



Séance académique

Academische zitting

16 juni - juin 2011

→ **K.U.Leuven**

- Prof. dr. Claudia Bagni
mRNA metabolism at synapses and spine remodeling: insights into fragile X, autism and Schizophrenia.
- Prof. dr. Danny Huylebroeck
Developmental origin of multiple defects of the nervous systems in Mowat-Wilson syndrome and its new insights for normal embryonic and adult neurogenesis.

→ **UA**

- Prof. dr. Marc Cruts
Molecular genetics and functional genomics of frontotemporal lobar degeneration.
- Prof. dr. Vincent Timmerman, PhD
Charcot-Marie-Tooth neuropathies: from genes to protein networks and disease mechanisms.

→ **UCL**

- Dr. Fadel Tissir
Celsr genes in brain development and function.

→ **UGent**

- Prof. dr. Christophe Ampe
 β -actin in neural crest cell migration and brain development.
- Prof. dr. Geert van Loo
Study of the role of the NF- κ B regulatory protein A20 in autoimmune central nervous system inflammation.

→ **ULB**

- Prof. dr. Eric Bellefroid
Role of DMRT transcription factors in the development of the cerebral cortex.
- Prof. dr. Serge N. Schiffmann
Roles of specific genes and neuronal populations in functions and disorders of basal ganglia.
- Prof. dr. Pierre Vanderhaeghen
From stem cells to cortical networks.

→ **ULg**

- Prof. dr. Pierre Maquet
Characterization of human sleep/Wake regulation using multimodal functional imaging in populations stratified on the polymorphism of PERIOD3 gene.
- Prof. dr. Laurent Nguyen
Unravelling the roles of lysine acetylation in neural development.

→ **VUB**

- Prof. dr. Ilse Smolders
Unveiling the role of the cystine/glutamate antiporter (system X_c^-) in hippocampal functioning, mechanisms of epilepsy and its comorbidities: a new era for future drug treatment.

→ **UCB Award 2011 – € 100.000**

- Laureaat - Lauréat: prof. dr. Bart De Strooper (K.U.Leuven)

Potential role of dysregulation of the microRNA network in Alzheimer's disease.

Hier wordt onderzocht hoe de expressie van eiwitten in de hersenen van patiënten met de ziekte van Alzheimer door veranderingen in microRNA kan veroorzaakt worden. Dit werk zal niet alleen helpen om te begrijpen hoe microRNA de hersenfunctie beïnvloeden, maar ook leiden tot nieuwe diagnostiek en hopelijk behandelingen voor de ziekte van Alzheimer.

→ **Solvay Prize – € 25.000**

- Laureaat - Lauréat: prof. dr. Pierre Vanderhaeghen (ULB)

Mechanisms of the development and evolution of the cerebral cortex.

Le projet de l'équipe de Pierre Vanderhaeghen vise à identifier les mécanismes génétiques et cellulaires du développement des neurones du cortex cérébral. Il combine des approches de génétique chez la souris et l'utilisation de cellules souches pluripotentes murine et humaines.

→ **Prijs - Prix ING – € 15.000**

- Laureaat - Lauréat: prof. dr. Serge N. Schiffmann (ULB)

Roles of specific neuronal populations in functions and disorders of basal ganglia: a transgenic and molecular approach.

Noyaux de la base: réseau de neurones sous-corticaux

Fonctions et dysfonctions: contrôle et apprentissage moteurs, comportements motivationnels, maladie de Parkinson, toxicomanies.

Projet: Propriétés fonctionnelles différentielles de populations neuronales, implications en pathologie.

Approche : Identification de gènes spécifiques par “*profiling*” génétique, ablation spécifique de populations neuronales, inactivation neurone-spécifique de gènes, activation *in vivo* par optogénétique

→ **Prijs - Prix van Gysel de Meise – € 12.500**

- Laureaat - Lauréat: prof. dr. Pierre Maquet (ULg)

Characterization of spontaneous brain activity in unconscious participants by multimodal functional neuroimaging.

Notre projet vise à déterminer l'influence de la pression de sommeil et de l'horloge circadienne sur le fonctionnement cérébral régional en recourant à des techniques de neuroimagerie multimodale et des populations de volontaires sains caractérisés sur le plan génétique et étudiés dans des conditions contrôlées.

→ **Prijs - Prix Janine et Jacques Delruelle – € 12.500**

- Laureaat - Lauréat: prof. dr. Wim Vanduffel (K.U.Leuven)

Large-scale causal functional interactions between cortical areas: from anatomy to neuro-pharmacology.

Functionele reorganisatie na een omkeerbaar letsel in de hersenschors.

Taak-afhankelijke adaptieve veranderingen in het functioneren van de hersenschors na een klein letsel.

Causale interacties tussen gebieden van de frontale en occipitale hersenschors gemeten door middel van fMRI-microstimulatie technieken.

Frontaal-gedreven modulatie van signaal verwerking in de occipitale hersenkwab.

→ **Prijs - Prix CBC Banque – € 10.000**

- Laureaat - Lauréat: prof. dr. Christine Van Broeckhoven, PhD, DSc (UA)
Onderzoeksgroep Neurondegeneratieve Hersenziekten, VIB, Instituut Born-Bunge en Universiteit van Antwerpen

Progranulin in neurodegenerative dementia: genetic, functional and neuropathological characterization.

De genetische identificatie van progranuline koppelde voor de eerste keer neurodegeneratie aan het verlies van een groeifactoractiviteit. Begrip van de biologische rol van progranuline zal naar verwachting nieuwe wegen openen voor de behandeling van het toenemende aantal in onze samenleving van ouderen met dementie.

→ **Prijs - Prix Cercle Gaulois - Thierry Speeckaert – € 9.000**

- Laureaat - Lauréat: prof. dr. Rufin Vogels (K.U.Leuven)

Coding of biological motion in macaque monkeys: relating perception and neuronal selectivity.

Registratie van actiepotentialen van neuronen in de temporale visuele cortex van de wakere, getrainde aap: hoe coderen deze neuronen dynamische beelden van acties? Coding via twee mechanismen: momentane lichaamshouding – snapshots van de actie - en sequentie van lichaamshoudingen –specifieke opeenvolging van snapshots.

