Iron as a driver of fibrosis and regeneration

Fact Sheet

Project Information

IRONAGE

Grant agreement ID: 794744

Closed project

Start date
1 April 2018

End date
26 May 2020

Funded under
H2020-EU.1.3.2.

Overall budget
€ 158 121,60

EU contribution
€ 158 121,60

Coordinated by
FUNDACIO INSTITUT DE RECERCA BIOMEDICA (IRB BARCELONA)
Spain

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
Spain

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

iMAC-FUN

Grant agreement ID: 864957

DOI
10.3030/864957

Start date
1 September 2020

End date
31 August 2025

Funded under
EXCELLENT SCIENCE - European Research Council (ERC)

Total cost
€ 2 000 000

EU contribution
€ 2 000 000

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

Address

Address

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

Project Information

IRMIDYN

Grant agreement ID: 788009

Start date
1 November 2018

End date
30 April 2024

Funded under
H2020-EU.1.1.

Overall budget
€ 3 154 658

EU contribution
€ 3 154 658

Hosted by
EIDGENOESSISCHE TECHNISCHE HOCHSCHULE ZUERICH
Switzerland

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 micro-spectroscopy 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
Switzerland

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

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

Fact Sheet

Project Information

IRONLAKE

Grant agreement ID: 706244

Closed project

Start date
1 June 2016

End date
31 May 2018

Funded under
EXCELLENT SCIENCE - Marie Skłodowska-Curie Actions

Total cost
€ 175 419,60

EU contribution
€ 175 419,60

Coordinated by
UNIVERSITE DE GENEVE
Switzerland

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

Project Information

MERIR

Grant agreement ID: 818450

Start date
1 April 2019

End date
31 March 2024

Funded under
H2020-EU.1.1.

Overall budget
€ 2 000 000

EU contribution
€ 2 000 000

Hosted by
BEN-GURION UNIVERSITY OF THE NEGEV
Israel

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
Israel

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

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84105 Beer Sheva

Activity type

Higher or Secondary Education Establishments

Contact the organisation Website

H2020 collaboration network

Last update: 24 February 2021
Record number: 221768

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