

**BIOMEDICINA SPAZIALE PER LE FUTURE MISSIONI DI ESPLORAZIONE
UMANA DELLO SPAZIO: A CALL TO ACTION**

Agenzia Spaziale Italiana

Roma, 15 marzo 2023

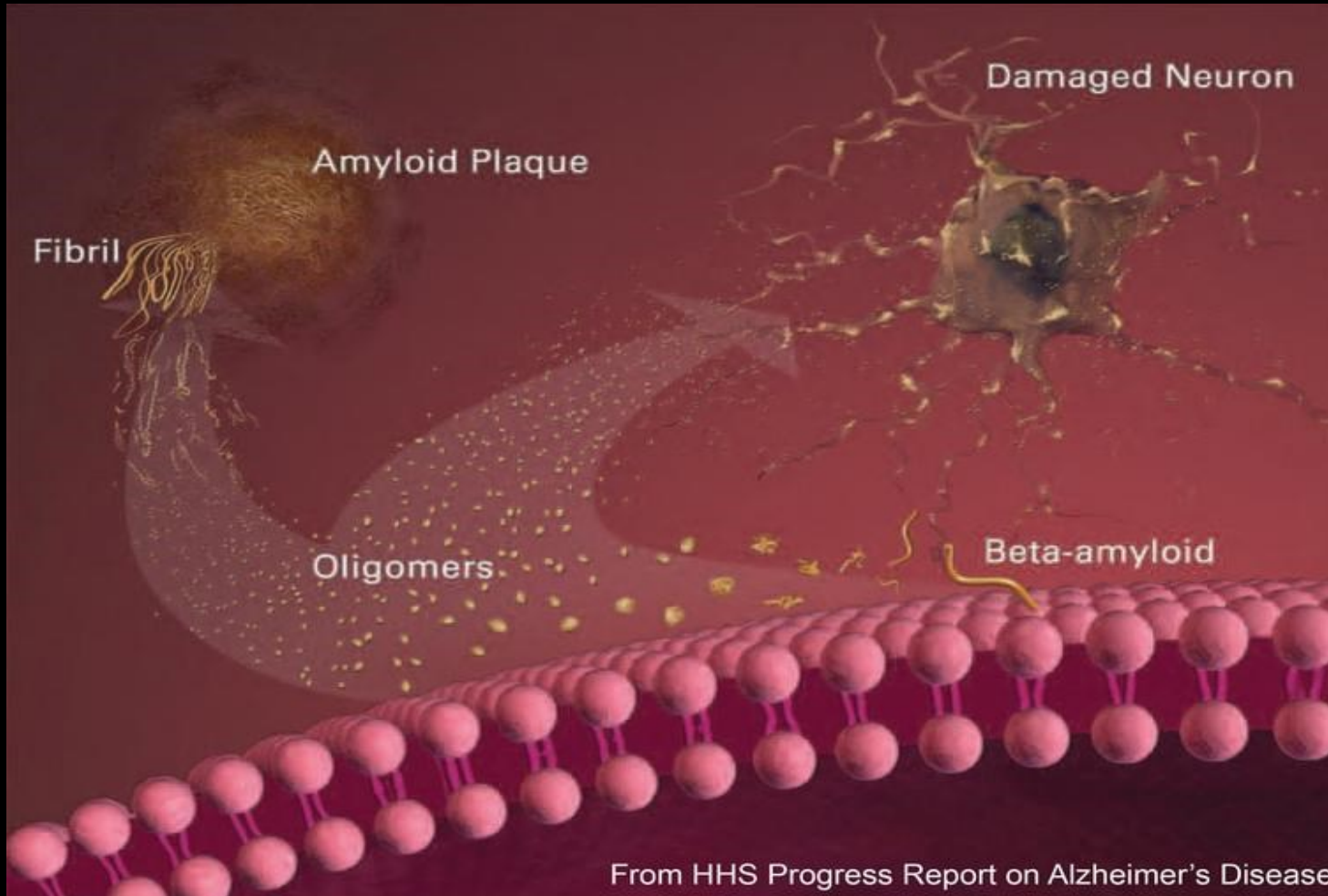
**STUDIO DEGLI EFFETTI DELLA
MICROGRAVITÀ E DELLE RADIAZIONI IN
MODELLI ANIMALI DI AGGREGAZIONE
PROTEICA E NEURODEGENERAZIONE**