Programme - Programma

15:00

→ Inleiding - Introduction

- De heer - monsieur Alain Siaens

Voorzitter van de Raad van Bestuur - Président du Conseil d'Administration

→ Voorstelling van de onderzoeksploegen - Présentation des équipes de recherche – 2011-2013

- Prof. em. dr. Baron de Barsy

→ Uitreiking van de onderzoekskredieten - Remise des crédits à la recherche

- H.K.H. Prinses Astrid en prof. em. dr. Baron de Barsy

→ Voorstelling van de weerhouden onderzoeksprojecten voor de wetenschappelijke prijzen van de GSKE - Présentation des projets retenus pour les prix scientifiques de la FMRE

- Prof. em. dr. Baron de Barsy

→ Overhandiging van de prijzen - Remise des prix

- H.K.H. Prinses Astrid en de prijsgevers - S.A.R. la Princesse Astrid et les donateurs de prix:
 - Solvay Prize: Graaf - Comte Bernard de Laguiche, CFO and member of the executive committee at Solvay S.A.
 - Prix ING: de heer - monsieur Dembour.
 - Prix van Gysel de Meise: Baron van Gysel de Meise.
 - Prix Janine et Jacques Delruelle: Baron et Baronne Delruelle.
 - Prix CBC Banque: Chevalier Fernand de Donnea.
 - Prix Cercle Gaulois-Thierry Speeckaert: de heer - monsieur Thierry Speeckaert.

→ Voorstelling van - Présentation du prof. dr. Bart De Strooper

- Prof. em. dr. Baron de Barsy

→ Voorstelling - Présentation UCB Award

- Dr. Roch Doliveux: CEO UCB Group

→ Overhandiging van de UCB Award - Remise du UCB Award

- H.K.H. Prinses Astrid - S.A.R. la Princesse Astrid en dr. Roch Doliveux

→ Conférentie - Conférence

- Prof. dr. Bart De Strooper, laureaat van de UCB Award

Nieuwe inzichten in de ziekte van Alzheimer: een rol voor micro RNA?

16:30

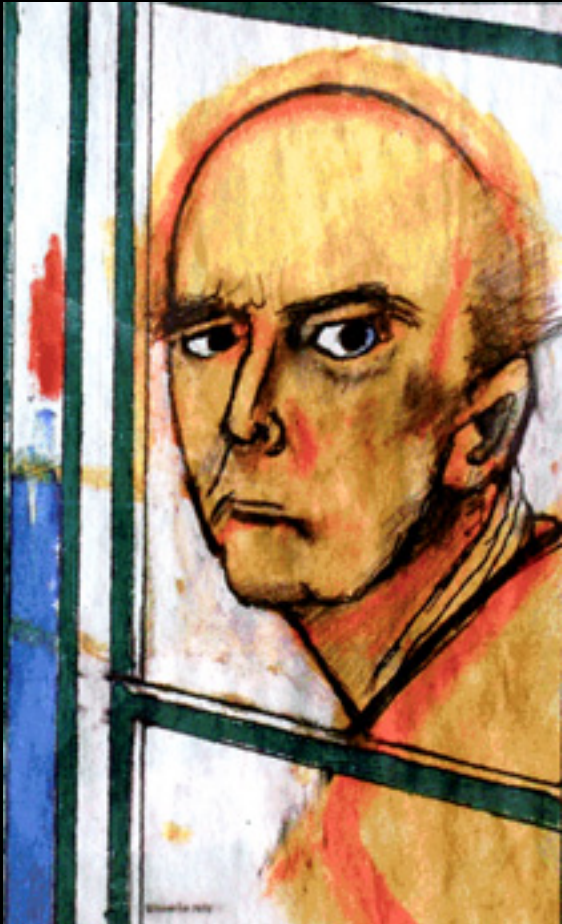
→ Receptie - Réception



Potential role of dysregulation of the microRNA network in Alzheimer's Disease



William Utermohlen



1996



1997



2000

Alzheimer's Disease

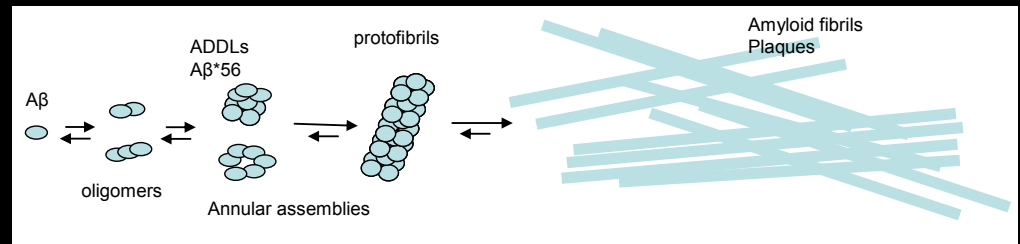
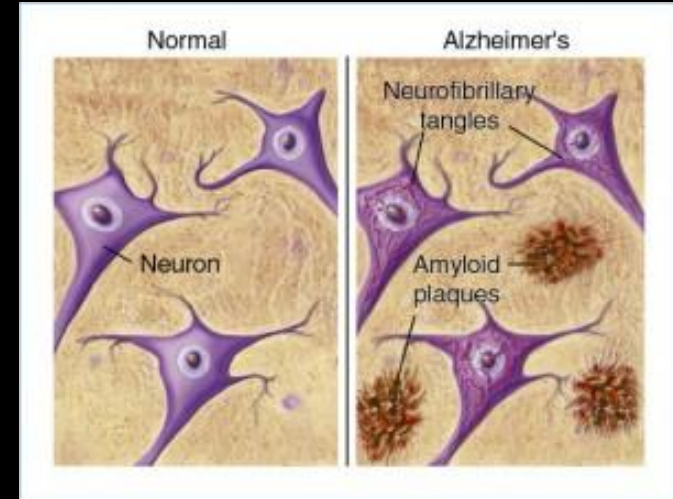
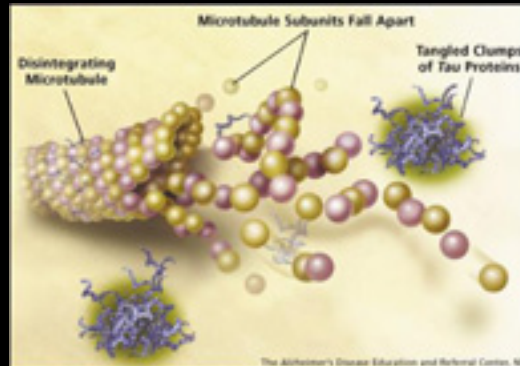


Symptoms:

- Cognition problems
- Memory loss
- Progressive dementia

Pathological hallmarks:

