

Fisiopatología celular durante el desarrollo y la enfermedad

Cell Biology 210

BIO-336

(Desarrollo y enfermedades musculares)

José A. Sánchez Alcázar, PhD, MD



ciberer

Centro de Investigación Biomédica En Red
de Enfermedades Raras



Fisiopatología celular durante el desarrollo y la enfermedad

Cell Biology 210

David Cotán, PhD

Manuel Oropesa Avila, PhD student

Juan Garrido Maraver, PhD student

Mario De la Mata, PhD student

Ana Delgado Pavón, PhD student

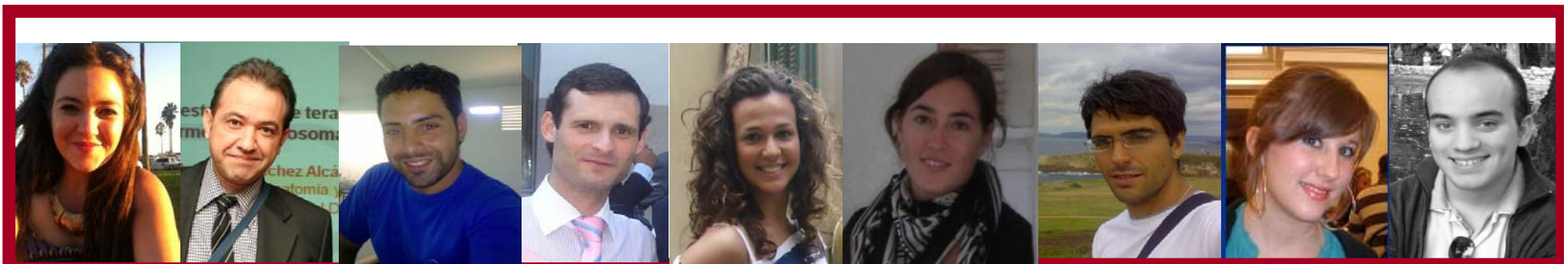
Alejandro Fernández Vega, PhD student

Carmen Pérez Calero, PhD student

Macarena Alanís Sánchez, , PhD student

Marina Villanueva Paz, student

José A. Sánchez Alcázar, PhD, MD



Research project:

Cell death during development and disease



Cell death during development and disease

GENERAL AIM

To study cell death in development and disease

SPECIFIC AIMS

-**APOPTOSIS**

-**AUTOPHAGY/MITOPHAGY IN MITOCHONDRIAL DISEASES**

-**MITOCHONDRIAL DISEASES TREATMENT**

-**PRONACERA**

Cancer project

Lysosomal diseases

- **FAMILIAL HYPERCHOLESTEROLEMIA**

-**FIBROMYALGIA AND CHRONIC FATIGUE** (in collaboration with Mario D. Cordero)

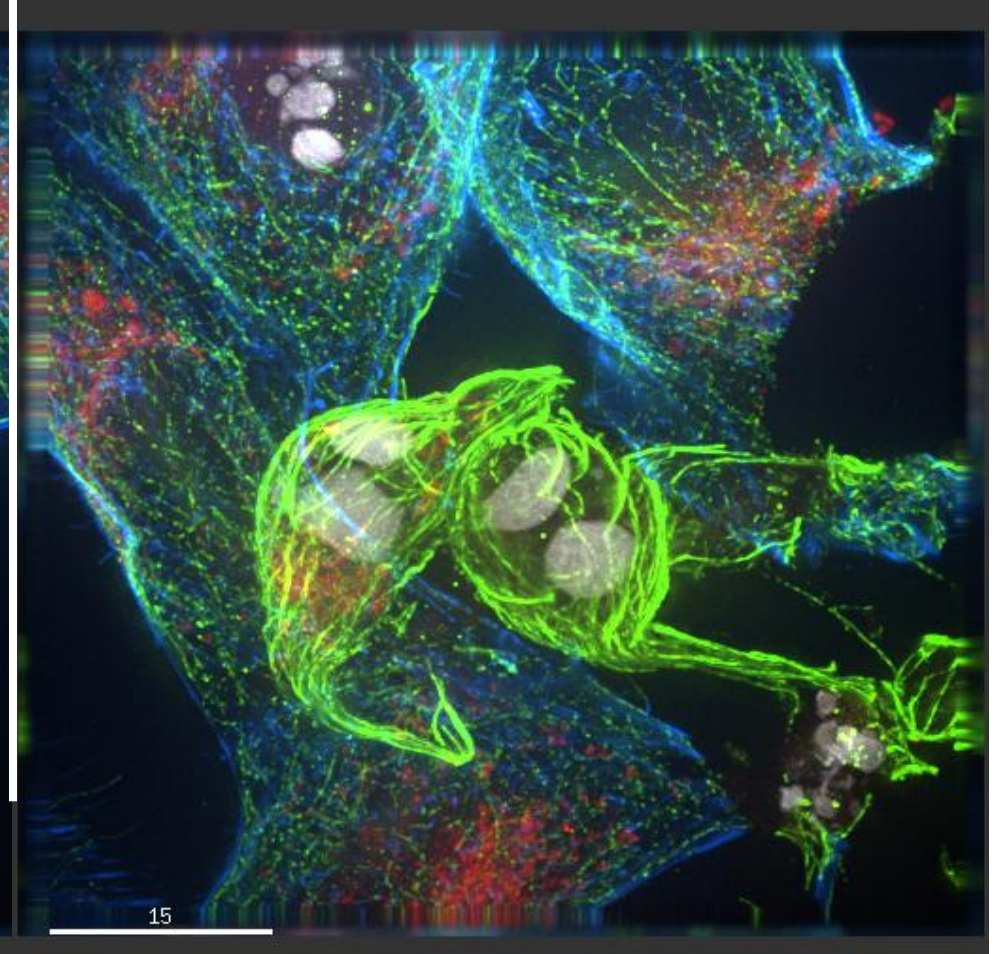
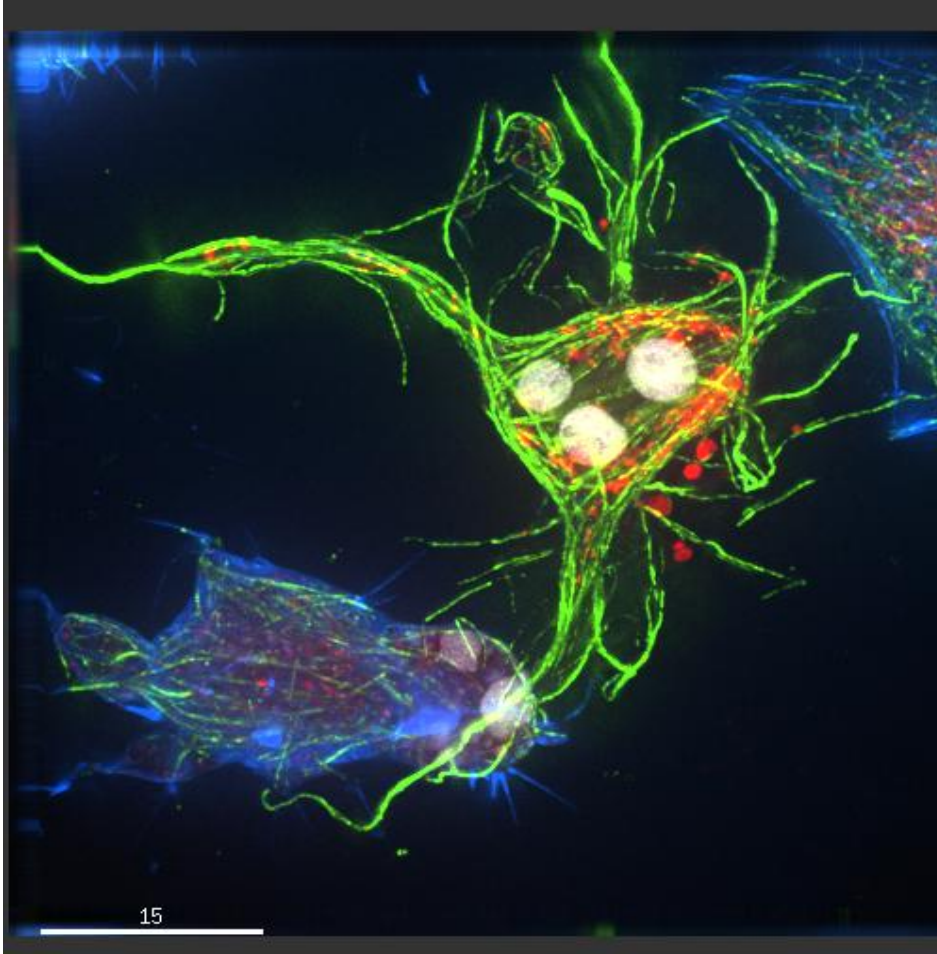
APOPTOSIS: CYTOSKELETON REORGANIZATION



