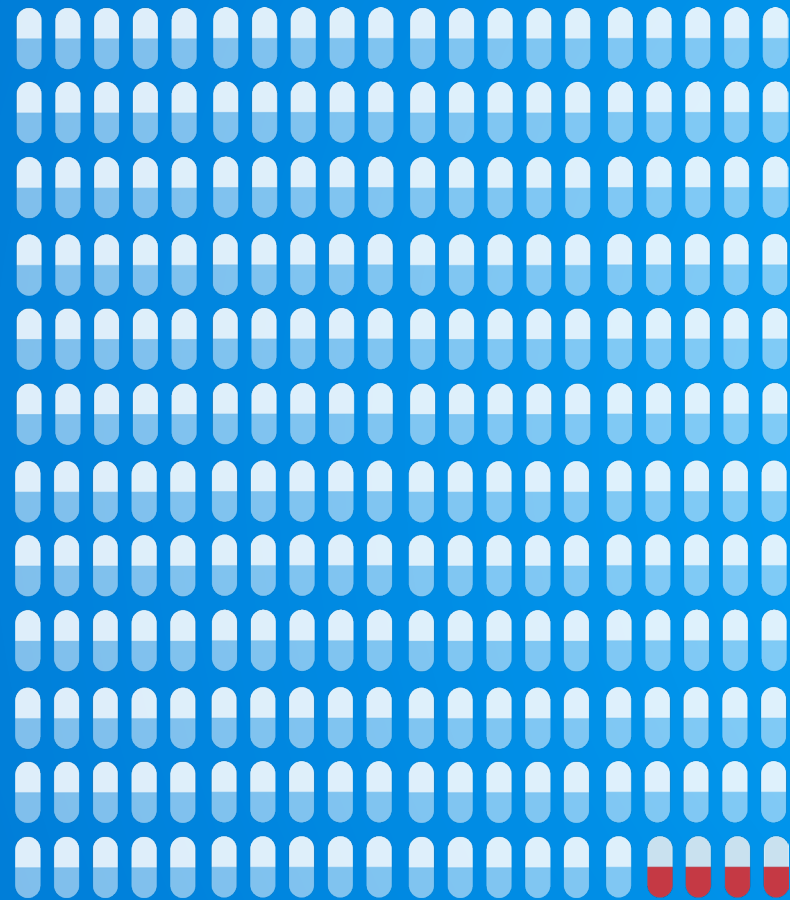
2013

Idalopirdine enters phase 3.

2015

Biogen begins a phase 1 study of Aducanumab with increasing doses up to 6 mg/kg in 25 patients with mild to moderate AD.





2017

Between 1998 and 2017 there have now been 146 drugs which have failed to achieve FDA approval.

2018

Idalopirdine and Solanezumab fail in phase 3 clinical trials.



Mar 2019

Biogen announces they are terminating all currently ongoing aducanumab trials, following an interim analysis that predicted EMERGE and ENGAGE would miss their primary endpoints.

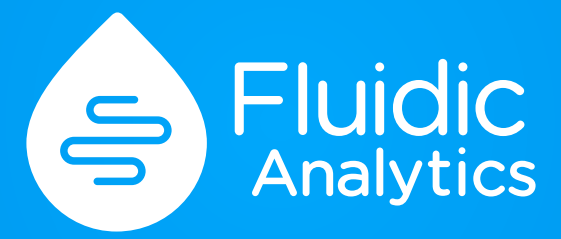
Oct 2019

Biogen announce that the interim futility analysis was incorrect, and that subsequent analysis of a larger data set instead showed EMERGE had met its primary endpoint.



2020

Prof Linse to release a paper to show for the first time, the mechanism of action that aducanumab takes to reduce the flux of oligomeric forms of amyloid β .



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