

NECTAR

Neutron Capture-Enhanced
Treatment of neurotoxic
amyloid aggregates

A revolutionary strategy to address
Alzheimer Disease treatment

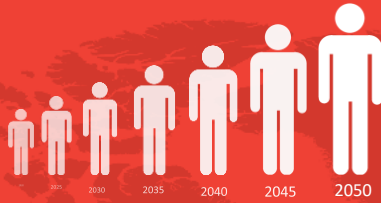


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and innovation programme
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58.67 million people worldwide are living with dementia in 2020.

This number will almost double every 20 years.



Someone in the world develops dementia every 3 seconds.

Already 60% of people with dementia live in low and middle income countries.

By 2050 this will rise to 71%.



Dementia disease primarily affects older people.

Up to the age of 65, dementia develops in only about 1 person in 1000.

Alzheimer Disease

- ▶ Today, only one drug has been approved by Food and Drugs Administration (FDA), but it must be conducted a post-approval clinical trial to verify the drug's clinical benefit.
- ▶ NECTAR project proposes an alternative and revolutionary strategy to address AD, investigating the safety, feasibility and effectiveness of a **Capture-Enhanced Neutron Irradiation (CENI)** to structurally damage A β aggregates.

NECTAR idea: bimodal treatment

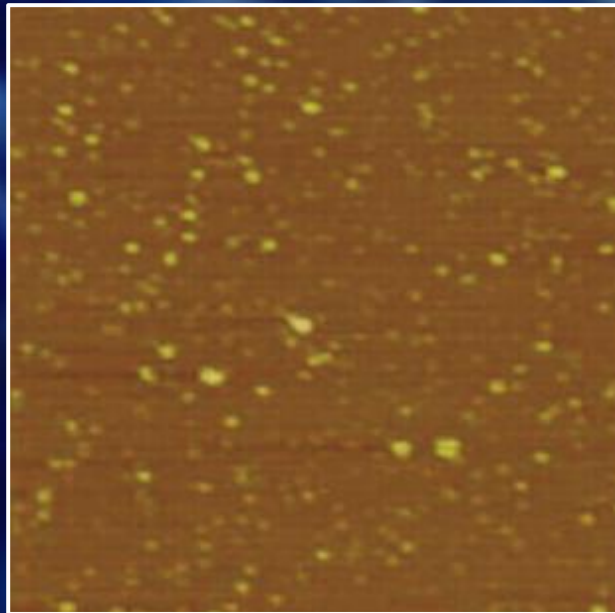
The $A\beta$ peptide is considered to be the main culprit of the neuropathological processes of Alzheimer Disease.

NECTAR idea: bimodal treatment

Thanks to the mixed **high** and **low** LET radiations field set in correspondence of $A\beta$ aggregates by the neutron irradiation, a bimodal treatment is expected to take place:

- ▶ a local depolymerisation of $A\beta$ aggregates by the highly biological effective charged particles
- ▶ a long distance stimulation of the brain tissue by penetrating photons