Manuel Oropesa Ávila



Alejandro Fernández Vega



Apoptotic microtubules network (AMN) in developmental apoptosis

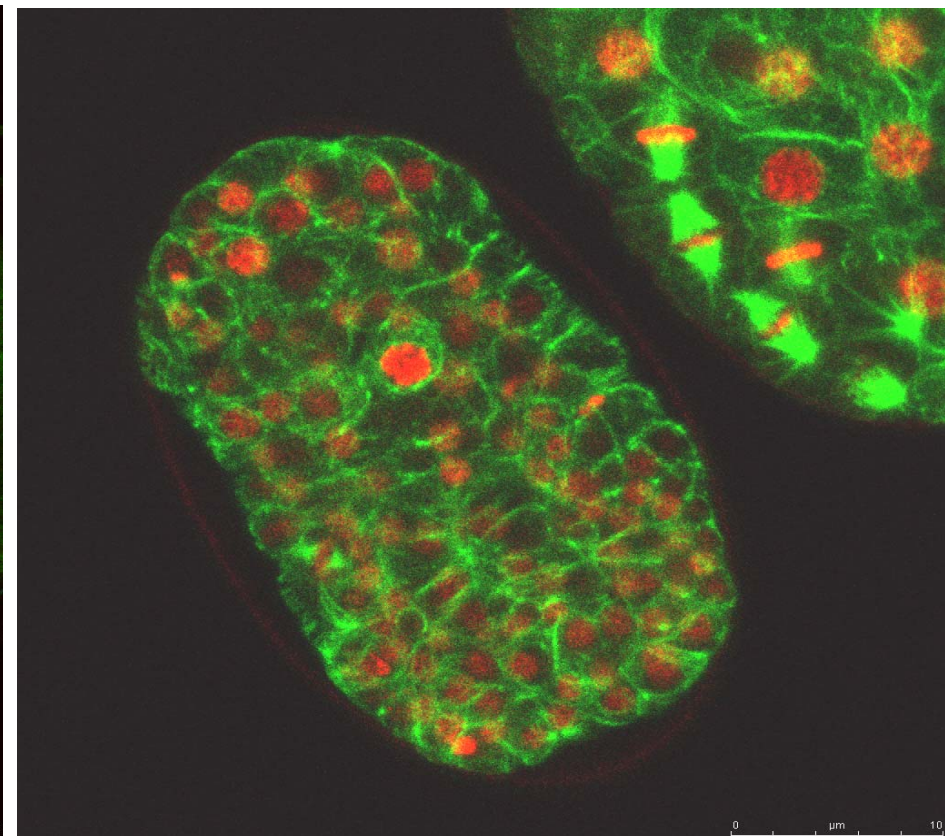
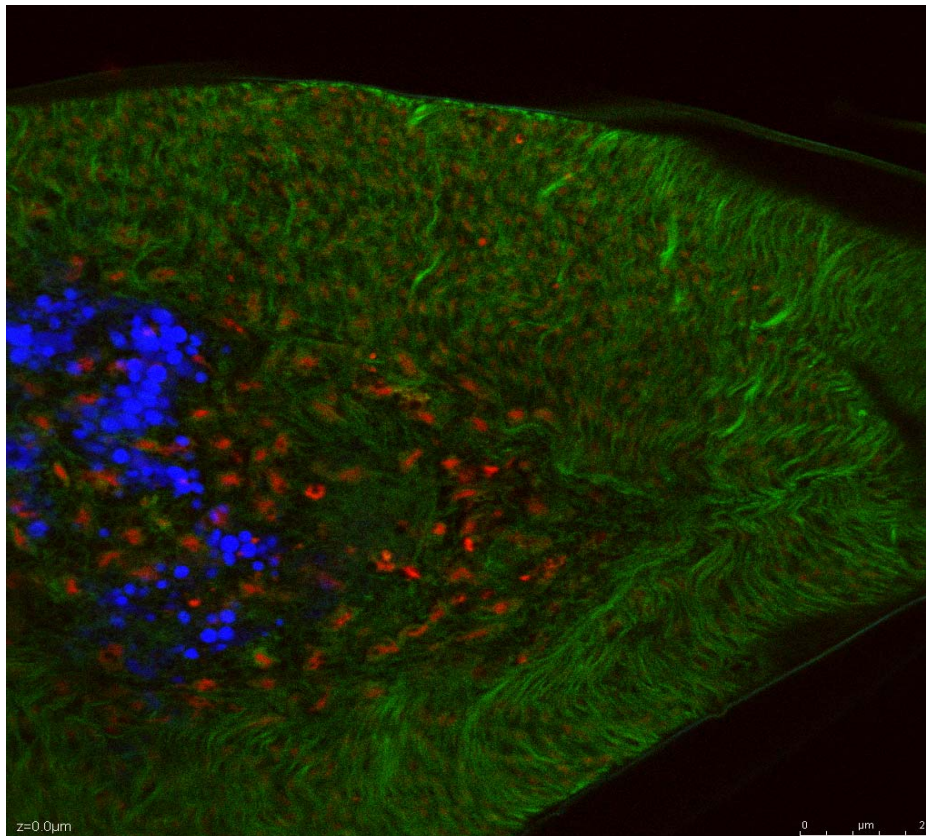


1. DROSOPHILA
2. C. ELEGANS
3. ZEBRAFISH

Is AMN important in developmental apoptosis?

What is its functional relevance?

Juan Garrido Maraver



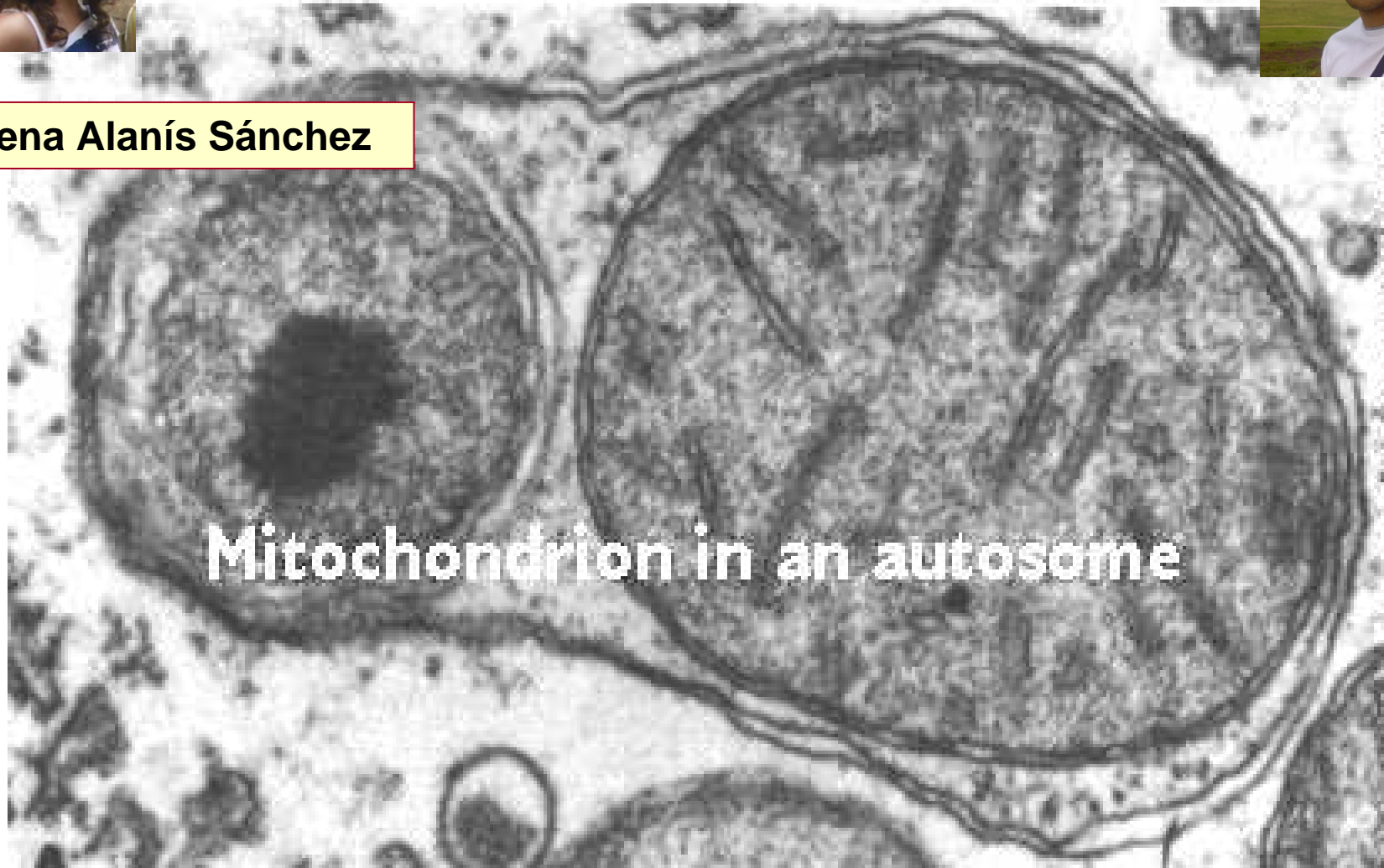
AUTOPHAGY AND MITOCHONDRIAL DISEASES (COENZYME Q DEFICIENCY, MELAS, MERRF...)