- Phosphorylated tau
- A β plaques



Social impact

1. Psychological, moral and financial heavy burden for caring partner and family

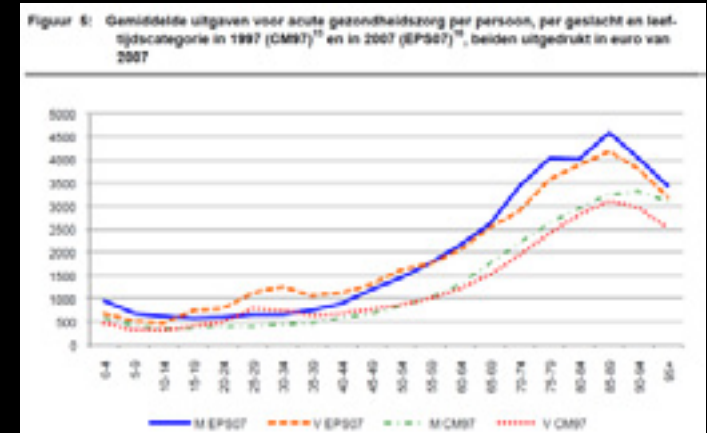
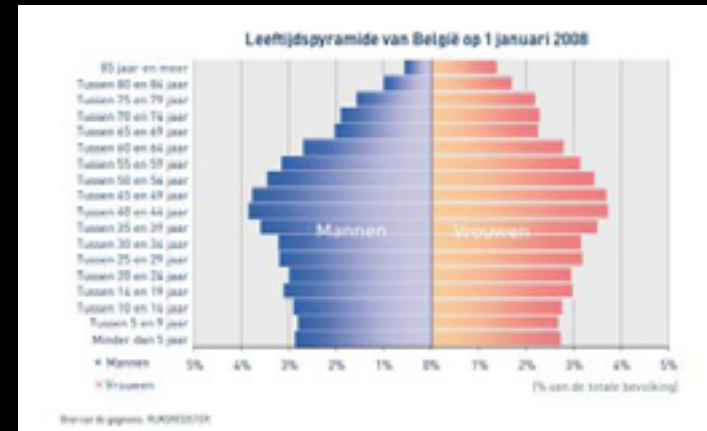
- +formal care: 14.550 euro/year, 3.116 euro to be paid by the family
- +institutional care: 22.585 euro/year, 9.600 euro to be paid by the family
- +1.72 billion euro's year

2. A heavy burden for our next generation

- +160.000 demented patients now;
- 251.000 patients in 2030

3. Ethical and social choices have to be made; this is a political urgency !)

- +Migration
- +Medical care at the end of life
- +Euthanasia



Research into the cause of Alzheimer's Disease

Hope for therapy

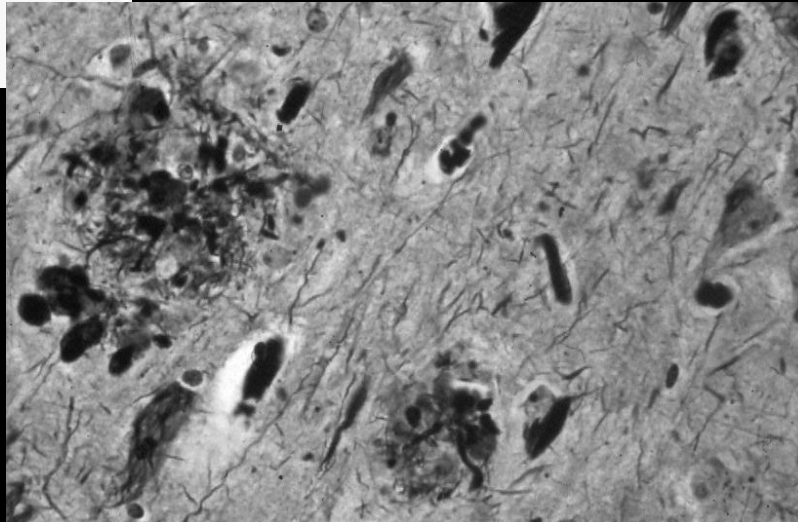
1. The microscope – diagnosis
2. Biochemistry – first treatment

Alzheimer's Disease

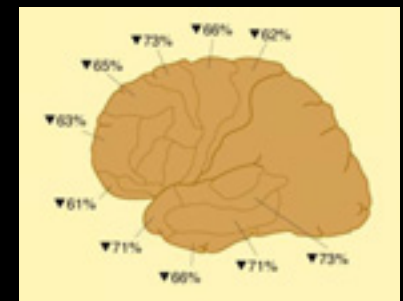
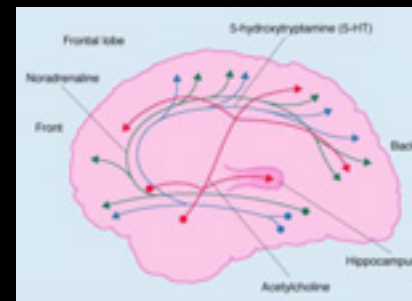
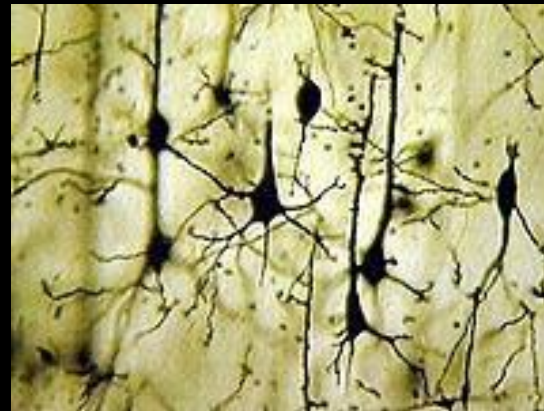
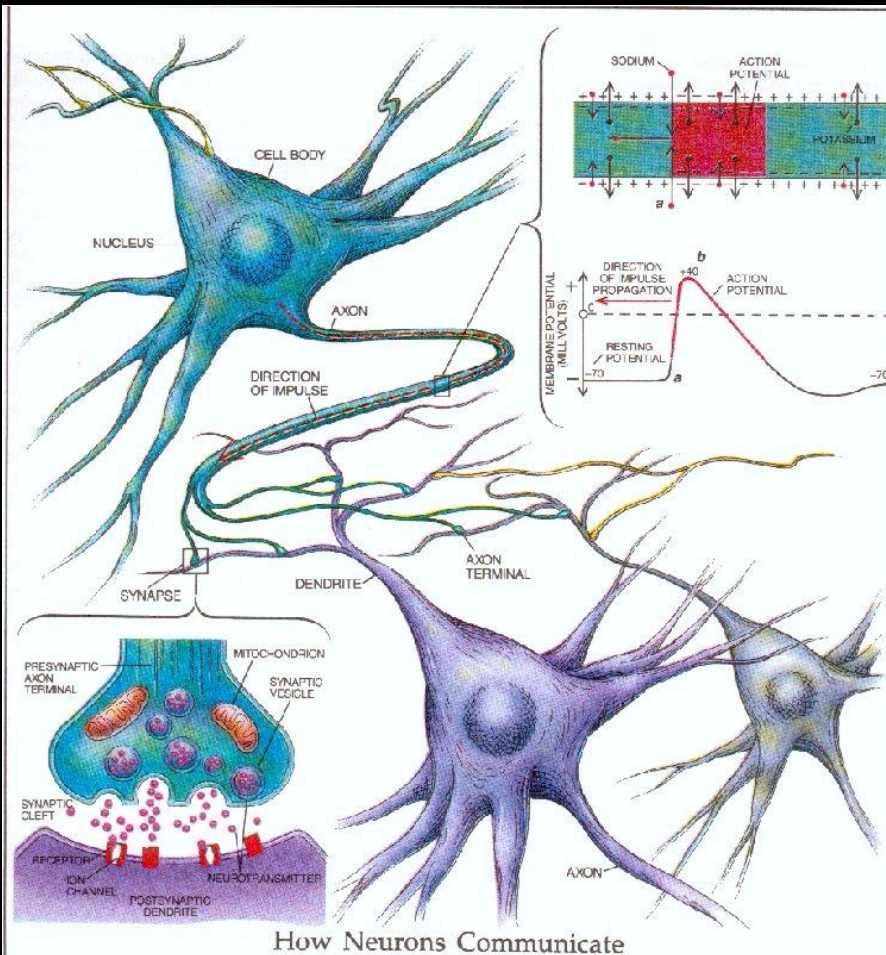


