Cryo Electron Microscopy Workshop:
“Enabling Portugal to Become a World Player in Biological Research and Health”

Exploring the advantages of using CryoEM in health-related projects

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Departments:

- Food and Nutrition
- Infectious Diseases (DDI)
- Epidemiology
- Human Genetics (DGH)
- Environmental Health (DSA).
- Health Promotion and Prevention of Noncommunicable Diseases

Mission: to contribute to public health gains

- Research and technological development activities,
- Laboratory activity reference,
- Observation of health and epidemiological surveillance,
- Coordinating external evaluation of laboratory quality

Instituto Nacional de Saúde Dr. Ricardo Jorge
Lysosomal Storage Diseases (LSD) are inherited metabolic diseases

- Deficiency of a single enzyme
- Mutation in an activator protein
- Disorders of lysosomal membrane transport

Phenotypes may range from extremely severe and early presentations with multi-systemic and neuronal involvement, leading to death in the first years of life or even in the neo-natal period, to later onset milder disease.

Enzyme replacement therapy has become available for several LSD.
Lysosomal Storage Diseases: Diagnosis and innovative therapeutic approaches.

**Discovery of novel gene defects:** Standard molecular biology techniques and NGS

**Development of novel therapeutical approaches (Personalized Medicine Approach):** Antisense U1 snRNAs, antisense oligonucleotides and RNA interference (RNAi) technology.

**Perform molecular/biochemical/cellular studies for the most promising identified mutations:** After identification of a novel variant with pathogenic features its impact is studied on mRNA, protein and cellular levels.

*Electron microscopy is very useful* to study ultrastructural morphology of distended lysosomes and their tissue distribution.

**Working closer to native state**

**Thicker sections (plastic)**


*Zebra bodies (Fabry Disease)*
Virus structures and design of better therapeutic approaches

Atomic resolution structures of viruses is a powerful tool for vaccine design.

Cryo-EM and X-ray crystallography (Complementary methods)

Challenging production (Low conc.)

Lack homogeneity

Images available at: http://www.ebi.ac.uk/pdbe/emdb/
Influenza virus characterization and surveillance.
Monitoring influenza vaccine effectiveness during influenza seasons and pandemics in the European Union (I-MOVE) - Laboratory component

Influenza-specific bioinformatics free web-based designed for effective and timely influenza laboratory surveillance. Data integration is continuously scalable, fitting the need for a real-time epidemiological surveillance during the flu epidemics.

https://insaflu.insa.pt/

Improve vaccine design
Central venous catheter-related bloodstream infection (CRBSI) is a healthcare associated infection (HAI) responsible for high rates of morbidity and mortality in critically ill patients, namely those in intensive care units (ICU).

Staphylococcus spp are the major etiological agent of CRBSI.

Structure of bacteriophage and S. aureus pathogenicity islands.

Biofilm control strategies
Final Remarks: Why Cryo-EM?

- Innovative therapeutic and diagnosis approaches
- New viruses
- Better vaccine design
- Treatment of biofilm associated infections
- Prevention of biofilm formation