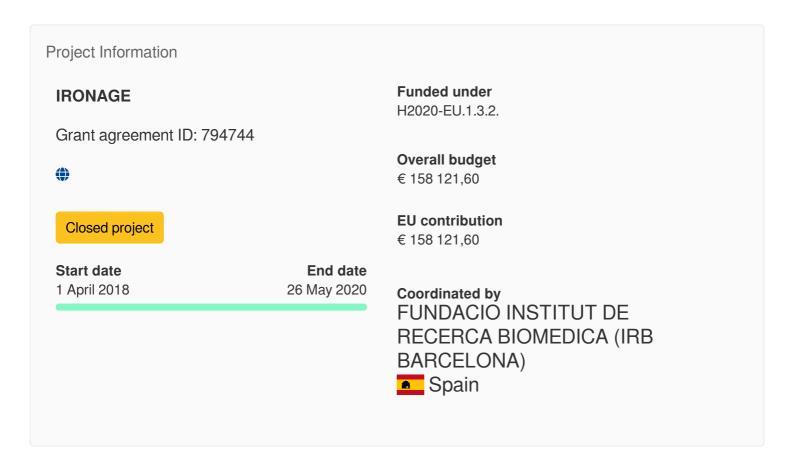




Iron as a driver of fibrosis and regeneration

Fact Sheet



Objective

"I have worked over the last five years on understanding how ion channels control inflammation, immunity, metabolism and cancer, with a strong emphasis on Ca2+ signaling. Now, I would like to take advantage of my diverse background in cation signaling and inflammation and integrate it with the outstanding expertise of Manuel Serrano's lab in regeneration and aging, to ask fundamental questions on the role of iron in regulation of plasticity and fibrosis. Clinical reports have described local deposition of iron around fibrotic tissues, although the significance of this remains poorly understood and unexplored. My unifying hypothesis is that fibrosis is the manifestations of ongoing free-iron release into injured organs and tissues, which without clearance maintains chronic inflammation and prevents regeneration. The project is divided as follows: Objective #1 – Iron induced inflammation: the impact of

free-iron on inflammatory cytokine and chemokine expression and signaling pathways. I have preliminary data indicating that free-iron is a potent inducer of inflammatory cytokines in fibroblasts. Objective #2 – Free-iron as a causative of fibrosis: effect of iron on cellular senescence and on mouse models of fibrosis; and iron homeostasis in human patients with fibrosis. In vitro, I have found that free-iron is an inducer of senescence. Furthermore, in a pilot study, I have found that bleomycin-induced lung fibrosis in mice is accompanied by high levels of iron deposition. Objective #3: Iron clearance and regeneration: Effects of free-iron and iron induced cytokines on acquired plasticity in vitro and on wound healing. Surprisingly, my preliminary data indicate that chelation of free-iron completely blocks acquisition of pluripotency, but has no effect on expansion of stem cells. I anticipate that the completion of this action will yield new fundamental insights into the underlying mechanisms of fibrosis and regeneration, and will allow me the transit to independence."

Fields of science

medical and health sciences > medical biotechnology > cells technologies > stem cells medical and health sciences > clinical medicine > oncology medical and health sciences > basic medicine > physiology > homeostasis

Programme(s)

H2020-EU.1.3.2. - Nurturing excellence by means of cross-border and cross-sector mobility

Topic(s)

MSCA-IF-2017 - Individual Fellowships

Call for proposal

H2020-MSCA-IF-2017 See other projects for this call

Funding Scheme

MSCA-IF-EF-RI - RI - Reintegration panel

Coordinator



FUNDACIO INSTITUT DE RECERCA BIOMEDICA (IRB BARCELONA)

Address

Carrer Baldiri Reixac 10-12 Parc Scientific De Barcelona 08028 Barcelona



Activity type

Research Organisations

Contact the organisation Website H2020 collaboration network

EU contribution

€ 158 121,60

Last update: 15 September 2020

Record number: 214146

Permalink: https://cordis.europa.eu/project/id/794744





Dissecting novel mechanisms of iron regulation during macrophage-fungal interplay