Alzheimer

*Über eine eigenartigen schweren
Krankheitsprozess der Hirnrinde.*
Neurolisches Zentralblatt, Leipzig,
1906, 25: 1134.



The cholinergic hypothesis of the '70s

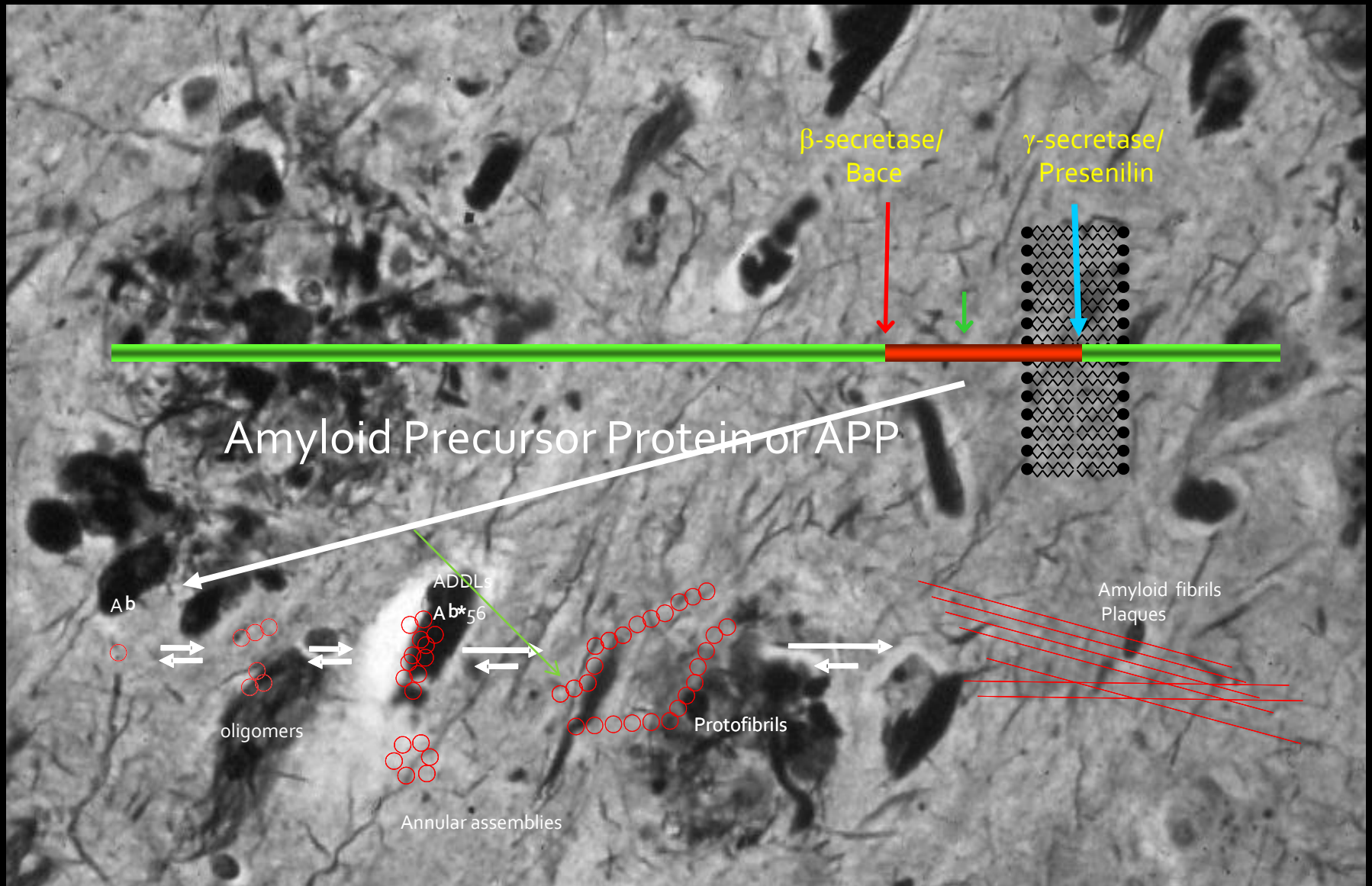


Cholinesterase inhibitors

Cognex (tacrine); Aricept (donepezil), Exelon (rivastigmine)
and Reminyl (galantamine)

Poorly active: work in less than half of the patient population
Gain: only a few months in the decline process

