

**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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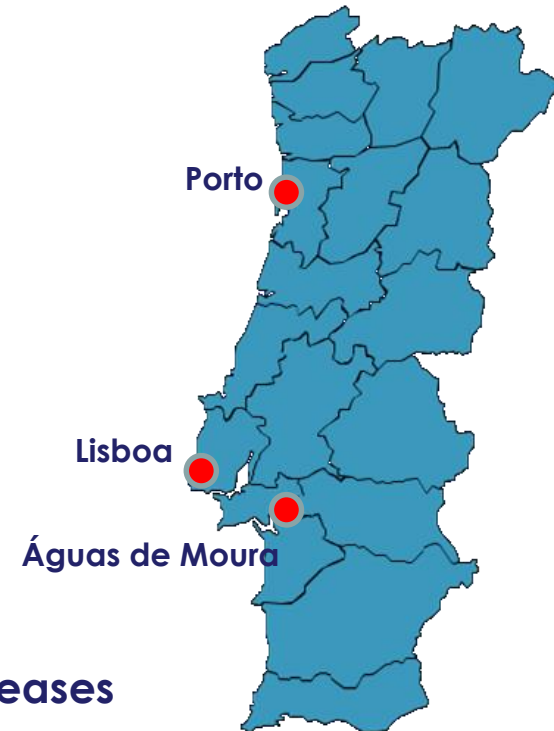


Mission: to contribute to **public health gains**

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

Departments:

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

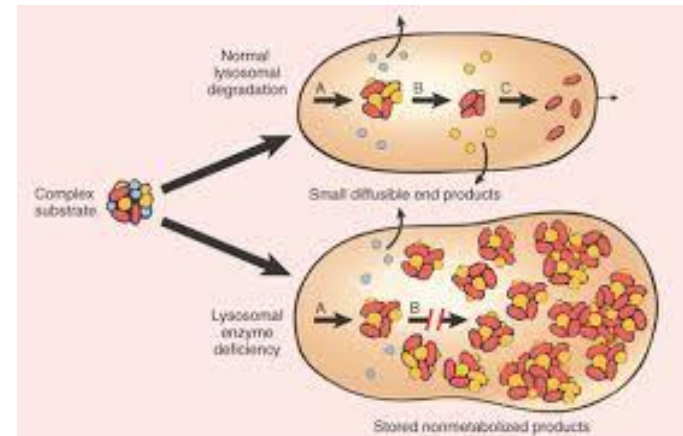




Sandra Alves
DGH-Porto

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.



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

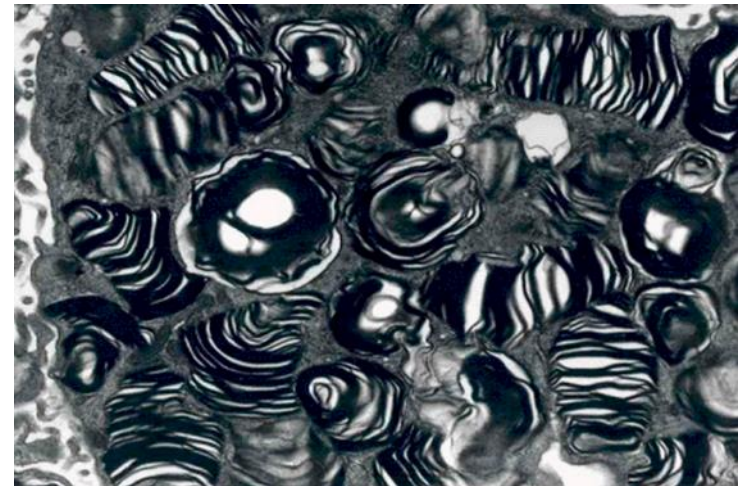
Development of novel therapeutical approaches (Personalized Medicine Approach): Antisense U1 snRNAs, antisense oligonucleotides and RNA interference (RNAi) technology.

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)



Chung et al, *Child Kidney Dis* 2016.
Zebra bodies (Fabry Disease)

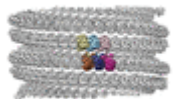
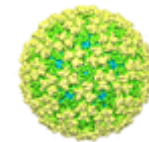
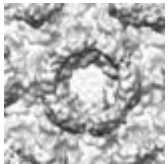
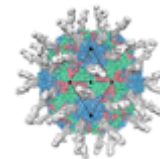
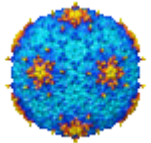
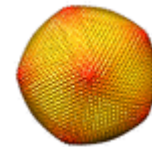
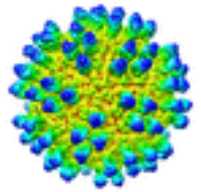
Virus structures and design of better therapeutic approaches

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

JP Gomes
DDI



Raquel Guiomar
DDI

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.



Sumário	
1 Vigilância clínica Taxa de incidência de SG	■ A taxa de incidência de síndrome gripal (SG) foi de 4,5 por 100.000 habitante, valor abaixo da linha de atividade basal.
2 Vigilância laboratorial Diagnóstico do vírus da gripe e outros vírus respiratórios. Caracterização do vírus da gripe	■ Na semana 12 observou-se uma tendência decrescente no número de vírus da gripe detetados, tendo sido o vírus do subtipo A(H3) o identificado com maior frequência, especialmente na Rede Portuguesa de Laboratórios para o Diagnóstico da Gripe (Hospitais). O vírus da gripe do tipo B da linhagem Yamagata foi o predominante, na presente época.
3 Severidade Internamentos por gripe em UCI	■ Foram reportados 2 casos de gripe pelas 20 Unidades de Cuidados Intensivos que enviaram informação. Foi identificado o vírus Influenza A num doente e o B noutra. A proporção de casos de gripe admitidos em UCI nesta semana (1,0%) decresceu face à semana anterior (1,7%).
4 Impacte Mortalidade por todas as causas	■ Mortalidade observada por todas as causas com valores de acordo com o esperado.
5 Monitorização da temperatura ambiente, taxa de incidência de SG e mortalidade	■ O valor médio da temperatura mínima do ar na semana 12 de 2018 foi de 4,55°C, a que correspondeu uma anomalia de -2,28°C relativamente ao valor normal 1971-2000 para o mês de março.
6 Situação Internacional	■ Na semana 11 de 2018 a maioria dos países continuou a reportar atividade gripal disseminada de intensidade baixa ou moderada.

Laboratorial
surveillance

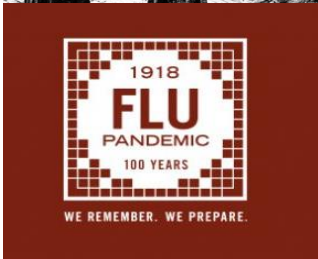
Detection of
new/emergent
viruses

Respiratory
viruses
collection



<https://insaflu.insa.pt/>

Improve vaccine design

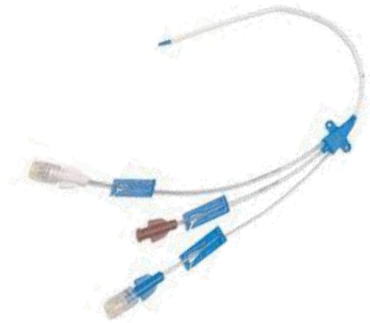




DSA

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?