A β aggregates

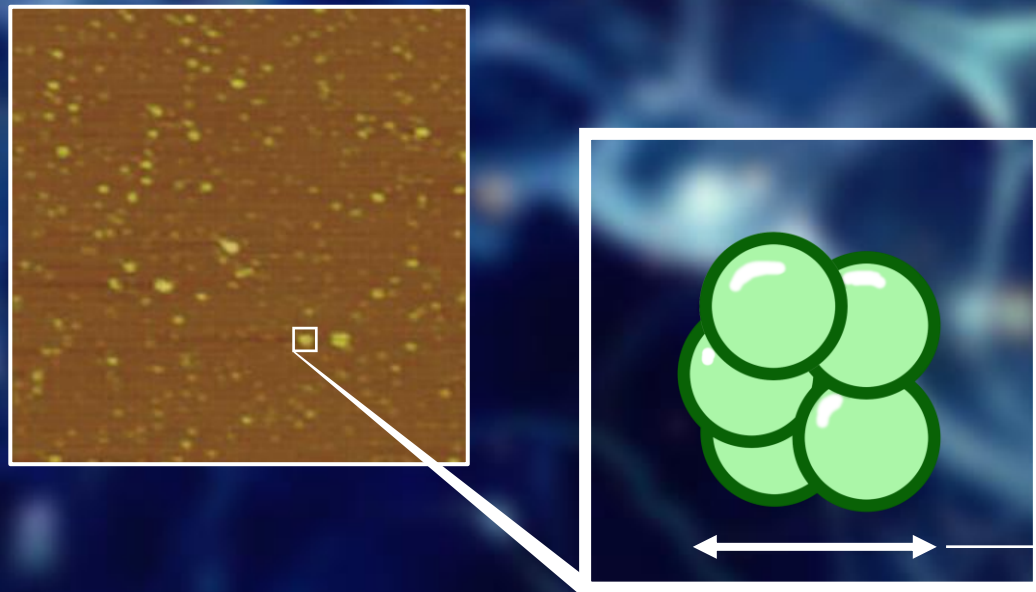


A β oligomer

The brain damage leading to Alzheimer's disease is instigated by soluble, ligand-like amyloid beta oligomers.

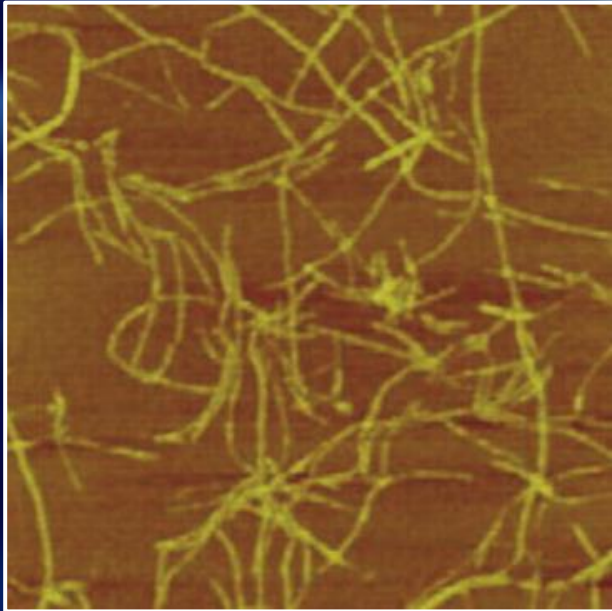
A β aggregates

A β oligomer



A few *nm* in diameter

A β aggregates

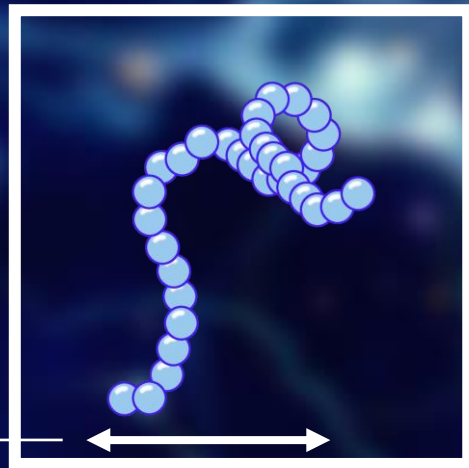


A β fibril

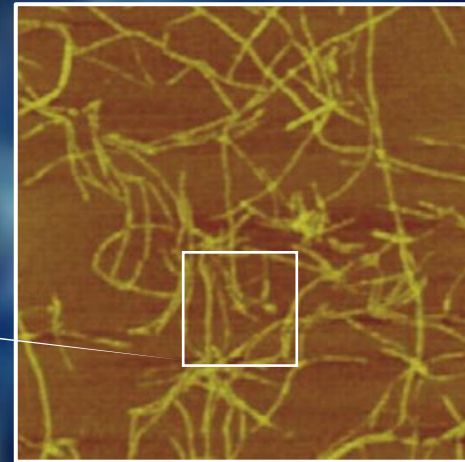
Amyloid monomeric proteins can oligomerize into destructive amyloid fibrils.