Fact Sheet

Project Information Funded under iMAC-FUN EXCELLENT SCIENCE - European Research Council (ERC) Grant agreement ID: 864957 **Total cost** DOI € 2 000 000 10.3030/864957 **EU** contribution Start date **End date** € 2 000 000 1 September 2020 31 August 2025 Hosted by IDRYMA TECHNOLOGIAS KAI **EREVNAS** Greece

Project description

Understanding invasive mould infections



Objective

Airborne filamentous fungi (molds) are major causes of respiratory diseases in an expanding population of patients with complex immune and metabolic defects. Invasive mold infections (IMI) are associated with substantial mortality and enormous economic impact. Understanding pathogenesis of IMI is an unmet need for design of better therapies. We have put forward a novel mechanism for the pathogenesis of IMI, according to which development of IMI requires two discrete mechanisms (a) phagosome maturation arrest via inhibition of LC3-associated phagocytosis (LAP), which allows intracellular persistence of fungal conidia (spores), and (b) alteration in iron homeostasis, resulting in invasive fungal growth and lysis of the macrophage. On the pathogen site, fungal melanin targets LAP and affects macrophage metal homeostasis. On the macrophage site, iron distribution in subcellular compartments of all eukaryotic cells is controlled by ferric reductases and divalent cation transporters, in a process that remains molecularly unexplored. During mold infection a group of ferric reductases represent the most prominently transcriptionally modulated iron regulatory genes in macrophages. Thus, iron regulation is the critical determinant of macrophage-fungal interplay and is the focus of this project. We will use molds as model pathogens to (i) dissect the role of selected ferric reductases in infection, (ii) identify novel iron transporters implicated in host defense (iii) and explore mechanisms of melanin interference with iron regulation in macrophages. To this end, we will employ a robust, unbiased, approach combining transcriptomics, metalloproteomics, in vivo RNAi screening in Drosophila model of IMI, and validation studies in transgenic mice and eventually in human patients ex vivo. Dissecting the function of novel iron regulators in the macrophage will have profound impact on iron biology and is likely to have direct therapeutic implications for the management of IMI.

Fields of science

social sciences > sociology > demography > mortality
natural sciences > biological sciences > microbiology > mycology
medical and health sciences > health sciences > infectious diseases > RNA viruses > coronaviruses
medical and health sciences > basic medicine > physiology > homeostasis

Programme(s)

H2020-EU.1.1. - EXCELLENT SCIENCE - European Research Council (ERC)

MAIN PROGRAMME

Topic(s)

ERC-2019-COG - ERC Consolidator Grant

Call for proposal

ERC-2019-COG

See other projects for this call

Funding Scheme

ERC-COG - Consolidator Grant

Host institution



IDRYMA TECHNOLOGIAS KAI EREVNAS

Net EU contribution

€ 2 000 000,00

Address

N Plastira Str 100 70013 Irakleio Greece №

Region

Ηράκλειο > Κρήτη > Νησιά Αιγαίου

Activity type

Research Organisations

Contact the organisation Website Participation in EU R&I programmes H2020 collaboration network

Non-EU contribution

€ 0,00

Beneficiaries (1)



IDRYMA TECHNOLOGIAS KAI EREVNAS

Greece

Net EU contribution

€ 2 000 000,00

N Plastira Str 100 70013 Irakleio

Region

Ηράκλειο > Κρήτη > Νησιά Αιγαίου

Activity type

Research Organisations

Contact the organisation Website Participation in EU R&I programmes H2020 collaboration network

