

GEMSTONE

1st COST Action Meeting



November 27 – 29, 2019

St Julian's, Malta

MEETING VENUE

Marina Hotel Corinthia
Mistral Conference Hall



COST Action CA18139
GEMSTONE
Genomics of Musculoskeletal
Traits Translational Network



L-Università
ta' Malta



Funded by the Horizon 2020
Framework Programme of the
European Union

COST Action GEMSTONE (CA 18139)

Genomics of Musculoskeletal Traits Translational Network

Chair

Fernando Rivadeneira (The Netherlands)

Vice-Chair

Evangelia Ntzani (Greece)

Project Manager

Fjorda Koromani (The Netherlands)

WG1 'Study populations and expertise groups'

Nerea Alonso (United Kingdom)

Ivan Soldatovic (Serbia)

WG2 'Phenotyping'

Bente Langdahl (Denmark)

Barbara Obermayer-Pietsch (Austria)

WG3 'Monogenic conditions – human KO models'

Outi Mäkitie (Finland)

Melissa Formosa (Malta)

WG4 'Functional investigations'

David Karasik (Israel)

Martina Rauner (Germany)

WG5 'Bioinformatics'

Milana Frenkel-Morgenstern (Israel)

Mikhail Kolev (Bulgaria)

WG6 'Translational Outreach'

Maria Luisa Brandi (Italy)

Claes Ohlsson (Sweden)

STSM Coordinator

Kent S e (Denmark)

Science Communication Manager

Patricia Khashayar (Belgium)

Ines Alv s (Portugal)

Policy Implementation Manager

- **Gender & Age**
Anna Teti (Italy)
- **ITC**
Eirini Agapidaki (Cyprus)
Amina Valjevac (Bosnia & Herzegovina)



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MEETING VENUE & TIME

Mistral Conference Hall
Marina Hotel Corinthia Beach Resort
St George's Bay
St Julian's
Malta

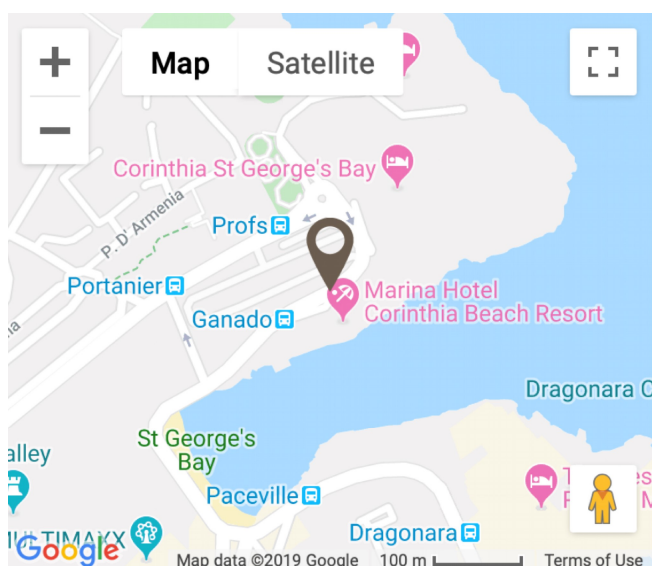
<https://www.marinahotel.com.mt>

Wifi name: MarinaHotel

Wifi username: marina

Wifi password: marina

Wednesday, 27th November	08:30 – 18:30
Thursday, 28th November	08:30 – 18:30
Friday, 29th November	08:30 – 15:00



LOCAL ORGANISER:

Melissa Formosa

email: melissa.m.formosa@um.edu.mt

Phone: +356 9988 0272



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MOVING AROUND IN MALTA

Transfers from Malta International Airport to Hotels:

Public Transport

Public transport is available from Malta International Airport (MIA) via X routes starting at c.05:30hrs with last trip at c.22:30hrs. Updated information regarding timings and routes can be accessed via the following link: <https://www.publictransport.com.mt/en/airport-services>