A β aggregates

A β fibril



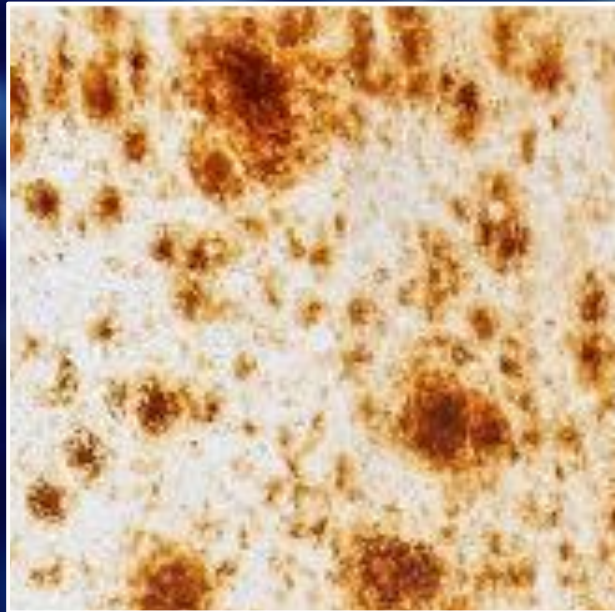
A few nm
in diameter
and several μm length



A β aggregates

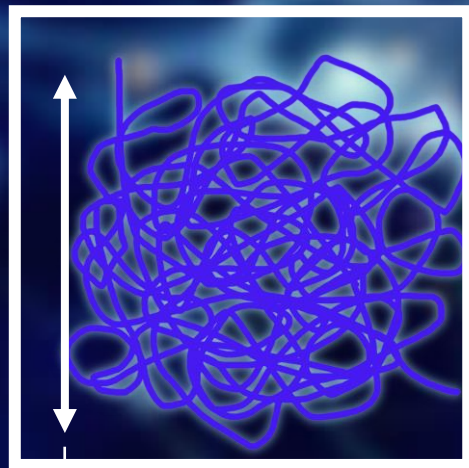
A β plaque

In the Alzheimer's brain, abnormal levels of beta amyloid protein clump together to form plaques that collect between neurons and disrupt cell function.

