PERoxisome, FUnction, MEtabolism (PERFUME)

Resumen:

The Marie Curie Initial Training Network PERFUME (PERoxisome Formation, Function, Metabolism) is an interdisciplinary and intersectoral initial stage training network (ITN) at the interface of medicine, plant and fungal biology, devoted to understanding the principles of peroxisome biology.

Peroxisomes are ubiquitous organelles that are essential in man. Yet, the importance of the organelles is strongly underestimated. This is evident from the recent identification of several novel crucial functions, for instance related to resistance towards various stress conditions. Due to earlier considerable technical challenges the atlas of peroxisome functions is still far from complete. Further understanding of the significance of the intact organelle for cell performance demands directed analyses, which require the combined expertise from different disciplines and sectors that cut across historically separated fields.

Objetivos:

The main objectives of the PERFUME program are to:

- Identify novel peroxisome functions. The recent identification of several novel peroxisome functions, a. o. related to stress adaptation and ageing, underline the still strongly underestimated significance of the key role of peroxisomes. Due to earlier considerable technical challenges the atlas of peroxisome functions is still far from complete.
- Understand the compartmentalization of functions in peroxisomes. For almost all peroxisomal metabolic pathways it is not understood why they are contained in these organelles. Moreover, recent observations indicate that peroxisome abundance also matters for optimal peroxisome metabolism and cell vitality.
- Unravel the principles of peroxisome proliferation. It has only recently been established that peroxisomes can proliferate in two ways (fission and formation from the endoplasmic reticulum, ER). Recent novel findings have opened up new outlooks to elucidate the molecular mechanisms of these important processes including also the signaling pathways that trigger peroxisome proliferation.

Objectivos contribución:

UPO will contibute to achieve the objectives by:

Analysing the function of a sub-set of newly identified proteins based on protein annotation, homology/phylogenetic analyses

Moreover, UPO will screen the promoter regions of peroxisomal genes through bioinformatics for response elements of corresponding transcription factors that will be verified by ChIP assays.

UPO is also in charge of the WP called: "Protein structure prediction using bioinformatics". This WP will characterize as completely as possible the sequence and structure of proteins important for peroxisome function and proliferation by a bioinformatics approach.

Entregables:

- D1.1: PTS tools developed also for fungi and mammals and application established
- D1.2: novel stress-inducible yeast and A. thaliana proteins identified
- D1.3: localisation of novel peroxisomal proteins and stress inducibility experimentally validated
- D1.4: Kinetic properties of novel peroxisomal enzymes determined
- D1.5:mutants generated and phenotype determined
- D1.6: Detailed characterization of the function of selected stress proteins in adaptation to abiotic stress and aging yeast, plant and mammals
- D1.7: five publications on novel peroxisomal proteins
- D2.1:Generic model of peroxisomal -oxidation constructed
- D2.2: Experimental determination and implementation of yeast and mammalian kinetic parameters
- D2.3: Yeast and mammalian metabolic fluxes determined
- D2.4: Yeast and mammalian metabolomics established
- D2.5: Prediction of metabolic impact of defects in enzyme localisation or organelle proliferation and experimental validation
- D2.6 four publications on the consequences of (defects in) peroxisomal enzyme or their compartmentalization
- D2.7: The consequences of differential compartmentalization of β-oxidation in peroxisomes versus mitochondria established
- D2.8: publication on mitochondrial versus peroxisomal β-oxidation
- D3.1: Repository of patient cell lines analysed for novel peroxisomal defects
- D3.2: Selected patient cell lines with novel peroxisomal defects characterized
- D3.3. three publications on novel peroxisomal defects
- D3.4. Improved diagnostic tools for laboratory identification of peroxisomal defects tested

- D3.5: Novel biomarkers for peroxisomal defects analyzed
- D3.6. Publication on improved diagnostic tools
- D3.7: Peroxisome proliferation assay developed and novel stimuli tested
- D3.8: Regulation pathways identified by transcriptome, promoter and network analysis
- D3.9: two publications on peroxisome proliferation stimuli and regulatory pathways
- D3.10. In vitro analysis of efficacy of putative therapeutic interventions in patient cell lines
- D3.11 publication on possible leads for novel therapeutic interventions
- D4.1: Yeast strains constructed with genomically tagged key proteins in peroxisome proliferation
- D4.2: Isolation and MS analysis of protein complexes of peroxisome proliferation machineries
- D4.3 Localization and characterization of newly identified proteins in peroxisome proliferation
- D4.4 three publications on novel proteins in peroxisome /proliferation
- D4.5. H. polymorpha and S. cerevisiae mutants for genetic screens constructed
- D4.6: Phenotypic analysis of mutants and selection of interesting candidates
- D4.7. Analysis and characterization of proteins involved in peroxisome proliferation completed
- D4.8: Four publications on mechanisms involved in peroxisome proliferation
- D4.9: Key proteins in peroxisome proliferation purified
- D4.10: Complex formation, characterization
- D4.11: Low resolution structure determination of selected proteins/protein complexes
- D4.12: High-resolution structure determination of selected proteins/ complexes
- D4.13. Three publications on the structure of selected proteins/protein complexes
- D4.14: Generation and characterization of structure-based variants of proteins
- D4.15: Two publications on structure-function relation of proteins required for peroxisome biogenesis
- D4.16: Peroxisome protein homologues collection prepared
- D4.17:Peroxisome proteins structure prediction performed
- D4.18: Definition of crystallizable domains/fragments establishedD4.19; Publication on predicted protein structures

Impacto:

This PERFUME ITN will make a major contribution to improve its attractiveness and competencies of life science researchers in medicine, agriculture and biotechnology by educating young excellent scientists in a training profile, which fulfills the demands of the private sector as well as from academia in an ideal way. The experience in advanced life sciences in the PERFUME program, together with a profound training-based knowledge, will provide the ESRs with excellent opportunities to develop their individual careers within a broad spectrum of scientific, industrial and public arenas.

Presupuesto: 3,911,064.03

Equipo de investigación

Nombre: Microbiology's platypus
PAIDI: 00000
Web: http://www.cabd.es/en-research_groups-104-247-microbiologys-platypus-summary.html
Investigador principal: Damien Devos (Investigador Principal)
Email: dpdev@upo.es
Presupuesto del equipo: 237,681.62

Universidad: Universidad Pablo de Olavide

Enlace: http://www.itn-perfume.eu/

Estado: published

Contacto Solicitar más información de PERoxisome, FUnction, MEtabolism