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Protein aggregation and neurodegenerative diseases (NDs) on Earth



- Alzheimer disease
- Parkinson disease
- Lewy-body dementia
- Prion disorders
- Frontotemporal dementia
- Huntington chorea

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Non ND protein-misfolding diseases

- Systemic amyloidosis
- Dialysis-related amyloidosis
- Diabetes-related amyloidosis
- Cataract

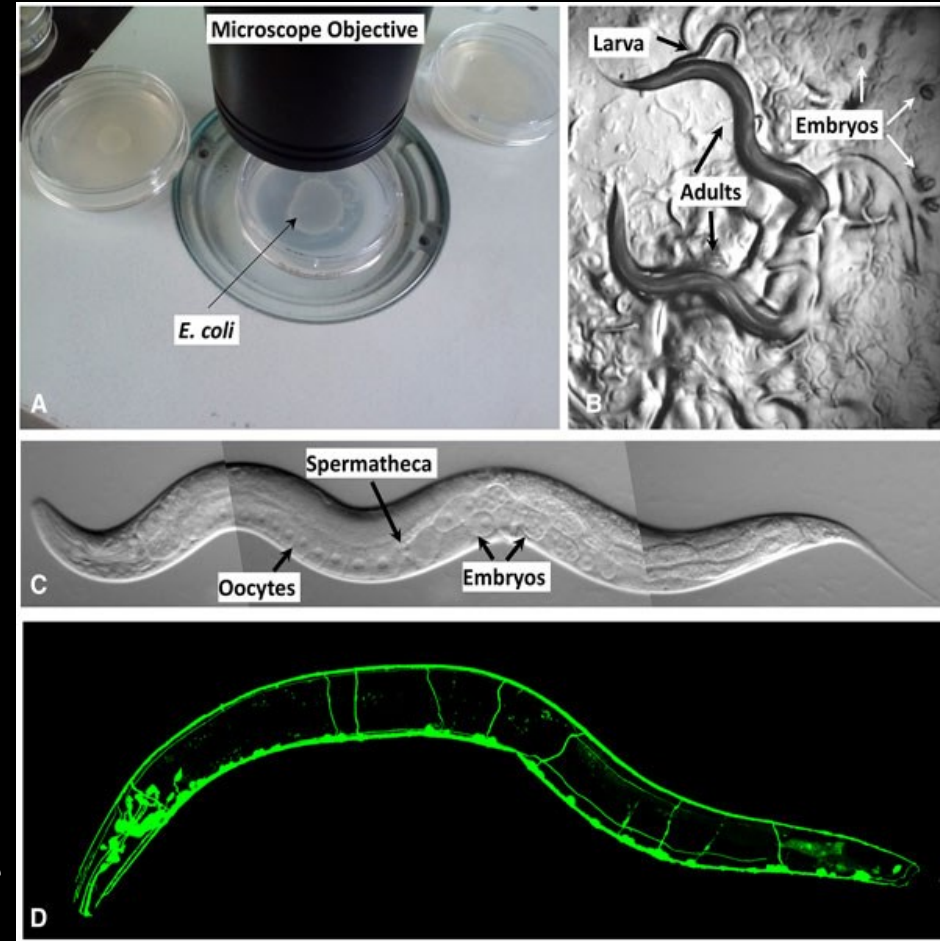
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Is neurodegeneration an issue in space?

- Changes in the brain of astronauts recall pathological conditions of the elderly that favour protein aggregation (*Wilson, 2023*)
- Increased levels of aggregation-prone proteins in brains of cosmonauts after 5-6 months on the ISS (*zu Eulenburg, 2021*)
- Simulated microgravity (μg) increases the possibility for neurons to degenerate (*Prasad, 2020*)
- Cognitive impairment and A β peptides plaques increase in AD mice after ^{56}Fe -particles irradiation (*Vlkolinsky, 2010; Cherry, 2012*)
- Proteins associated to AD and neurodegeneration have altered aggregation patterns in microgravity (*Berrone, 2020; Yagi-Utsumi, 2020; Matsushita, 2021*)