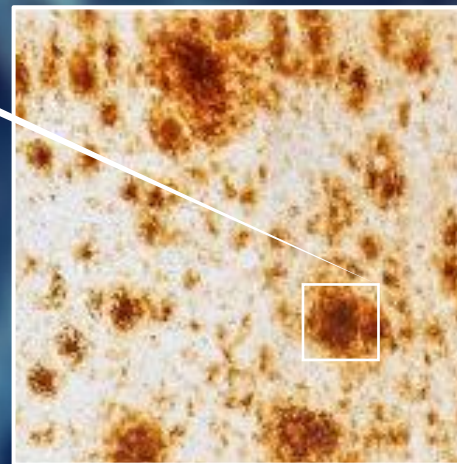


A β aggregates

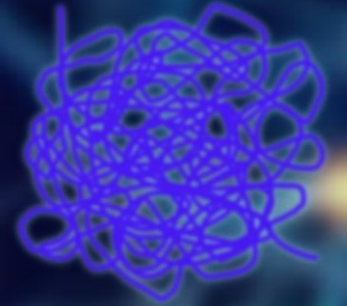
A β plaque



Several μm

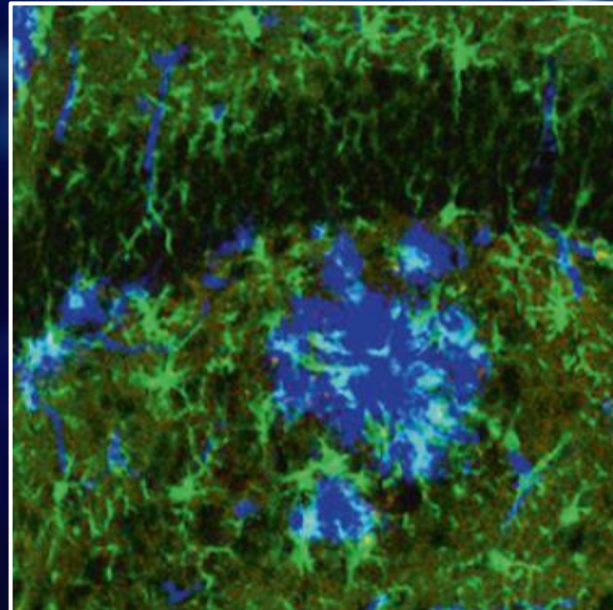


A β aggregates

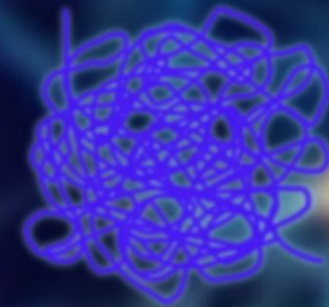


Microglia cell

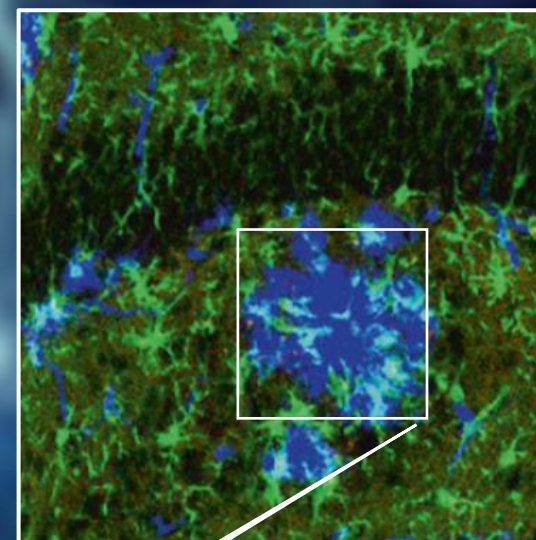
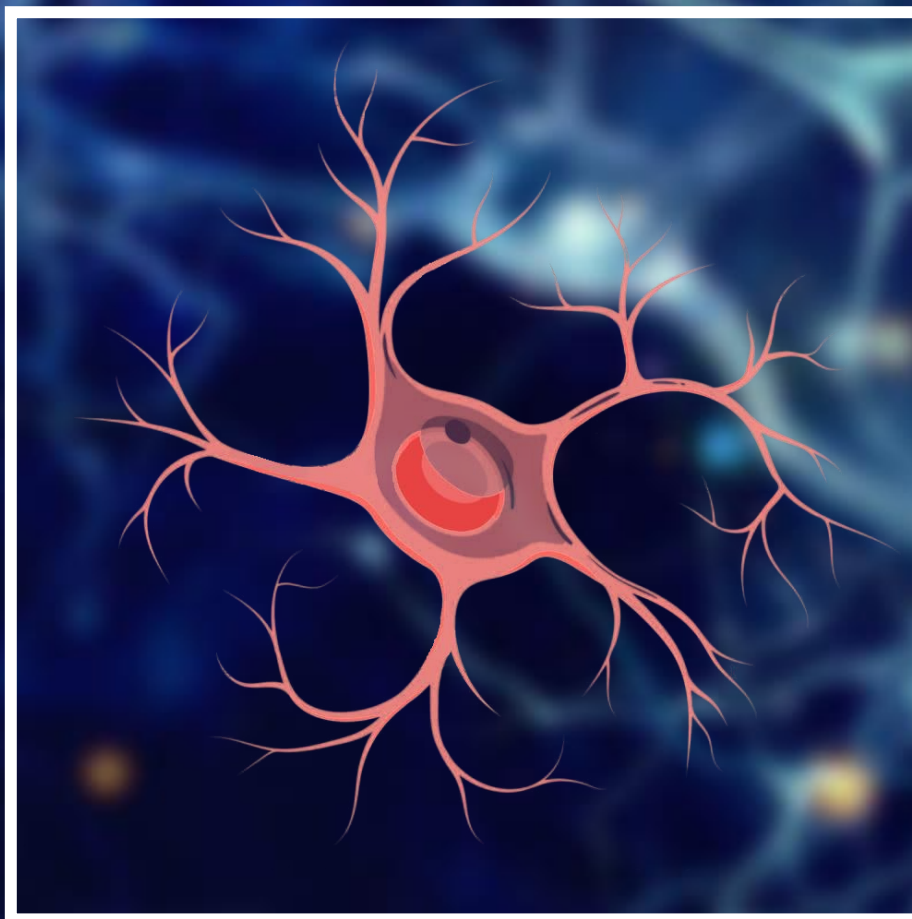
microglia protect neurons from physical and chemical damage and are responsible for clearing foreign substances and cellular debris from the brain.