Juan Garrido Maraver



Macarena Alanís Sánchez

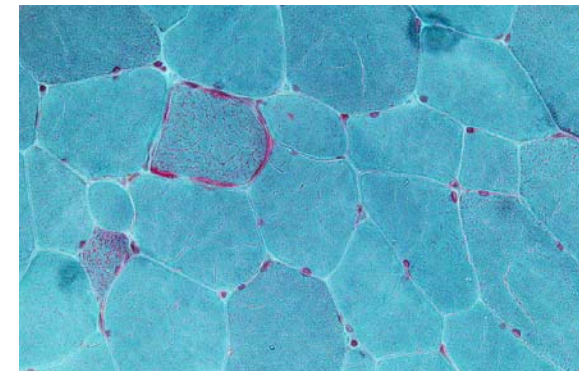
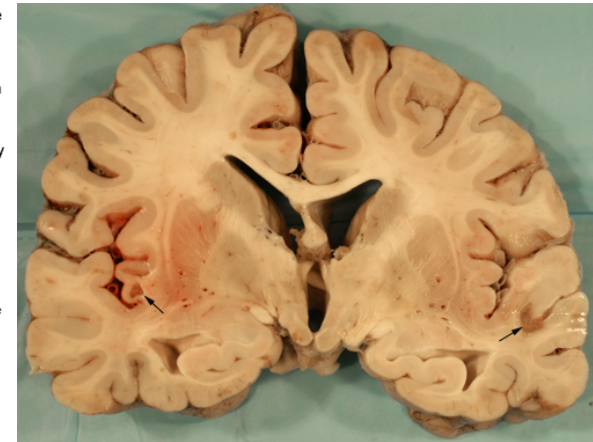
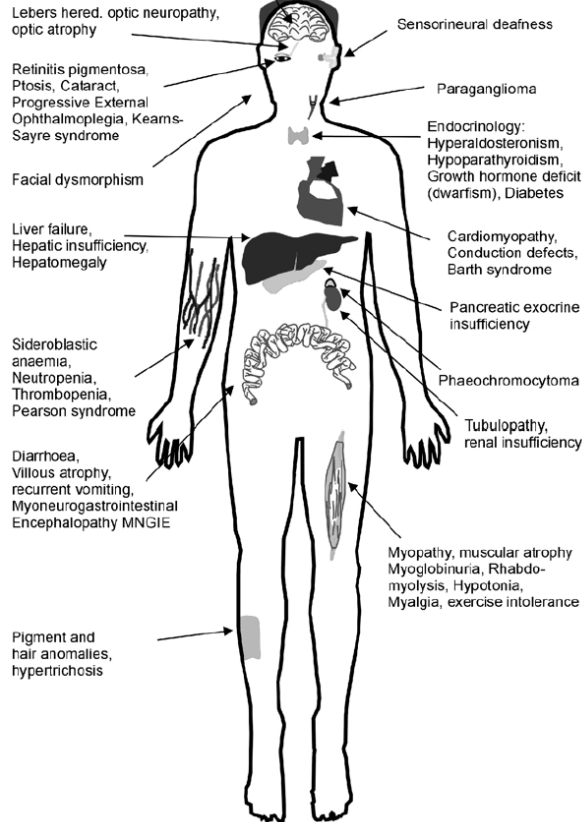


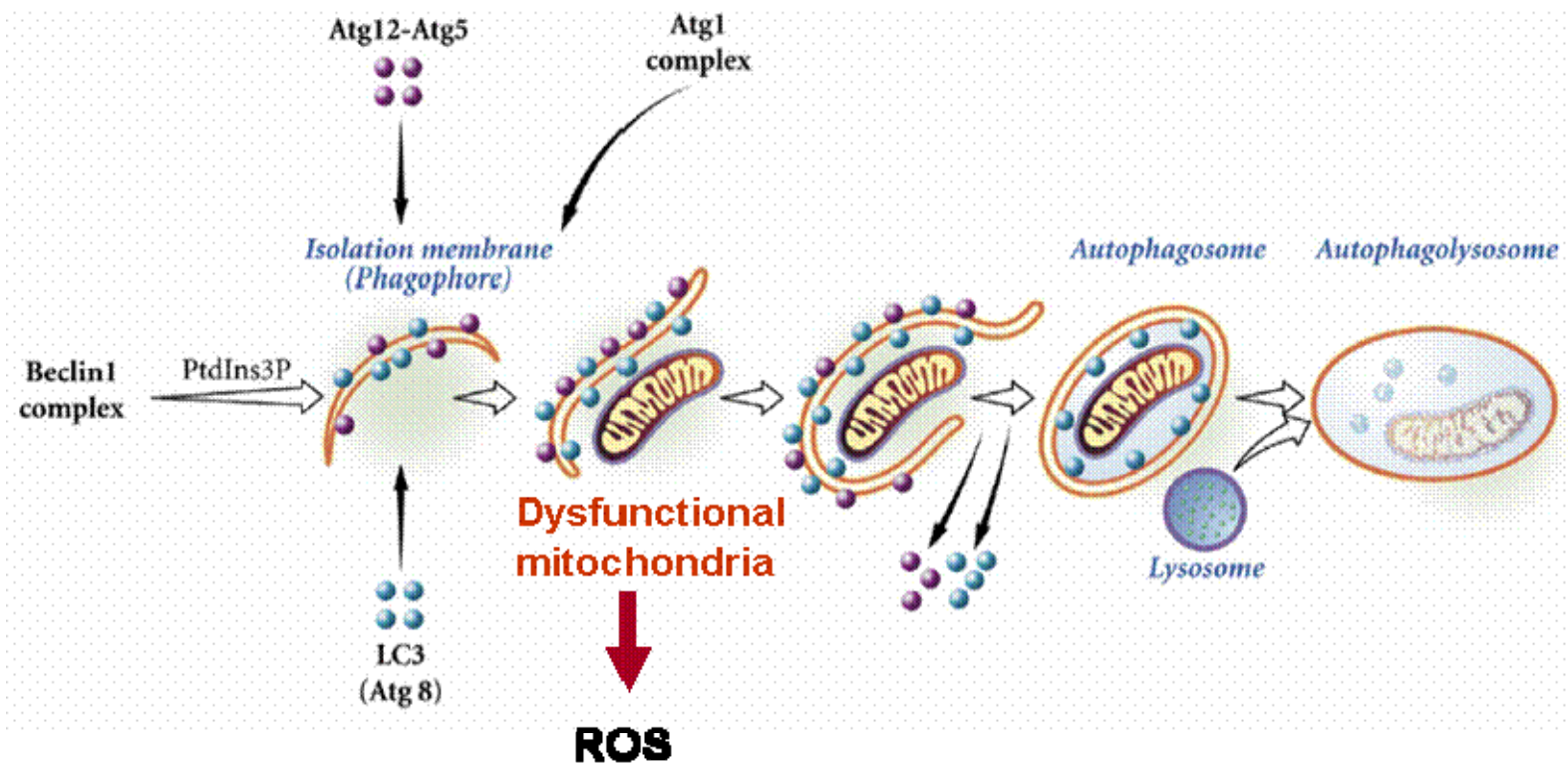
Mitochondrion in an autosome

MITOCHONDRIAL DISEASES



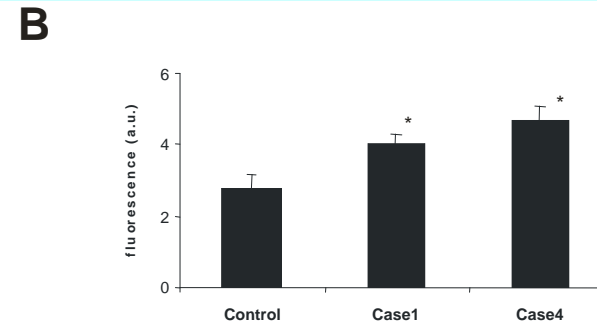
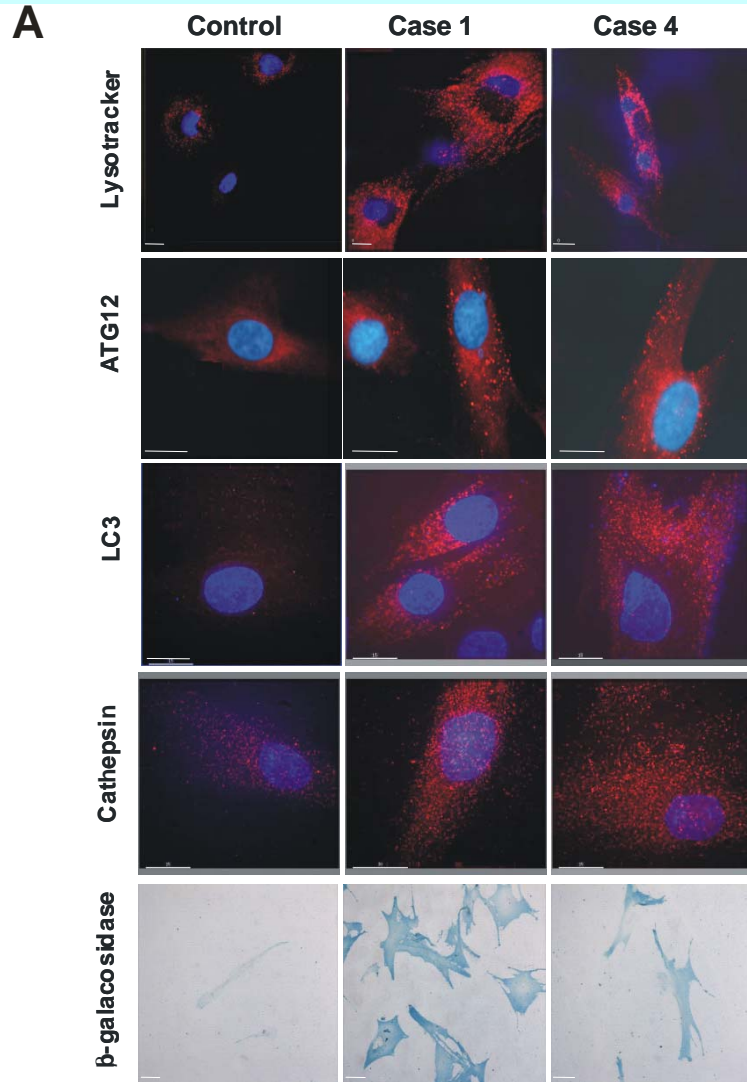
Neurology: Hypotonia, cerebellar ataxia, epilepsy, myoclonic seizures, spasticity, psychomotor and mental retardation, leucodystrophy, cortical atrophy, peripheral neuropathy, Leigh-Syndrom, Friedreich's ataxia, Alpers-Syndrom, hered. spastic paraplegia, MELAS, MERRF, NARP