Non-EU contribution

€ 0,00

EC signature date: 9 June 2020 Last update: 10 March 2022 Record number: 230059

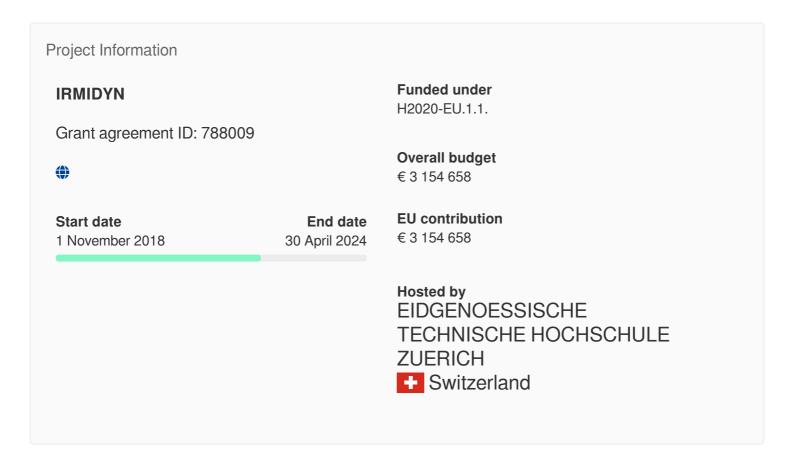
Permalink: https://cordis.europa.eu/project/id/864957





Iron mineral dynamics in redox-affected soils and sediments: Pushing the frontier toward in-situ studies

Fact Sheet



Objective

IRMIDYN will study the dynamics of redox-driven iron mineral transformation processes in soils and sediments and impacts on nutrient and trace element behavior using a novel approach based on enriched stable isotopes (e.g. 57Fe, 33S, 67Zn, 113Cd, 198Hg) in combination with innovative experiments and cutting-edge analytical techniques, most importantly 57Fe Mössbauer and Raman microspectroscopy and imaging. The thermodynamic stability and occurrence of iron minerals in sufficiently stable Earth surface environments is fairly well understood and supported by field observations. However, the kinetics of iron mineral recrystallization and transformation processes under rapidly changing redox conditions is far less

understood, and has to date mostly been studied in in mixed reactors with pure minerals or sediment slurries, but rarely in-situ in complex soils and sediments. Thus, we do not know if and how fast certain iron mineral recrystallization and transformation processes observed in the laboratory actually occur in soils and sediments, and which environmental factors control the transformation rates and products. Redox-driven iron mineral recrystallization and transformation processes are key to understanding the biogeochemical cycles of C, N, P, S, and many trace elements (e.g. As, Zn, Cd, Hg, U). In face of current global challenges caused by massive anthropogenic changes in biogeochemical cycles of nutrients and toxic elements, it is paramount that we begin to understand and quantify the dynamics of these processes in-situ and learn how we can apply our mechanistic (but often reductionist) knowledge to the natural environment. This project will take a large step toward a better understanding of iron mineral dynamics in redox-affected Earth surface environments, with wide implications in biogeochemistry and other fields including environmental engineering, corrosion sciences, archaeology and cultural heritage sciences, and planetary sciences.

Fields of science

engineering and technology > environmental engineering
humanities > history and archaeology > archaeology
natural sciences > earth and related environmental sciences > geochemistry > biogeochemistry

Programme(s)

H2020-EU.1.1. - EXCELLENT SCIENCE - European Research Council (ERC)

Topic(s)

ERC-2017-ADG - ERC Advanced Grant

Call for proposal

ERC-2017-ADG
See other projects for this call

Funding Scheme

ERC-ADG - Advanced Grant

Host institution



EIDGENOESSISCHE TECHNISCHE HOCHSCHULE ZUERICH

Address

Raemistrasse 101 8092 Zuerich



Activity type

Higher or Secondary Education Establishments

Contact the organisation Website H2020 collaboration network

EU contribution

€ 3 154 658

Beneficiaries (1)