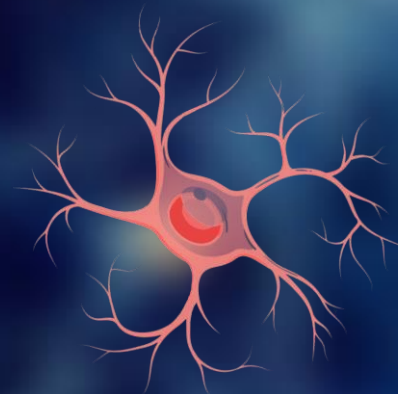
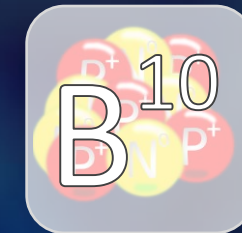
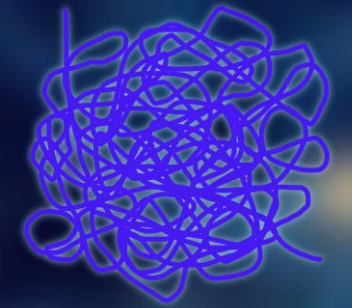
A β aggregates



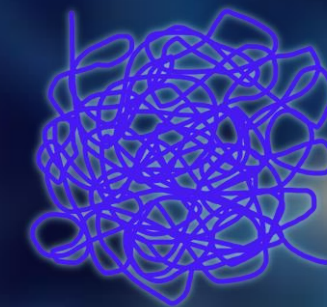
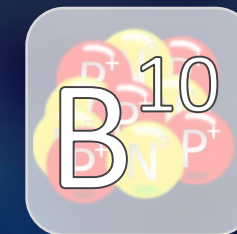
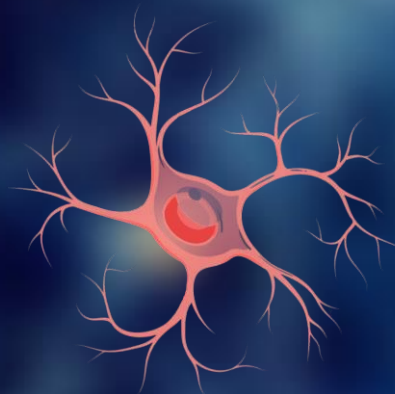
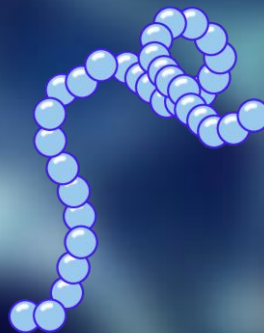
Microglia cell