Side effects are very moderate:
Nausea, gastro-intestinal cramps, vomiting

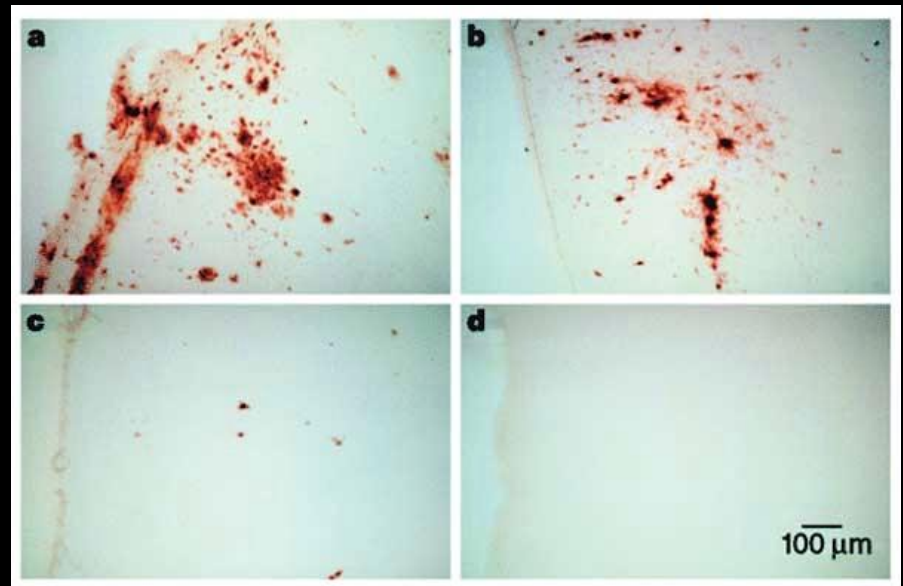


Anti-amyloid treatments

1. Vaccination
2. β -secretase inhibitors
3. γ -secretase inhibition or modulation

$A\beta$

Immunisation therapy



Dale Schenk, Nature 1999

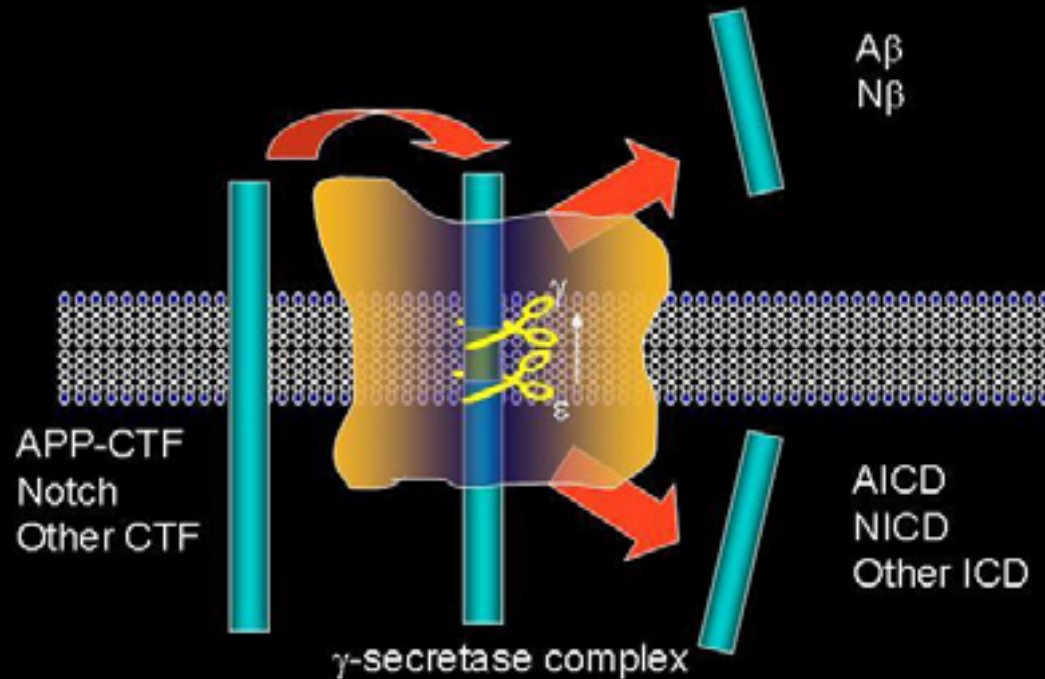
Vaccination

ELAN and Wyeth

1. Preclinical tests in mice: ok
2. Phase 1 (80 volunteers): ok
3. Phase 2a: 360 patients: trials stopped after 1 year:

Aseptic meningoencephalitis
clinical improvement/stabilisation in a few patients
(Hock et al, Neuron 2003)

Blocking of gamma-secretase



De Strooper et al, Nature, 1998
De Strooper et al., Nature, 1999
De Strooper, Neuron, 2003

Lilly Halts Development of Semagacestat for Alzheimer's Disease Based on Preliminary Results of Phase III Clinical Trials

Decision does not affect other Lilly Alzheimer's compounds in development.

"This interim analysis showed that, as expected, cognition and the ability to complete activities of daily living of placebo-treated patients worsened. However, by these same measures patients treated with semagacestat worsened to a statistically significantly greater degree than those treated with placebo. In addition, data showed semagacestat is associated with an increased risk of skin cancer compared with those who received placebo."

γ -Secretase Heterogeneity in the Aph1 Subunit: Relevance for Alzheimer's Disease

Lutgarde Serneels,^{1,2*} Jérôme Van Biervliet,^{1,2*} Katleen Craessaerts,^{1,2}
Tim Dejaegere,^{1,2} Katrien Horré,^{1,2} Tine Van Houtvin,^{1,2} Hermann Esselmann,^{3,4}
Sabine Paul,^{3,4} Martin K. Schäfer,⁵ Oksana Berezovska,⁶ Bradley T. Hyman,⁶
Ben Sprangers,⁷ Raf Sciot,⁸ Lieve Moons,⁹ Mathias Jucker,¹⁰ Zhixiang Yang,¹¹
Patrick C. May,¹¹ Eric Karran,^{12†} Jens Wiltfang,^{3,4} Rudi D'Hooge,¹³ Bart De Strooper^{1,2‡}