Coenzyme Q deficiency triggers mitochondria degradation by mitophagy

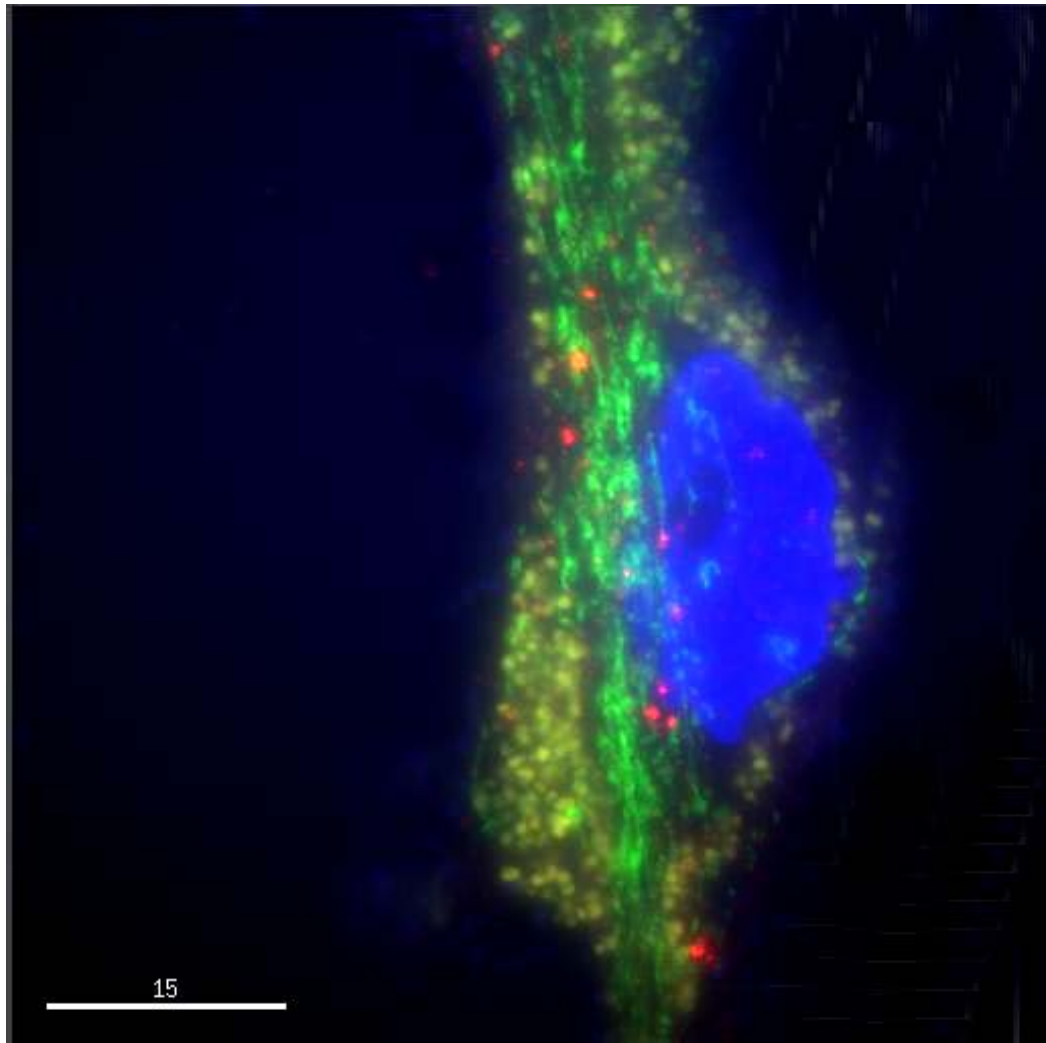
Ángeles Rodríguez-Hernández, Mario D. Cordero, Leonardo Salviati, Rafael Artuch, Mercé Pineda, Paz Briones, Lourdes Gómez Izquierdo, David Cotán, Plácido Navas, and José A. Sánchez-Alcázar.



Autophagy Journal, 2009

Secondary coenzyme Q10 deficiency triggers mitochondria degradation by mitophagy in MELAS fibroblasts

David Cotán, Mario D. Cordero, Juan Garrido-Maraver, Manuel Oropesa-Ávila, Ángeles Rodríguez-Hernández, Lourdes Gómez Izquierdo, Mario De la Mata, Manuel De Miguel, Juan Bautista Lorite, Eloy Rivas Infante, Sandra Jackson, Plácido Navas, and José A. Sánchez-Alcázar.



FASEB Journal, 2011

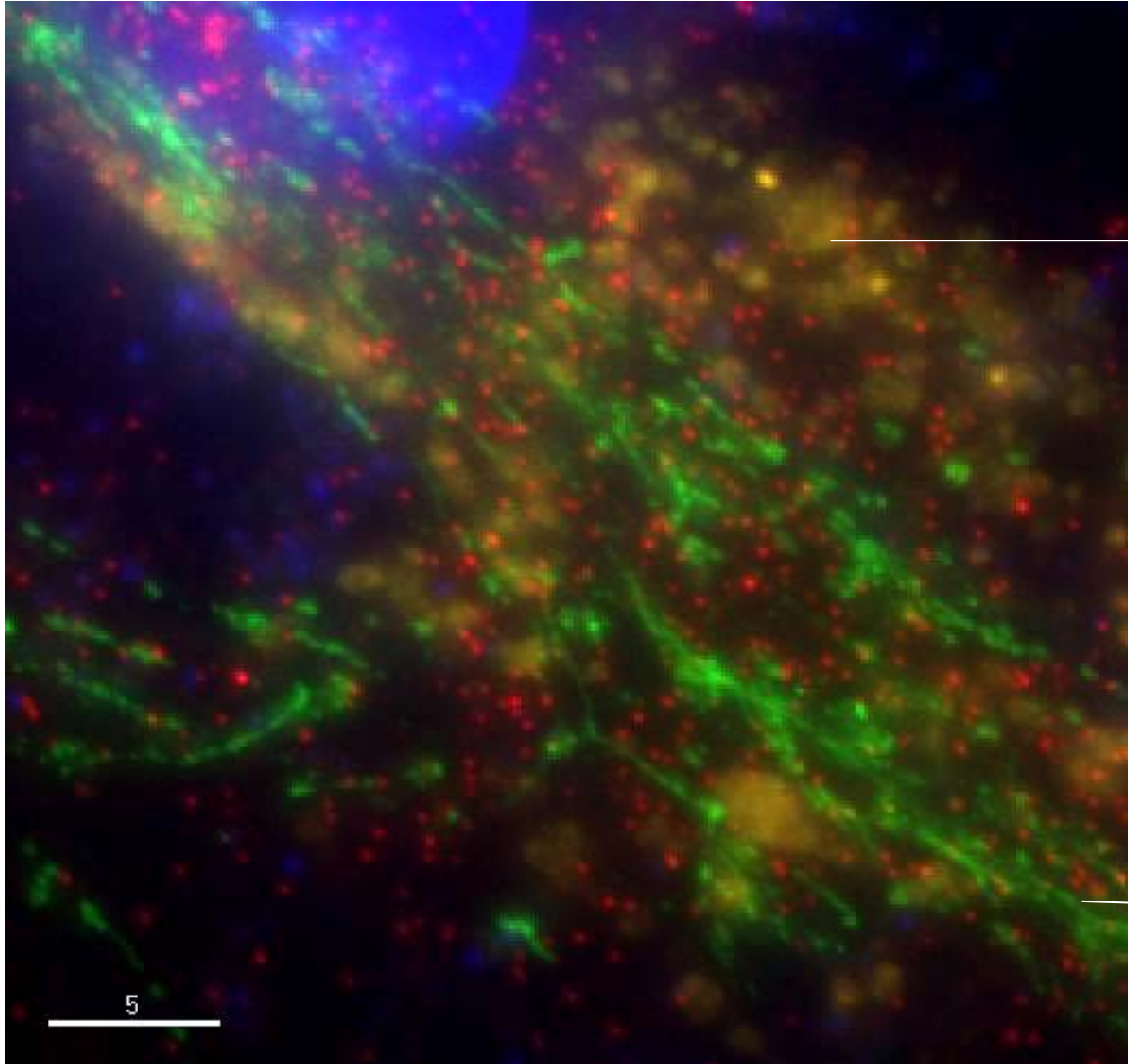


Image: MELASDD9_R3D.dv
Pearson Coefficient of Correlation: 0.8528

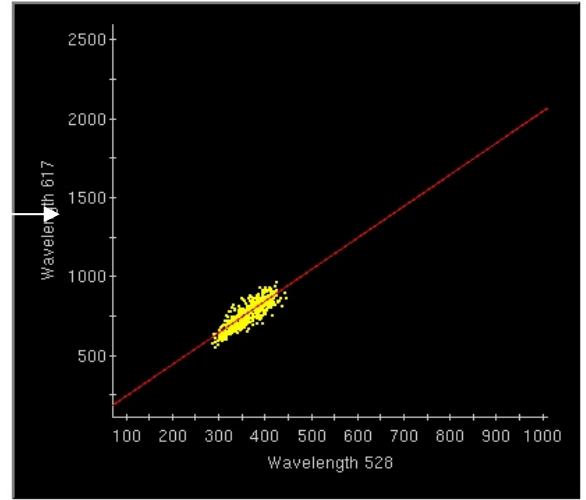
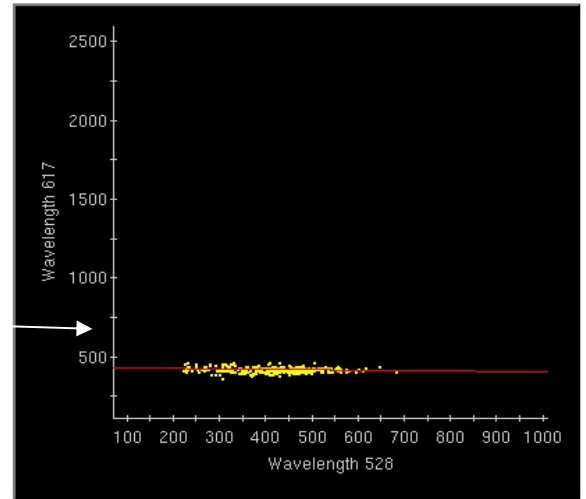