NECTAR idea:
bimodal treatment

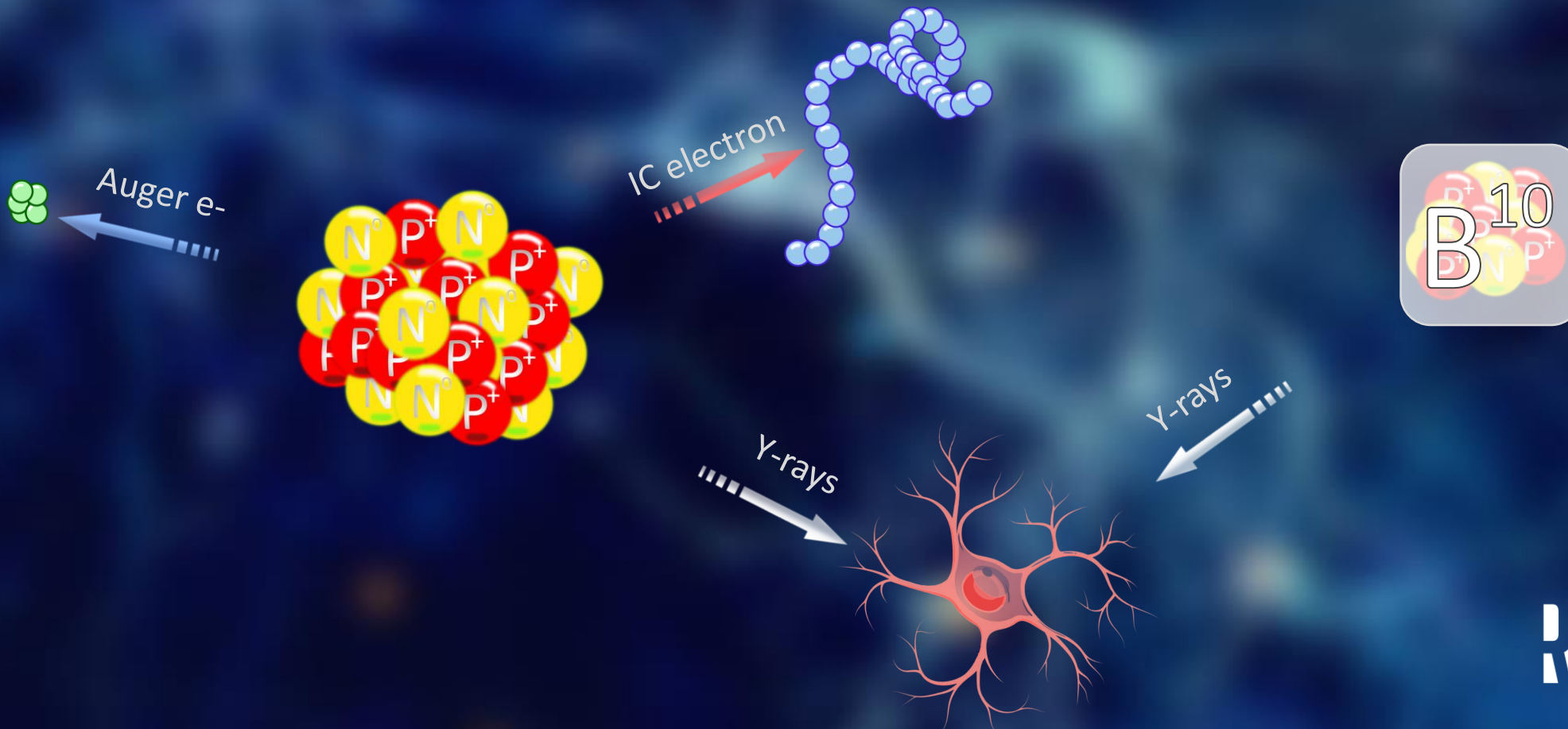
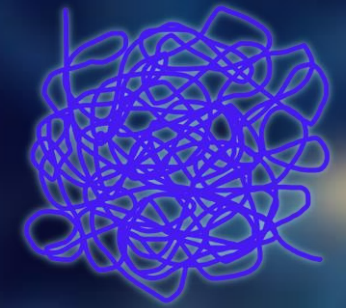