EIDGENOESSISCHE TECHNISCHE HOCHSCHULE ZUERICH

Switzerland

EU contribution

€ 3 154 658

Address

Raemistrasse 101 8092 Zuerich

Activity type

Higher or Secondary Education Establishments

Contact the organisation Website H2020 collaboration network

Last update: 4 June 2021 Record number: 216198

Permalink: https://cordis.europa.eu/project/id/788009

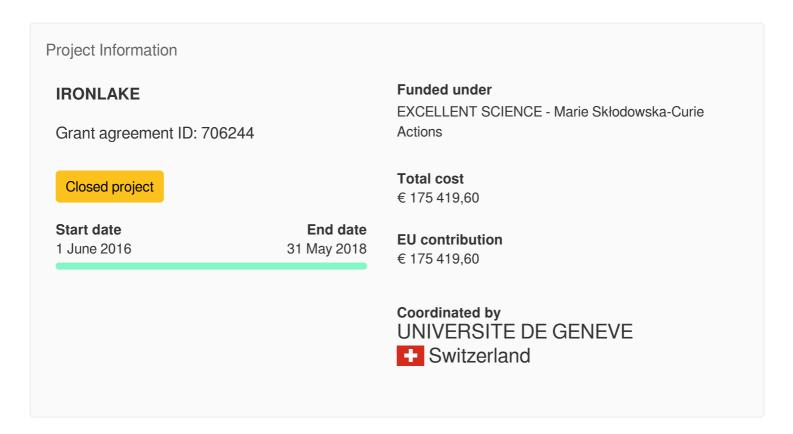
3 of 4





Establishing stable IRON isotopes of laminated LAKE sediments as novel palaeoclimate proxy

Fact Sheet



Objective

Under the pressure of human-induced climate change, it is essential to better understand the past natural climate variability. A broader global coverage of high-resolution palaeoclimatic proxy (indicator) data is urgently needed to improve climate projections and adaptation strategies to changing climate and environmental stress. Laminated lake sediments provide invaluable palaeoclimatic information with up to seasonal resolution. The IRONLAKE project aims to develop the innovative methodology of stable iron isotope measurements of laminated lake sediments as a novel proxy for past changes in temperature and wind. Only recently, first studies have hinted that variations in stable iron isotopes of marine and lake sediments reflect changing redox conditions in oceans and lakes, possibly linked to variations in

past wind and/or temperature. This project aims to test the hypothesis of a redox-climate-relationship mirrored in iron isotopes. The project will be carried out on existing sediment cores from Lago Fagnano (Tierra del Fuego, Argentina) exhibiting characteristic iron-rich laminae that are most suitable for the approach. In a multidisciplinary perspective, a combination of ultrahigh-resolution micro-facies analysis by thin section microscopy and micro-X-ray-fluorescence elemental scanning will be applied to fully understand the general sedimentological and geochemical processes and, specifically, possible seasonal/climatic variations influencing the formation and deposition of iron-bearing minerals in the lake. The gained knowledge will then be linked with mineral-selective iron isotope measurements to infer the sensitivity of stable iron isotopes to capture climatic variations. The interdisciplinary perspective of this project is designed to advance the innovative field of iron isotope geochemistry and to provide a novel wind/temperature proxy to the palaeoclimate and climate modelling communities .

Fields of science

natural sciences > earth and related environmental sciences > geology > sedimentology
natural sciences > earth and related environmental sciences > palaeontology > paleoclimatology
natural sciences > earth and related environmental sciences > geochemistry > isotope geochemistry
natural sciences > biological sciences > ecology > ecosystems
natural sciences > earth and related environmental sciences > atmospheric sciences > climatology >
climatic changes

Programme(s)

H2020-EU.1.3. - EXCELLENT SCIENCE - Marie Skłodowska-Curie Actions

MAIN PROGRAMME

H2020-EU.1.3.2. - Nurturing excellence by means of cross-border and cross-sector mobility

Topic(s)

MSCA-IF-2015-EF - Marie Skłodowska-Curie Individual Fellowships (IF-EF)

Call for proposal

H2020-MSCA-IF-2015

See other projects for this call

Funding Scheme

Coordinator



UNIVERSITE DE GENEVE

Net EU contribution

€ 175 419,60

Address

Rue Du General Dufour 24

1211 Geneve

Switzerland

Region

Schweiz/Suisse/Svizzera > Région lémanique > Genève

Activity type

Higher or Secondary Education Establishments

Contact the organisation Website Participation in EU R&I programmes H2020 collaboration network