Image: MELASDD9_R3D.dv
Pearson Coefficient of Correlation: -0.1145



KEY POINTS

Mitophagy is involved in many neurodegenerative diseases and aging

Modulation of mitophagy can be helpful in the treatment of mitochondrial diseases and others diseases in which mitochondria dysfunction plays a critical role

EVALUATION OF THE EFFECTIVENESS OF IN VITRO PHARMACOLOGICAL TREATMENTS OF FIBROBLASTS TAKEN FROM PATIENTS SUFFERING MITOCHONDRIAL DISEASES

Asociación de Enfermos Mitocondriales de España, AEPMI

Avoidance of dangerous drugs
Removal of noxious metabolites
Administration of electron acceptors

Valproic acid, aspirin, aminoglycosides
Lactate, thymidine
Vitamin E and C, succinate

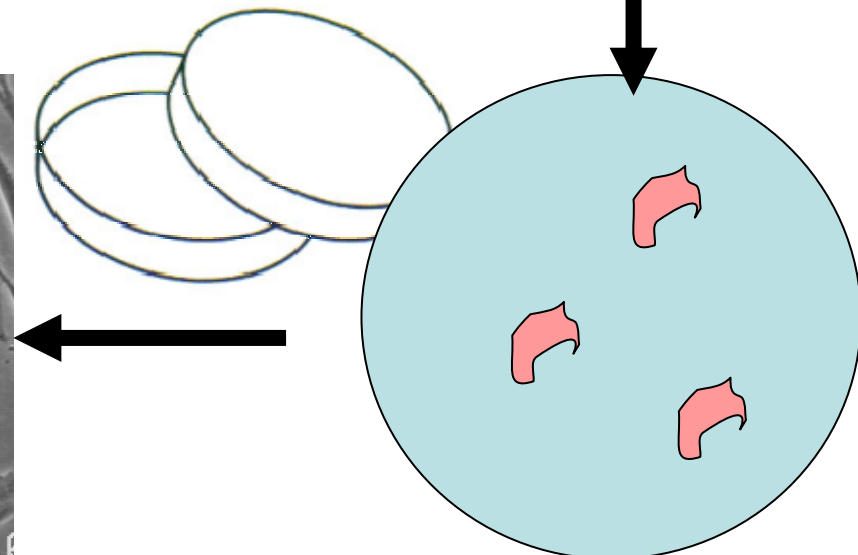
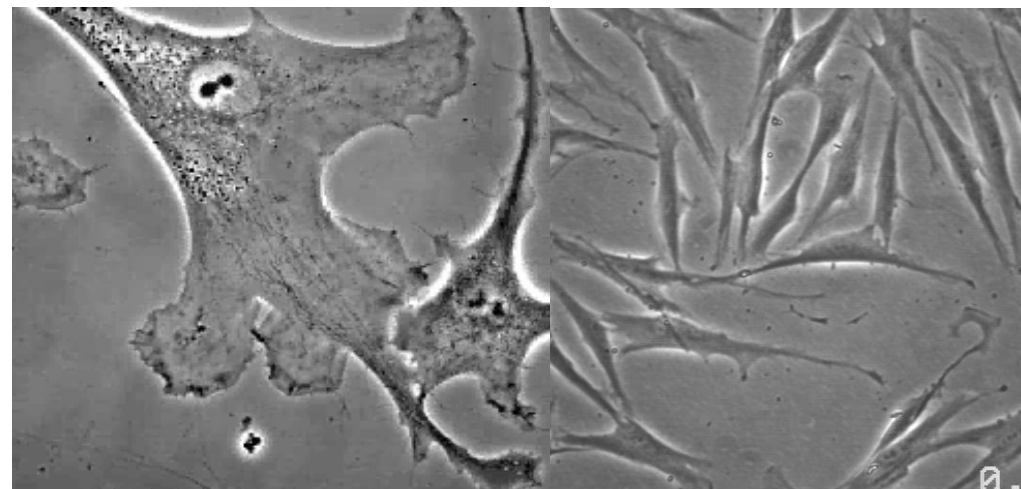
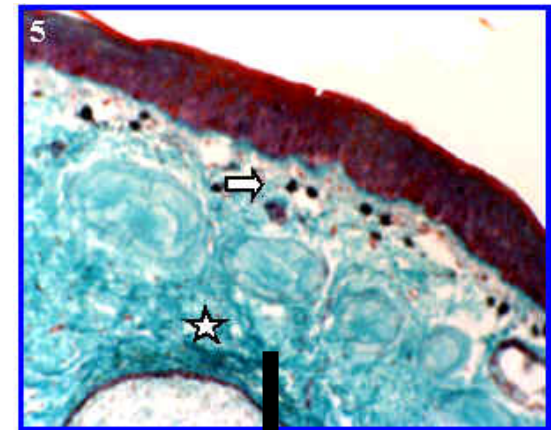
metabolites and

Vitamins, folic acid, Coenzyme Q10, L-carnitine

Coenzyme Q10, MitoQ, glutathione



Carmen Pérez Calero



TREATMENT OF MITOCHONDRIAL DISEASES

MELAS YEASTS: Yeast as a model of human mitochondrial tRNA base substitutions: Investigation of the molecular basis of respiratory defects.