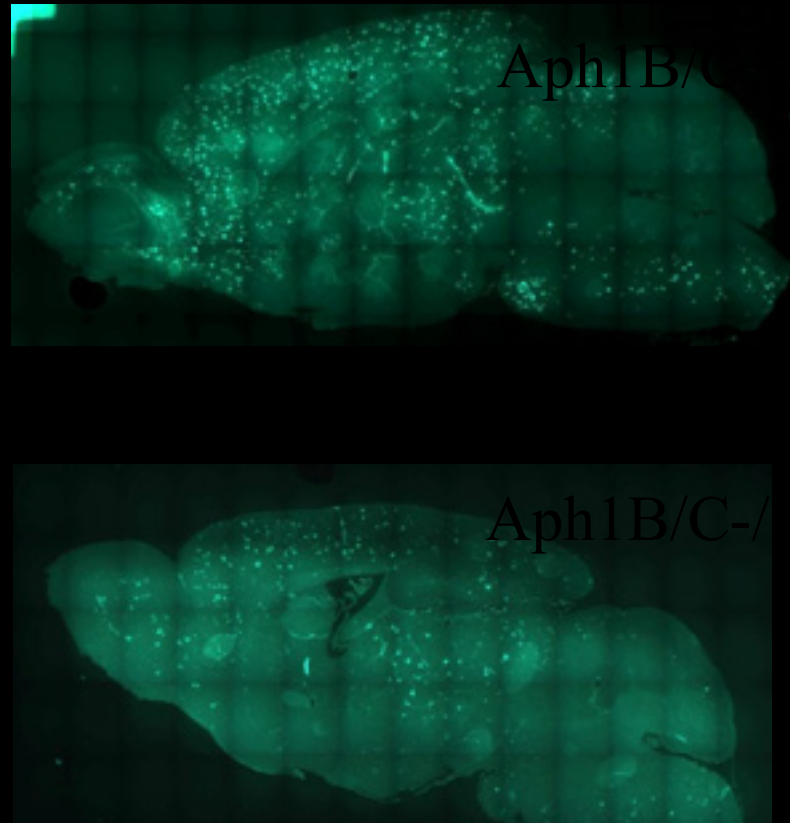
Science, 2009

The Orphan G Protein–Coupled Receptor 3 Modulates Amyloid-Beta Peptide Generation in Neurons

Amantha Thathiah,^{1,2} Kurt Spittaels,^{3*} Marcel Hoffmann,^{3†} Mik Staes,^{3‡} Adrian Cohen,^{3§}
Katrién Horré,^{1,2} Mieke Vanbrabant,^{1,2} Freya Coun,⁴ Veerle Baekelandt,⁴ André Delacourte,⁶
David F. Fischer,^{5||} Dirk Pollet,³ Bart De Strooper,^{1,2||} Pascal Merchiers^{3¶}

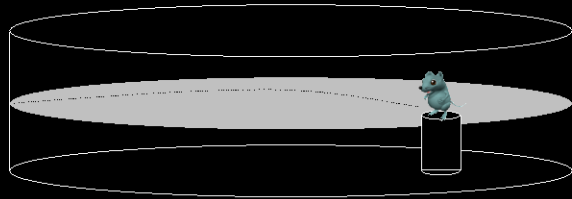
Science, 2009

Aph1B/C deletion protects against amyloid plaque formation



Learning and behavioral tests

MORRIS WATER MAZE



TRIAL 1



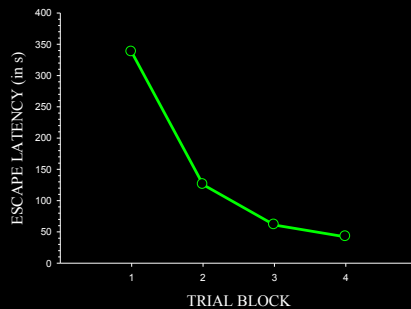
TRIAL 8



TRIAL 16

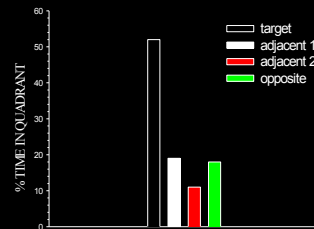


Acquisition

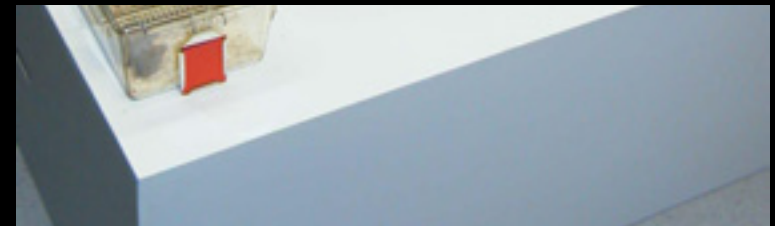


(path length, swimming velocity)

Testing (probe trial)



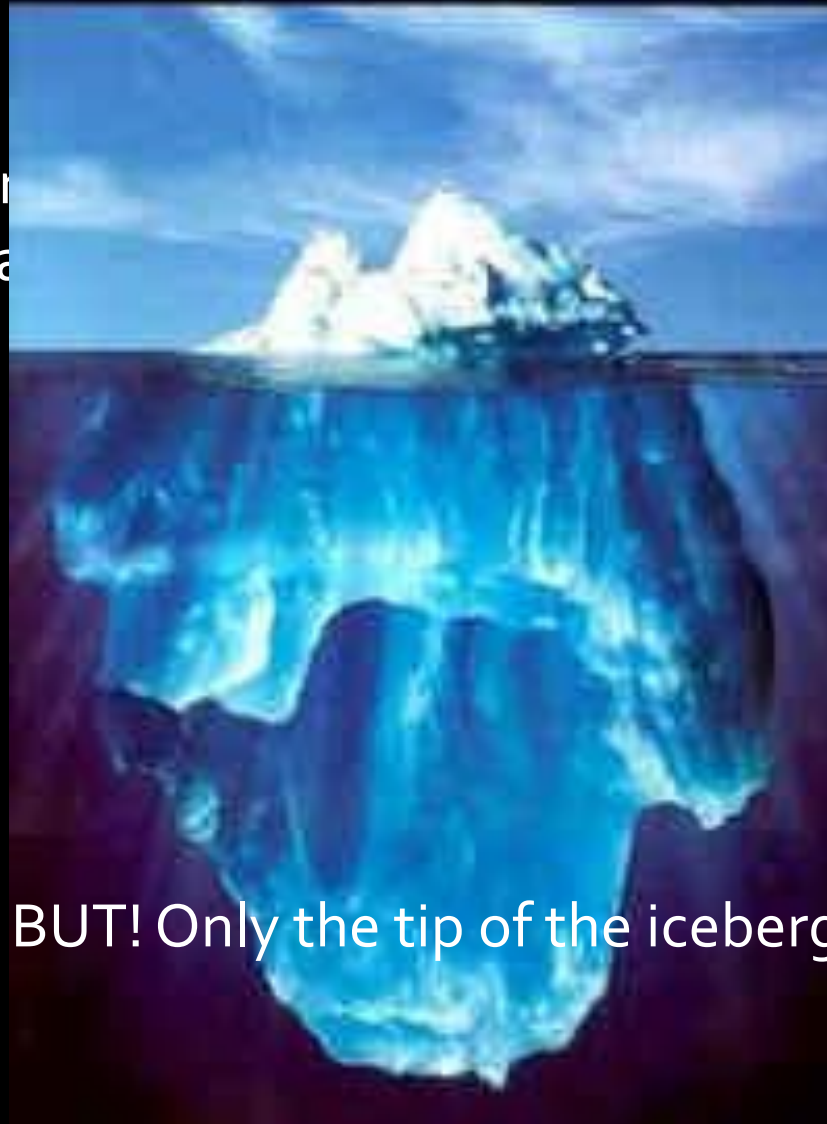
(target entries)