NECTAR idea:
bimodal treatment



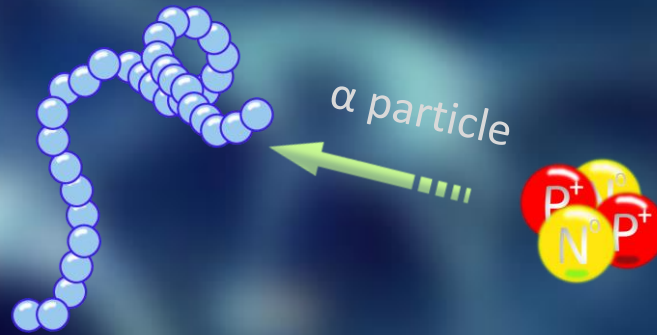
NECTAR idea:
bimodal treatment

Low LET
radiations

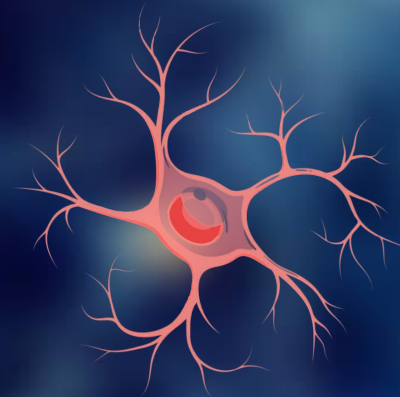
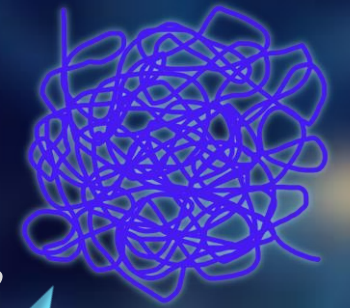


NECTAR idea:
bimodal treatment

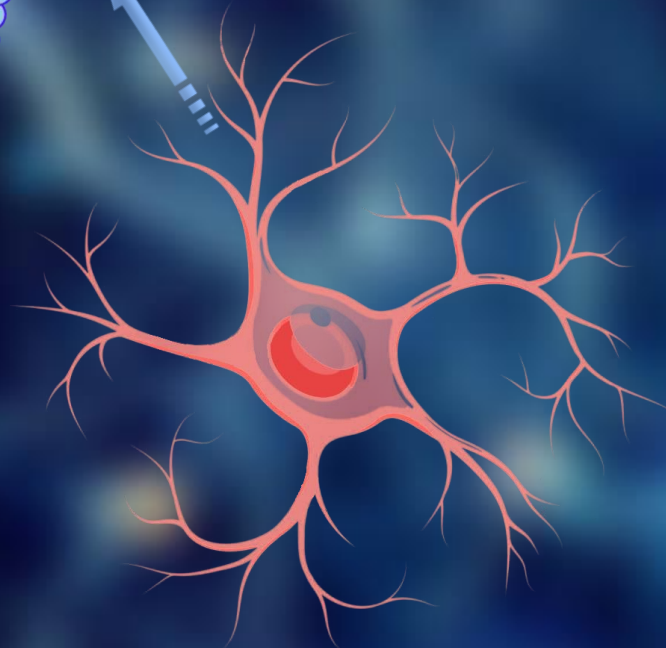
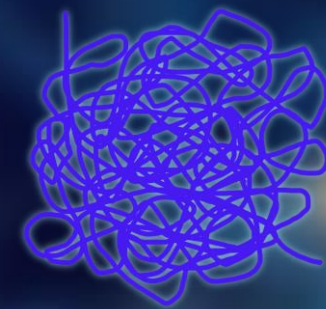
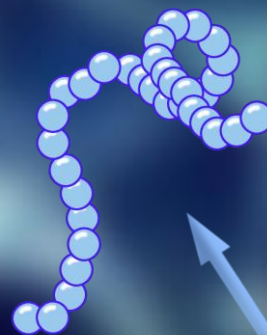
High LET
radiations