SILVIA FRANCISCI
University of Rome

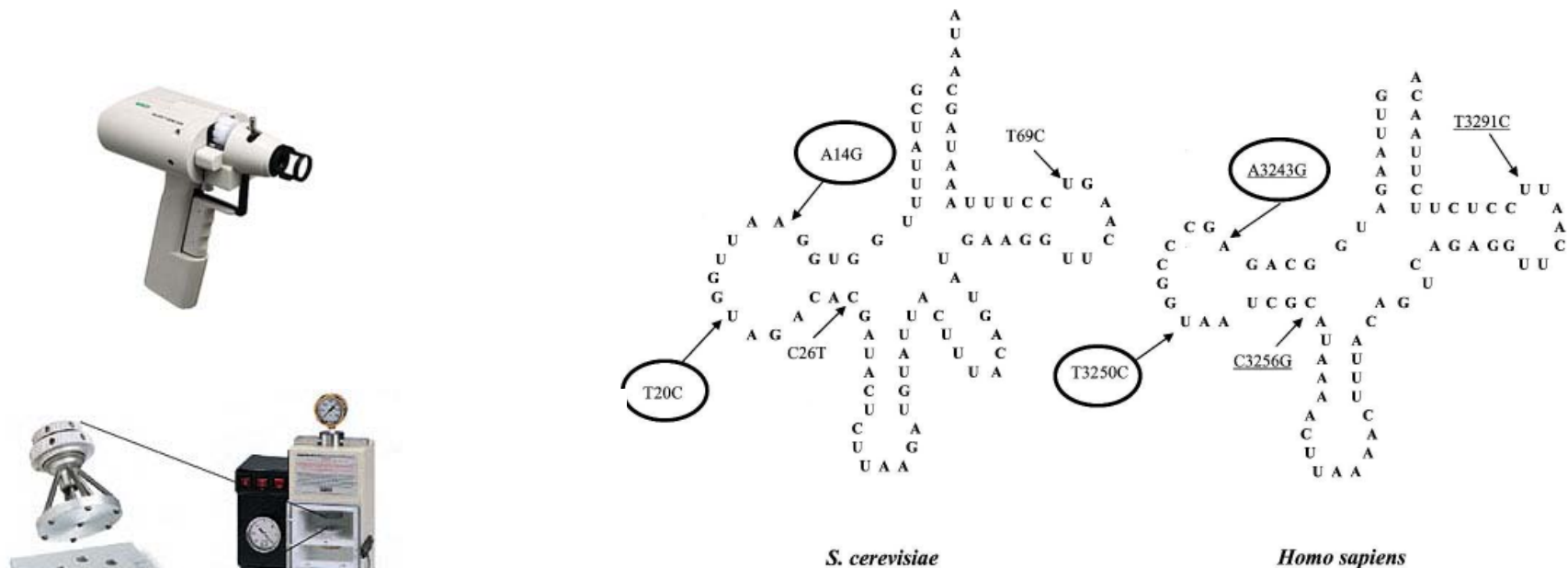
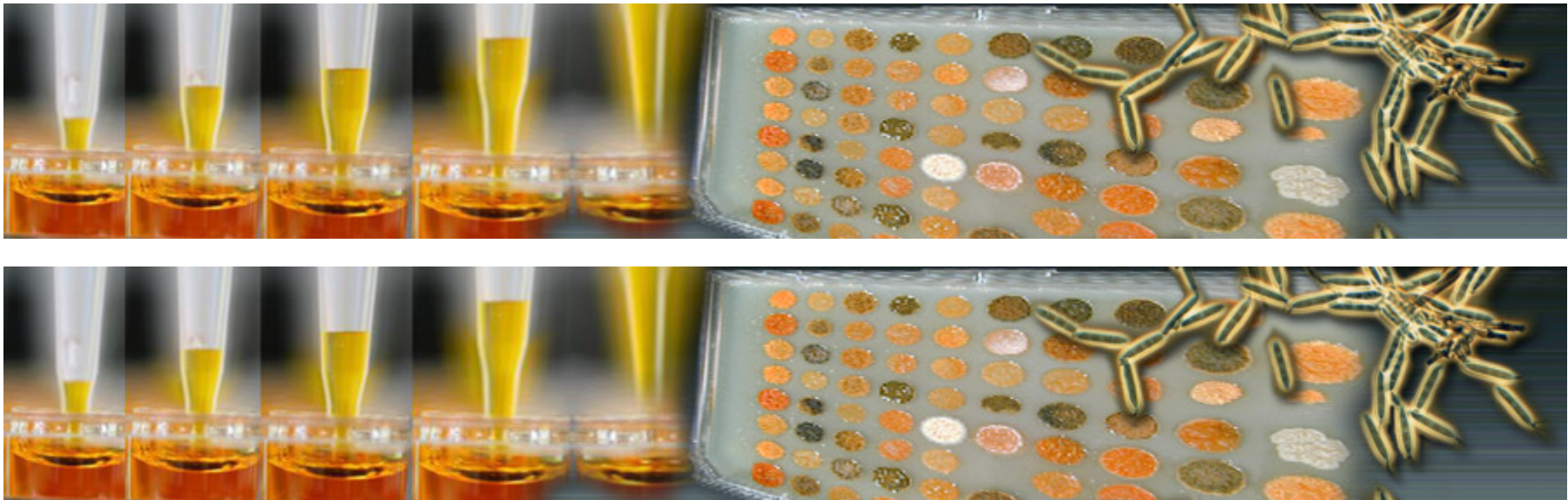
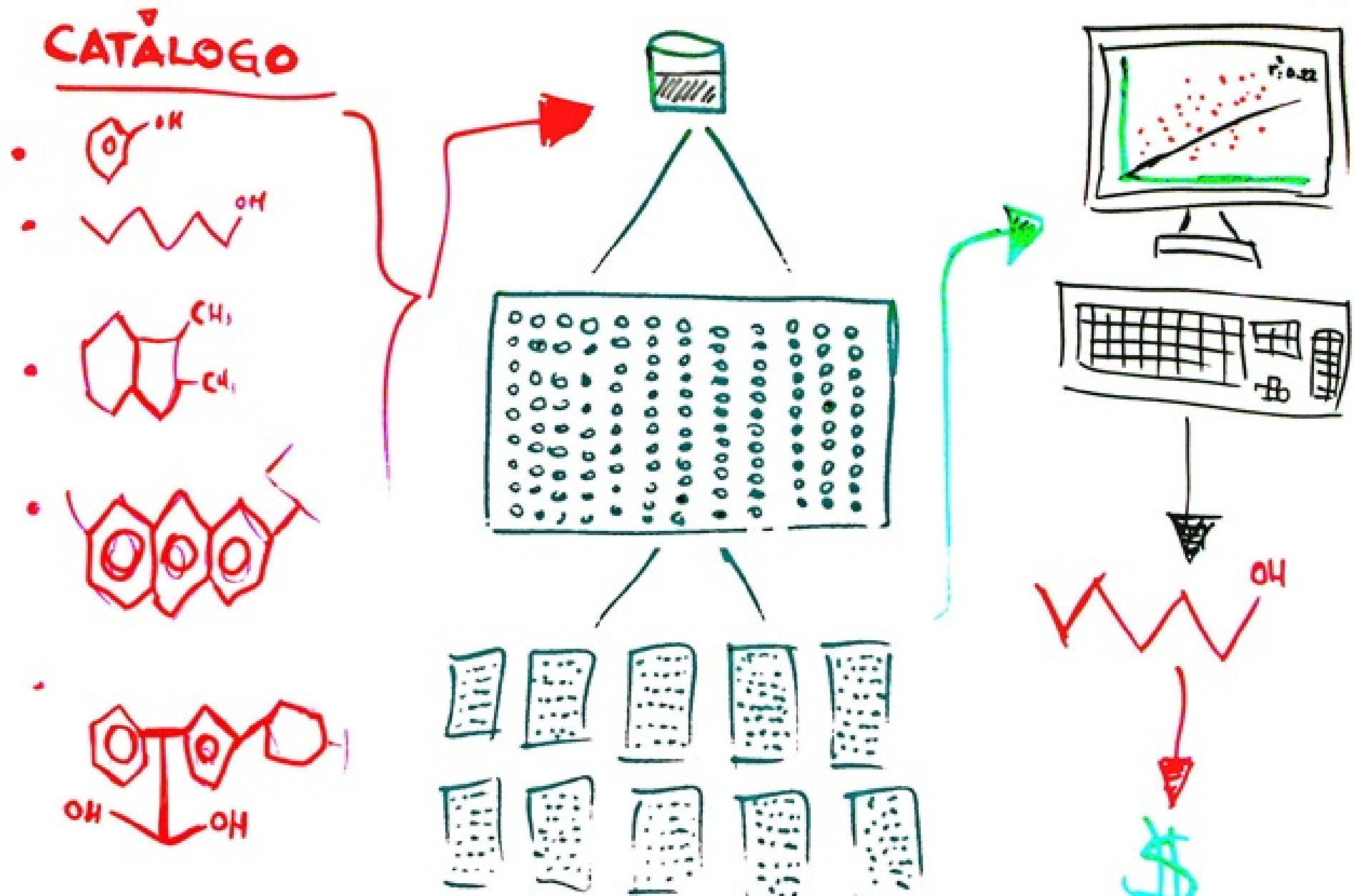


FIGURE 1. Comparison of yeast and human mt tRNA^{Leu}_{UUR} cloverleaf structures and mutations introduced in yeast mt tRNA^{Leu}_{UUR} by biolistic procedures. (Arrows) The “pathological mutations” described in Feuermann et al. (2003) and equivalent to MELAS base substitution (underlined) and the mutations analyzed in this work (circles).

High-throughput screening (HTS) for testing new drugs in the treatment of MELAS syndrome





Using robotics, data processing, liquid handling devices and sensitive detectors, HTS allows a researcher to quickly conduct million of pharmacological tests.

PRONACERA

Proteins

Nanotechnology

Cells

Mouse

Clinics



Mario de la Mata Fernández



David Cotán Marín

Cancer project

Lysosomal diseases project

RECOMBINANT PROTEIN PRODUCTION
NANOPARTICLES FUNCTIONALIZATION
ASSAYS IN CELLS
ASSAYS IN MICE

Delivery of proteins, drugs and genes to specific cellular targets

PRONACERA

In collaboration with BIONATURIS

PLATAFORMA FLYLIFE

David Cotán Marín



FLYLIFE es una plataforma tecnológica de fabricación a escala industrial de proteínas recombinantes de alto valor añadido. Se trata de un sistema versátil y eficiente, especialmente diseñado para proteínas difíciles de expresar en otros sistemas. **FLYLIFE** utiliza larvas de insectos como biofactorías no fermentativas. **Bionaturis** ofrece contratos de manufactura para entidades del sector farmacéutico, biotecnológico, veterinario y diagnóstico.

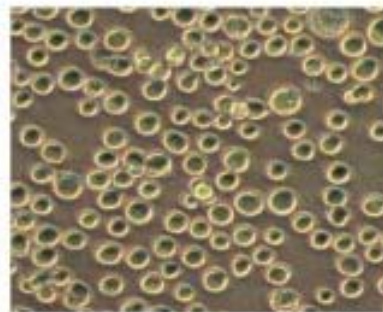
Principales características:



- **Gran versatilidad.** Diseñado de forma específica para proteínas de difícil expresión en otros sistemas convencionales como levaduras o bacterias
- **Funcionalidad.** Altos niveles de modificaciones postraslacionales (glicosilaciones y *foldings*)
- **Cost-effective.** Sistema de producción no fermentativo y fácil de escalar (desde mg a KG)
- **Seguridad biológica.** Uso de vectores de expresión baculovíricos



Uninfected insect cells



Insect cells infected with recombinant Baculovirus



Spodoptera frugiperda (J.E. Smith)



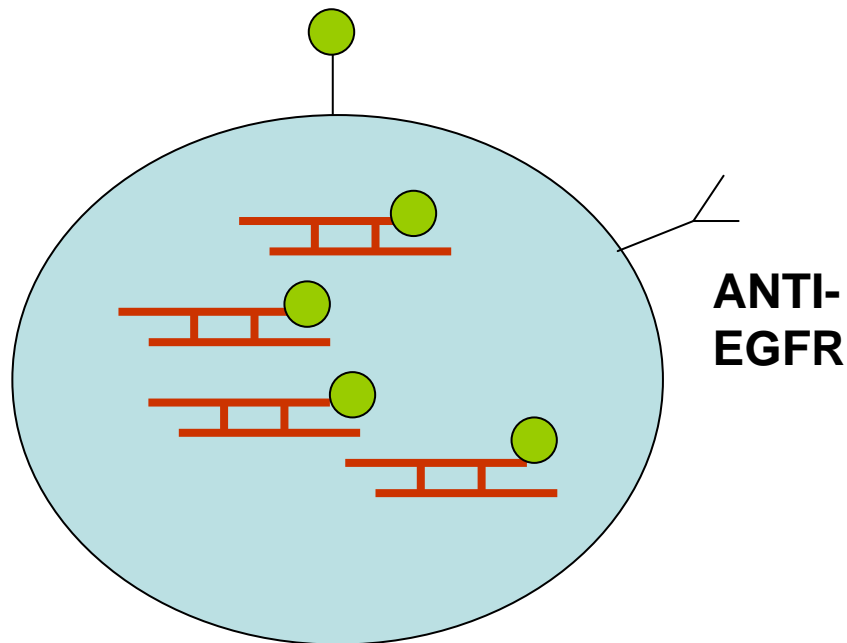
Spodoptera frugiperda

Cancer project

Ana Paula Zaderenko Partida, Principal Investigator of the project
Departamento de Sistemas Físicos, Químicos y Naturales