An intermediary balance of the genetic-biotechnological approach: (1987-2010)

1. An enormous
to a

white picture
sights



BUT! Only the tip of the iceberg

4. Modern times

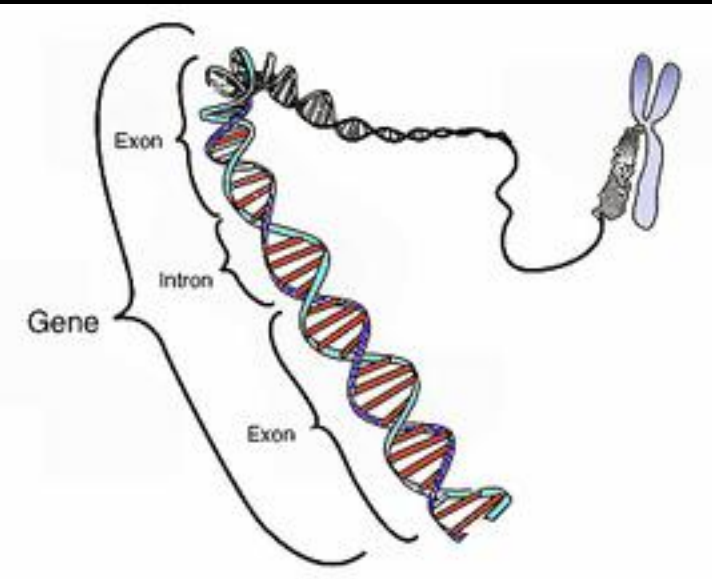
New technological revolutions make it possible
to study the complete brain
in a dynamic way