${}^7\text{Li}$ nucleus








NECTAR idea:
bimodal treatment



Microglia cells activation
against $A\beta$ by low LET IRs

NECTAR Objectives

-  Synthesis of biocompatible Radiation enhancer probes
-  In vitro A β depolymerization through high LET particles
-  n/ μ -dosimetric field quantities characterization
-  In vitro and in vivo CENI proof of concept using AD models
-  Safety and effectiveness evaluation for human AD cases

NECTAR Objectives

NECTAR aims to develop, test and prove the feasibility, safety and effectiveness of a **Capture-Enhanced Neutron Irradiation** (CENI) of A β aggregates exploiting the synergy between an external beam of low energy neutrons which irradiate the whole brain and specifically engineered radiation enhancers capable of increasing the administered dose only in the A β aggregate site.

NECTAR RoadMap

 **WP1**
Project Management

 **WP4**
High LET effects

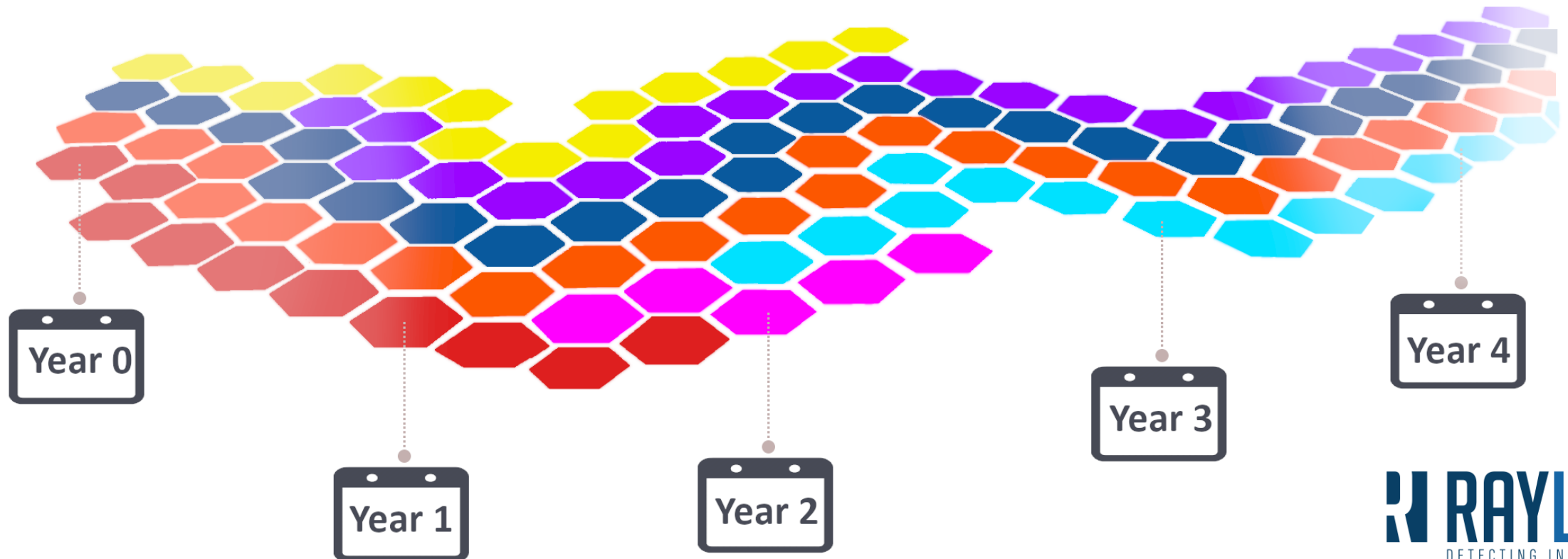
 **WP2**
CENI agents

 **WP5**
CENI safety

 **WP7**
Dissemination,
training and education

 **WP3**
Dosimetry and
CENI planning

 **WP6**
CENI efficacy





Partners



UNIVERSITÀ
DEGLI STUDI
DI TORINO



Stockholm
University



Universitätsklinikum
Essen



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