Non-EU contribution

€ 0,00

EC signature date: 31 March 2016

Last update: 26 May 2022 Record number: 202426

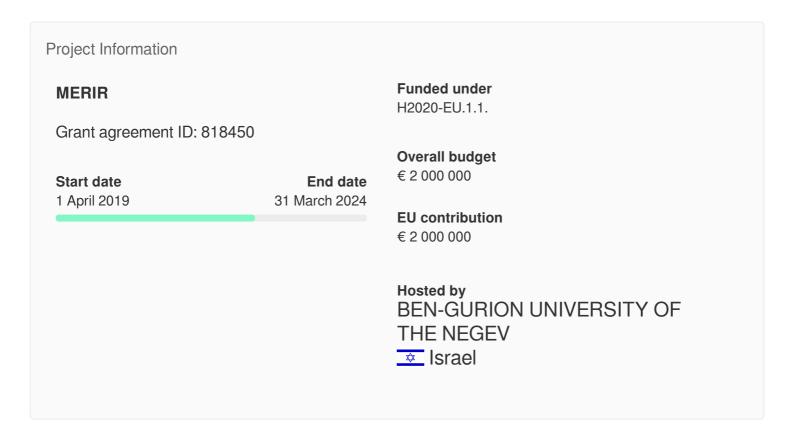
Permalink: https://cordis.europa.eu/project/id/706244





Methane related iron reduction processes in sediments: Hidden couplings and their significance for carbon and iron cycles

Fact Sheet



Objective

About one-third of annual methane (CH4) emissions to the atmosphere originate from natural, nonanthropogenic

sources. However, if all the naturally produced methane actually did reach the atmosphere, its

levels would increase by an order of magnitude, dwarfing anthropogenic CO2 emissions. Fortunately, natural

scavengers of this methane near its production zone limit its release. One of these scavengers, iron (Fe) oxide,

can become a major sink for methane when sulfate concentrations are low. Methane-

iron couplings in

established sediments, however, are poorly understood. Specifically, significant iron oxide reduction has been

observed in many aquatic sediments at depths well below its expected redox zone, where methane is produced

by methanogenesis, often accompanied by decreases in methane concentrations.

These observations challenge

our understandings of iron-methane couplings and microbial players in the deep methanogenic zone and their

impacts on the carbon, iron and other cycles. I aim in the proposed research to elucidate the unexplored

mechanisms of methane-related iron reduction (MERIR) in the methanogenic zone of established

sedimentary profiles under various environmental conditions and their impact on global biogeochemical

cycles. I will resolve two striking yet unexplained phenomena: (1) the active involvement of aerobic

methanotrophs in iron-coupled anaerobic oxidation of methane (AOM), and (2) the unusual reactivity

of iron minerals toward reduction that is accompanied by intensive authigenic magnetite precipitation, and

the effects of this mineralogy change on sedimentary magnetism. My expertise will enable me to achieve the

objectives of this interdisciplinary proposed work using novel approaches from different fields. The project

will likely lead to breakthroughs in our understanding of microbial survival strategies, reveal novel pathways

for aerobic methanotrophs, and change our perspectives on iron mineral reactivities and sedimentary magnetism.

Fields of science

natural sciences > chemical sciences > electrochemistry > electrolysis
natural sciences > earth and related environmental sciences > geology > mineralogy
natural sciences > chemical sciences > organic chemistry > aliphatic compounds

Programme(s)

H2020-EU.1.1. - EXCELLENT SCIENCE - European Research Council (ERC)

Topic(s)

ERC-2018-COG - ERC Consolidator Grant

Call for proposal

ERC-2018-COG
See other projects for this call

Funding Scheme

ERC-COG - Consolidator Grant

Host institution



BEN-GURION UNIVERSITY OF THE NEGEV

Address

84105 Beer Sheva

Activity type

Higher or Secondary Education Establishments

Contact the organisation Website H2020 collaboration network

EU contribution

€ 2 000 000

Beneficiaries (1)



BEN-GURION UNIVERSITY OF THE NEGEV

Israel

EU contribution

€ 2 000 000

Address

84105 Beer Sheva

Activity type

Higher or Secondary Education Establishments

Contact the organisation Website Website H2020 collaboration network

Last update: 24 February 2021

Record number: 221768

Permalink: https://cordis.europa.eu/project/id/818450