Alois Alzheimer = pictures of the brain

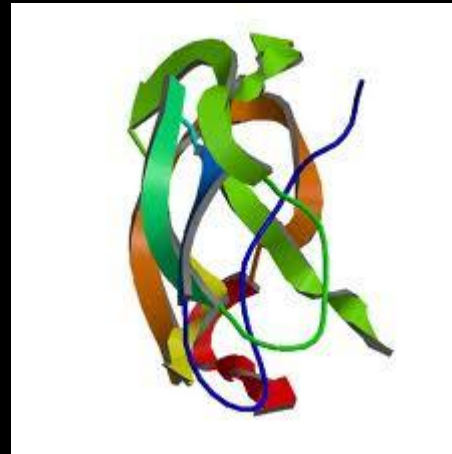


Now: 100.000 processes in parallel

Coding versus non-coding DNA

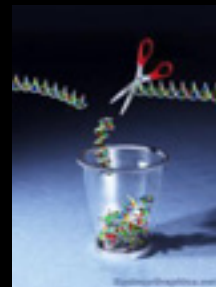


1.5 %



Coding
DNA

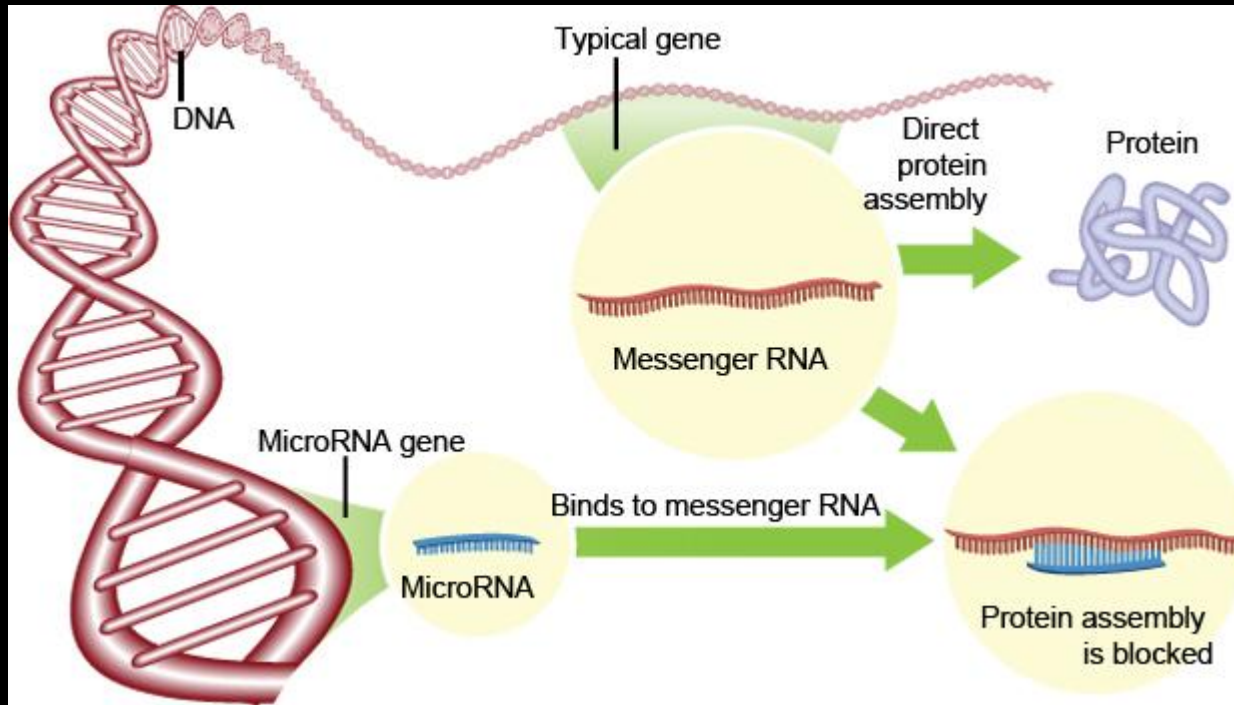
98.5 %



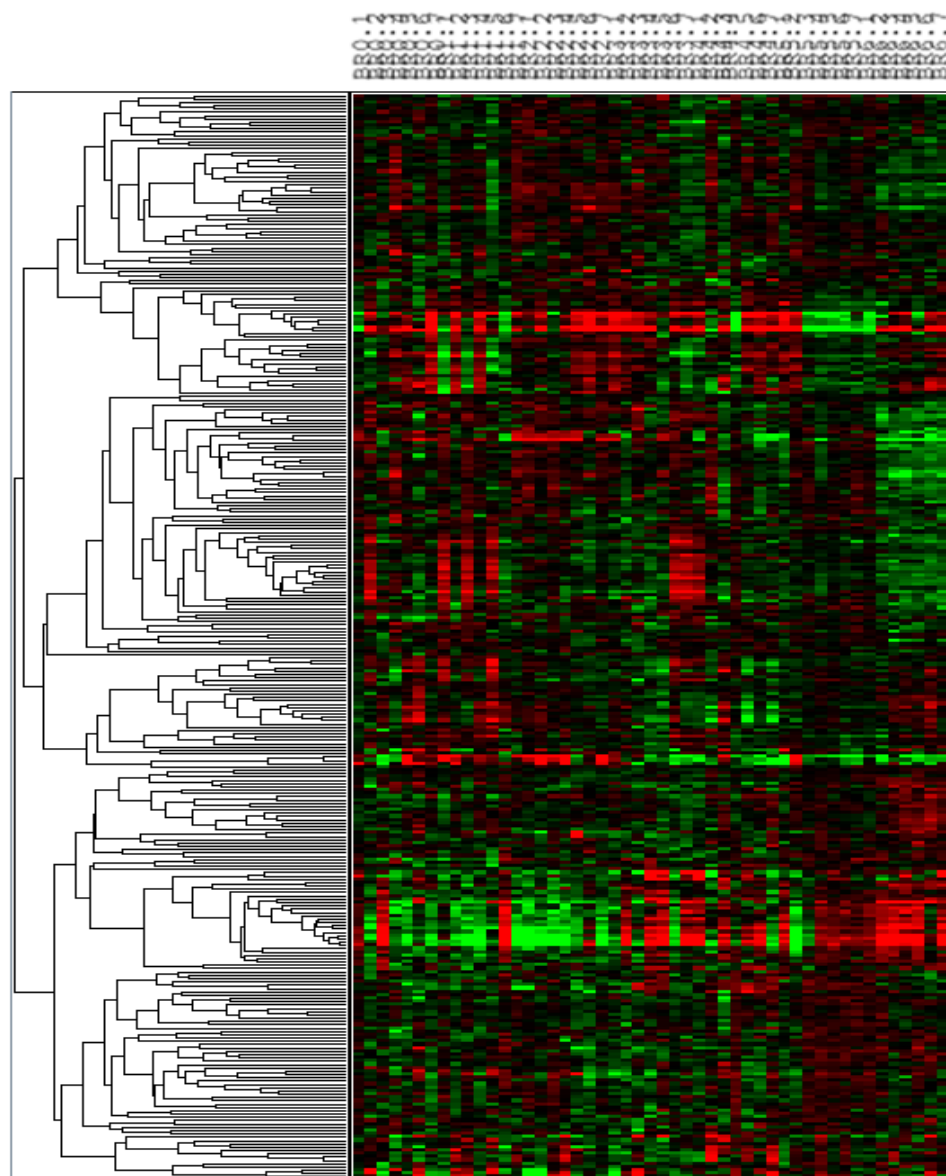
?

Non-coding DNA or 'Junk' DNA

MicroRNAs

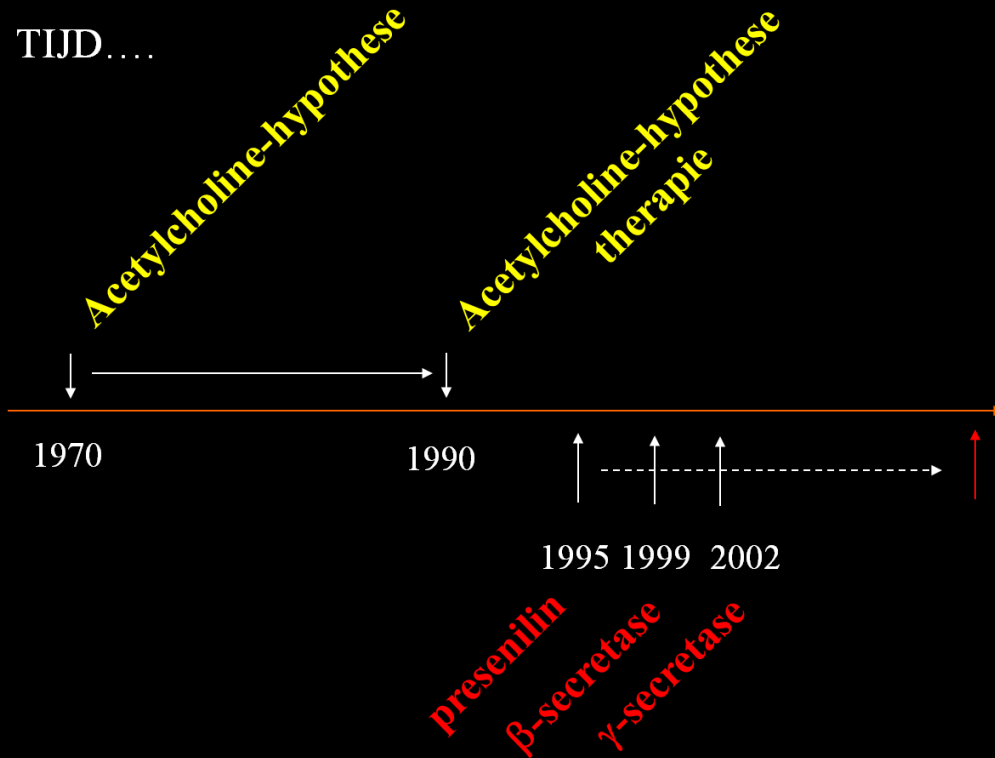


- Regulate gene expression during proliferation
- Involved in differentiation and development of CNS



Conclusions

1. Hope is raising : early diagnosis + early treatment



2. Only continuous engagement and funding will make a therapy possible

Thank you !!!!



Leuven, Belgium

That's it folks !!!



Arthur Bax and Anna Vanluffelen