New nanoparticles for selective therapy against cancer



PROYECTO DE EXCELENCIA 2011-2014

Grupo de Físico-Química

Bionaturis

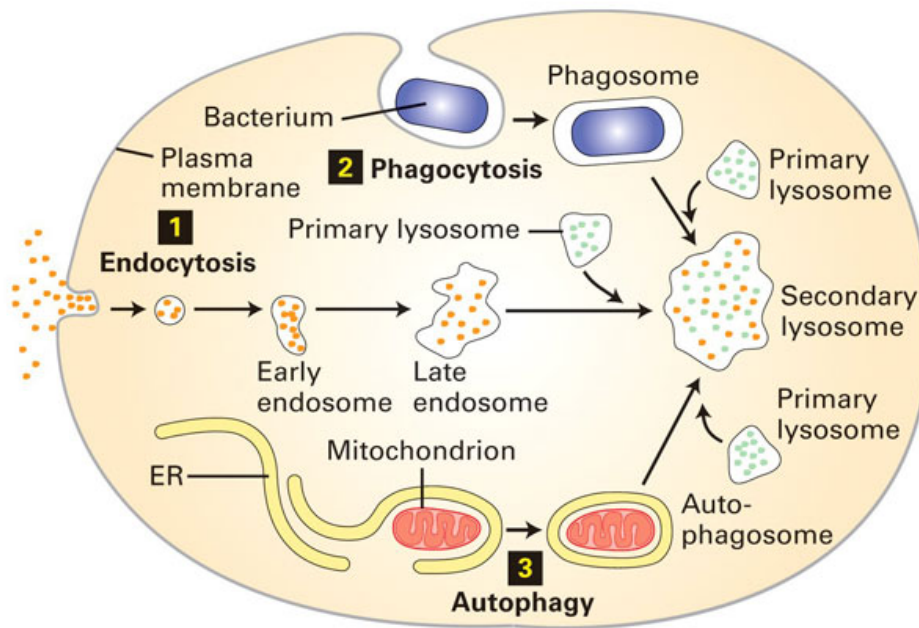
Biología Celular-Lab 210

Grupo Facultad de Medicina

Mario de la Mata Fernández

Self-assembling **nanoparticles** with siRNA or anticancer agents
Surface conjugation of antibodies

Development of new formulations of enzyme replacement therapy for the treatment of lysosomal diseases



PROYECTO DE EXCELENCIA 2011-2014

Grupo de Físico-Química

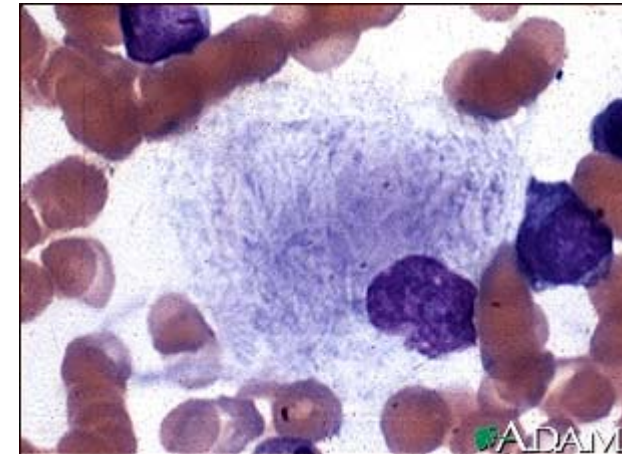
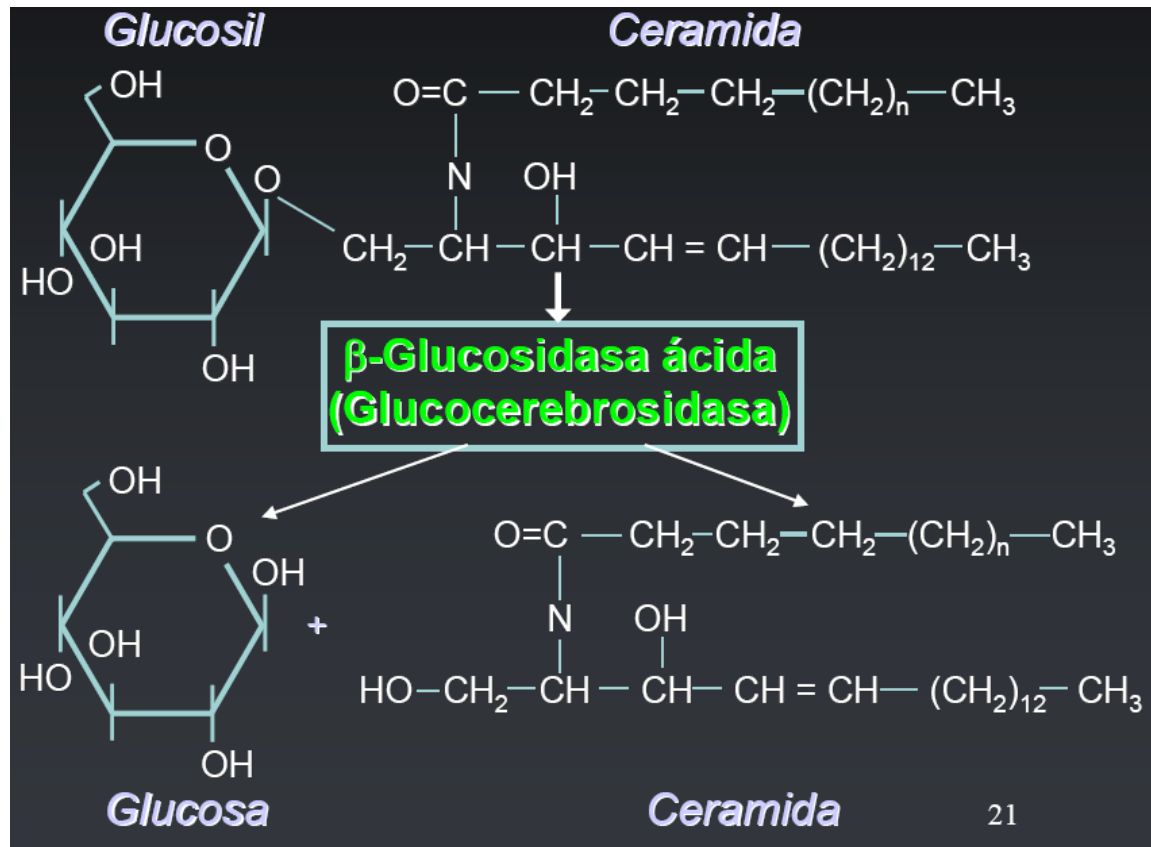
Bionaturis

Biología Celular-Lab 210

Grupo Facultad de Medicina

Mario de la Mata Fernández

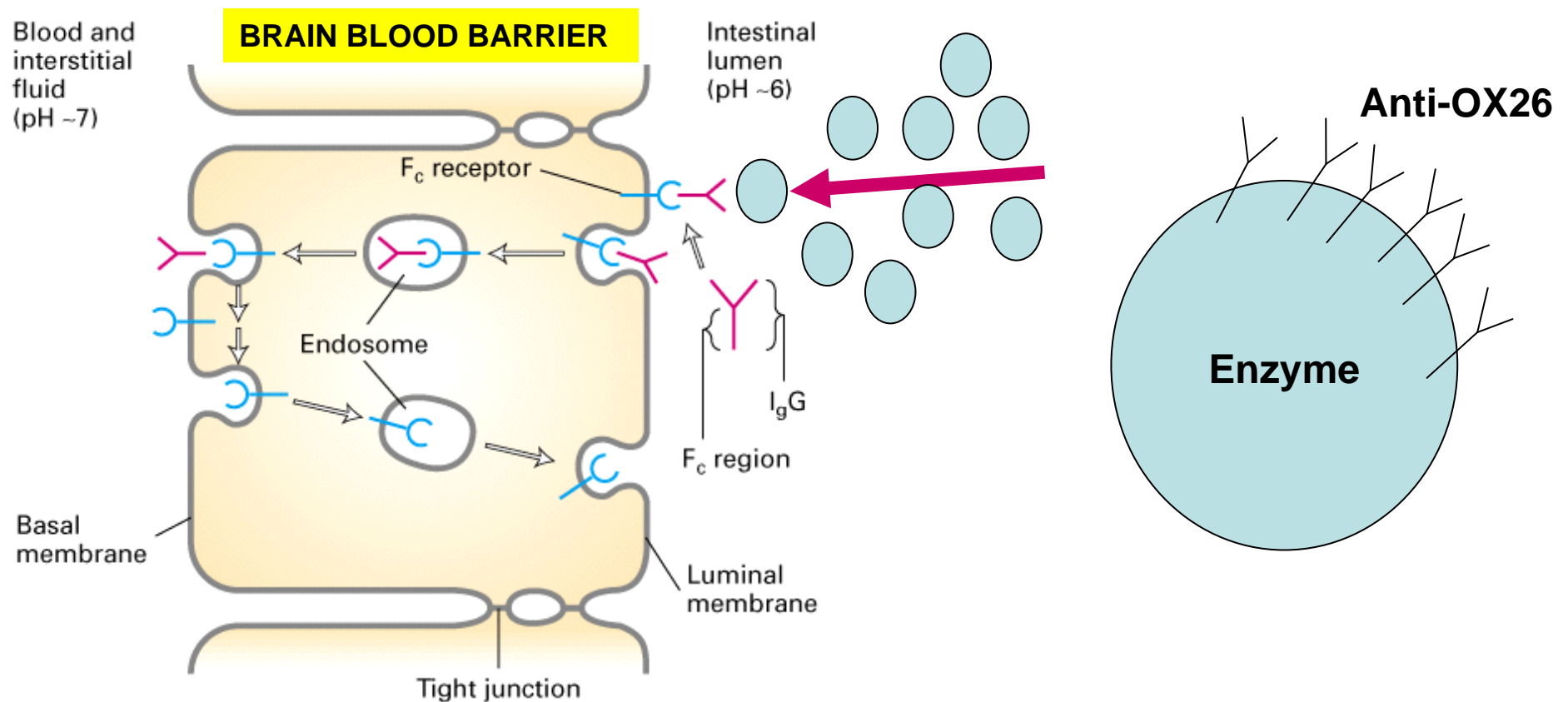
ENFERMEDAD DE GAUCHER



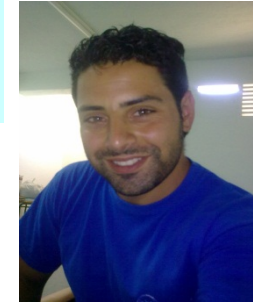
Pathophysiology of fibroblasts derived from patients

a) Establish an encapsulation procedure for the enzyme glucocerebrosidase, in biocompatible and biodegradable polymeric nanoparticles.

b) Functionalize the polymeric nanoparticles with antibodies against transferrin receptor (OX26) as active delivery agent.