C. elegans as a model organism

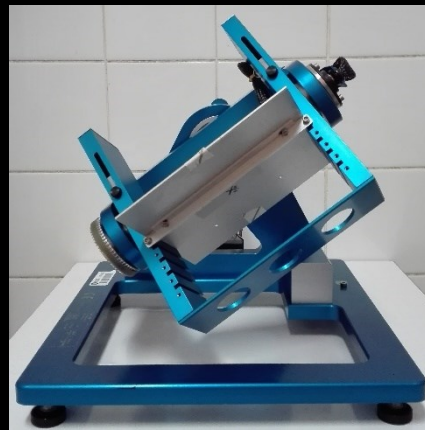
- Small and easy to cultivate
- Well-known physiology
- Hundreds of disease models
- Dozens of lab analysis tools
- Automated monitoring systems
- Wide bibliography and databases
- Model system on the Earth and in space biology



http://www.wormbook.org/chapters/www_celegansintro/celegansintro.html

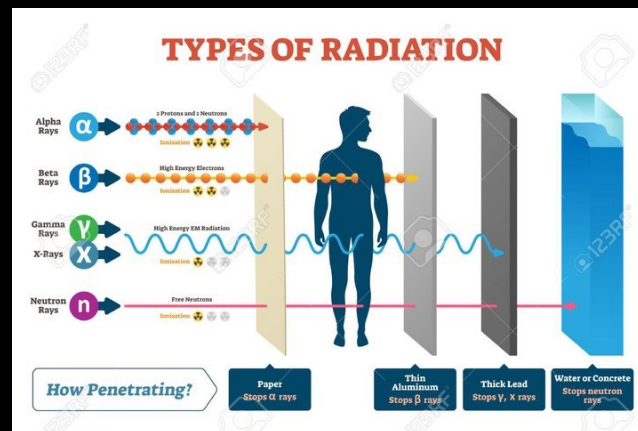
C. elegans in microgravity

- Downregulation of genes involved in neuronal/endocrine signaling associated with survival extension (*Honda, 2012*)
- Muscle physiology alterations (reduction of paramyosin and troponin T) (*Higashibata, 2013*)
- Alterations of neuronal physiology (impaired branching, dopamine decrease) (*Prasad, 2020; Laranjeiro, 2021; Sudevan, 2022*)
- Unaltered effectiveness of RNAi (*Etheridge, 2011*)
- Impaired neuronal degradative pathways (*Laranjeiro, 2021*)



C. elegans and radiations

- Acute irradiation decreases life duration and increases the death ratio, causes DNA damage and reduces reproduction rate (Dhakal, 2021)
- Chronic irradiation (at low doses) has milder effects than acute irradiation (at high doses) (Dhakal, 2021)
- Motor performance of *C. elegans* is reduced after irradiation (Sakashita, 2008, 2012)
- *C. elegans* miRNAs remain active after space radiation stimuli (Yan, 2020)



C. elegans models of protein misfolding and NDs

- Several Tg lines for:
 - Alzheimer disease
 - Parkinson disease/LB disease
 - Frontotemporal dementia
 - Amyotrophic lateral sclerosis
 - Prion diseases



- Protein misfolding phenotypes involving different cell types
- Neurobehavioral effects
- Increased spontaneous protein aggregation in aged worms

Keypoints for *C. elegans* studies of protein aggregation and cellular degeneration

- Establishment of *C. elegans* strains
- Validation of phenotypes
- Definition of combined μg and irradiation protocols
- Set up of analytical methods for biological evaluation, biochemical and histological studies, -omic analyses, oxidative stress status investigation

Aims and innovation areas

1. Definition of protein aggregation patterns, biochemical and genetic changes in NDs (and non-Tg) worm strains exposed to radiations in μg (μg -ray)
2. Comparison of the effect of acute vs chronic μg -ray exposure
3. Validation of worm strains for studies on NDs, protein aggregation, and preventive/treatment approaches after μg -ray exposure
4. Development of novel biological indicators to monitor at-risk conditions during space exploration

Logo, title, team, and facilities are ready

We just need some fuel to start!



S-WORM-S

Search for Worm Oddity after
Radiation and Microgravity Supply