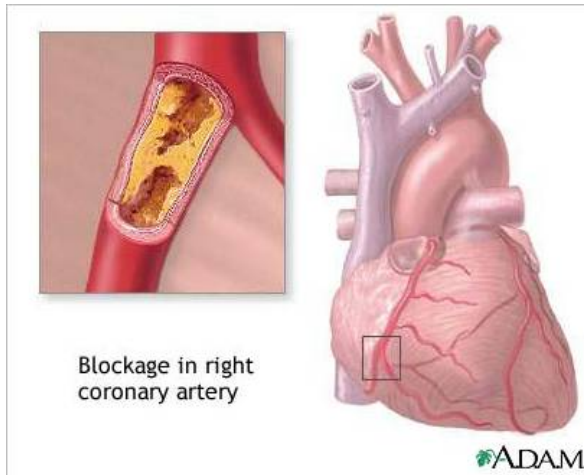
Familial Hypercholesterolemia as a model to understand atherosclerosis



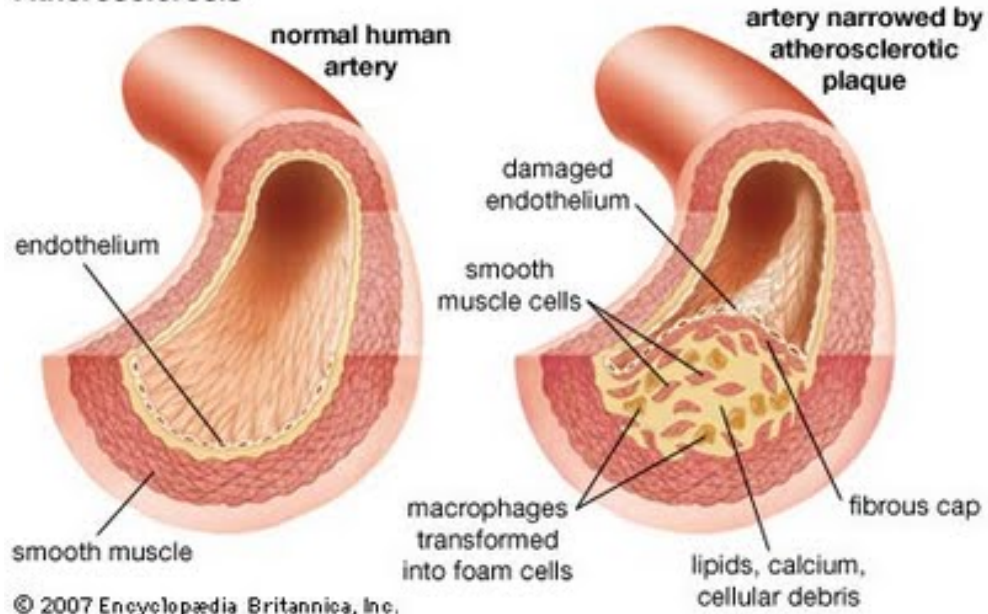
David Cotán Marín

Ana Delgado Pavón

Marina Villanueva Paz



Atherosclerosis

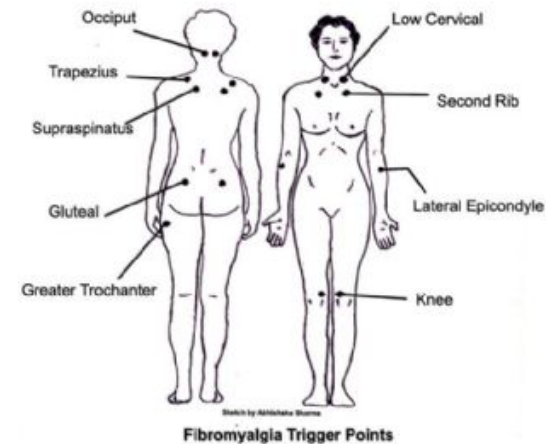


Collaboration with Mario D. Cordero (Universidad de Sevilla)

Mario D. Cordero Morales



Fibromyalgia and Chronic Fatigue

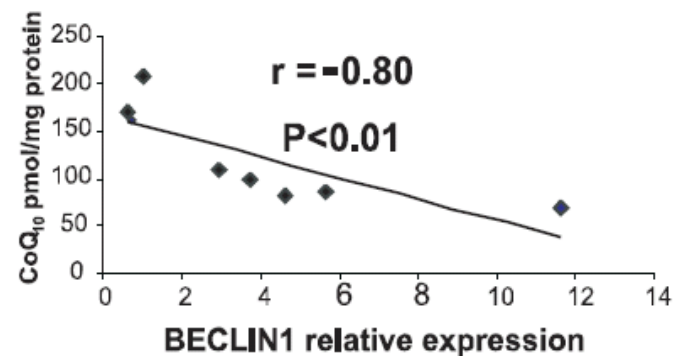
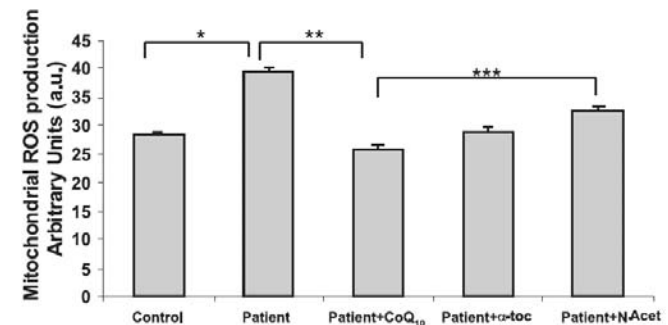
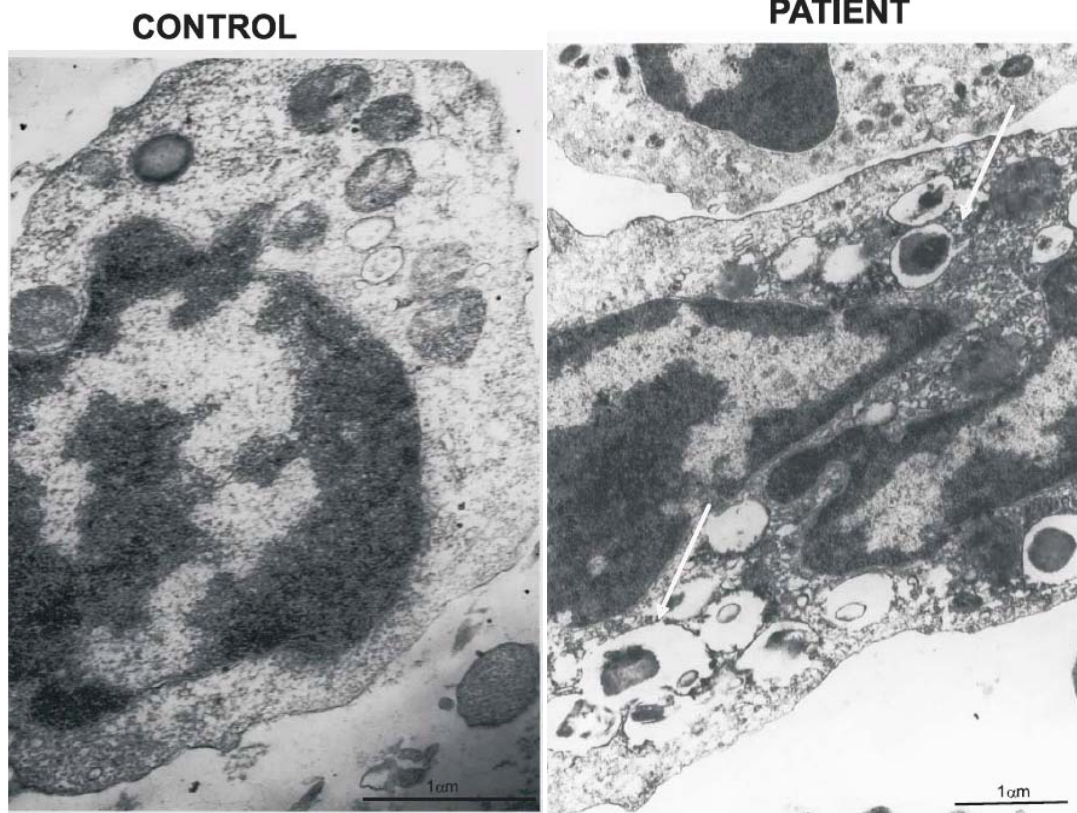


Mitochondrial dysfunction and mitophagy activation in blood mononuclear cells of fibromyalgia patients: implications in the pathogenesis of the disease.

Mario D Cordero, Manuel De Miguel, Ana M Moreno Fernández, Inés M Carmona López, Juan Garrido Maraver, David Cotán, Lourdes Gómez Izquierdo, Pablo Bonal, Francisco Campa, Pedro Bullon, Plácido Navas and José A Sánchez Alcázar .

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Highly accessed



Thanks to:

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MIGUEL A MARTIN CASANUEVA

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CELL BIOLOGY PEOPLE (Plácido Navas Group)

Thanks