There are two public transport bus routes that stop in the vicinity of the Marina Hotel Corinthia, 14 (which connects to Valletta) and 120 (which connect to the southern part of Malta). Both can be boarded by waiting on bus-stops 'Profs' and 'Ganado'. For more info re timings and latest info one can access the following links:

Route 14: <https://www.publictransport.com.mt/en/route/14>

Route 120: <https://www.publictransport.com.mt/en/route/120>

More routes may be availed of by walking down to nearby Paceville Centre (c.10 minutes walk from the hotel).

Malta Transfer

A shuttle service offering transfer from Malta airport to hotels, and vice versa for groups or single passengers. Tariffs are fixed and booking can be done online or on site at the airport stand. More information is available from the following link: <https://www.maltatransfer.com>

Taxi Service

Taxi stands are also found at the airport. Taxi service from the Airport is available 24 hours a day to any destination in Malta. Fixed rates are applicable and pre-paid tickets can be purchased from the ticket booth at Arrivals. The fares are usually around 20-25€ to Valletta/Sliema/St Julians. More information is available from the following link: <http://gettinghere.maltairport.com/en/white-taxi.htm>

The hotel also offers a taxi service (please contact the hotel directly for reservation).

There are a number of taxi and car hire companies in Malta and Gozo. Below find suggestions:

ECABS

Tel: (+356) 2138 3838

Web: <http://ecabs.com.mt/>

Percius Car Hire

Tel: (+356) 2144 2530

Web: <http://www.percius.com/>

REM: Taxi is NOT reimbursed by COST unless when public transportation is unavailable, or between 10 pm to 7 am, provided receipt shows the date, time, and amount paid.



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PRACTICAL INFORMATION ABOUT MALTA

Currency

The unit of currency in Malta is the Euro.

Electricity

Electricity supply is 220/240 volts, single phase, 50 cycle. The square fitting standard 3-pin plugs and sockets are used. **PLEASE BRING ADAPTERS FOR YOUR COMPUTERS AND LAPTOPS SINCE A BRITISH STYLE 3-PIN SOCKET IS USED IN MALTA.**

Health

Delegates should ensure that they are covered by adequate medical insurance. Health care in Malta is of a high level conforming to European standards. Mater Dei Hospital is the state hospital situated in Msida, whereas St James Capua is a private hospital.

Language

The national language is Maltese which is a complex derivative of Semitic and Romance languages using a primarily Latin alphabet but also including a number of additional letters which originate in the Arab language. English is also an official language and is widely spoken in Malta and will be the language of the conference.

Culture / Activities

Malta is rich of historical sites, prehistoric temples museums, churches and palaces. Check out <http://heritagemalta.org/> and www.visitmalta.com for more information on sites, activities and opening hours.



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Wednesday 27-11-2019

Scientific Program – Blazing the trail!

- 8:00 – 8:30: **Registration**
- 8:30 – 9:30: **Welcome & Introductions**
- 8:30: Fernando Rivadeneira
 - 9:00: Minister for Health Hon. Mr Chris Fearn
 - 9:10: Janet Mifsud (COST Country National Coordinator)
 - 9:20: Melissa Formosa (Chair Organising Committee)
- 9:30 – 10:45: **A glimpse to osteoporosis care in the year 2030**
Chair: André Uitterlinden
- 9:30: An Epidemiological & Clinical Perspective (John Kanis)
 - 10:00: A Genomics Perspective (Emma Duncan)
 - 10:30 – 10:45: Q/A with both speakers
- 10:45 – 11:00: **Coffee break**
- 11:00 – 12:15: **A glimpse to Fundamental -omics research in the year 2030: Models of skeletal function & disease**
Chair: Martina Rauner
- 11:00: From cells to organisms (Anna Teti)
 - 11:30: Technological innovations (Ralph Muller)
 - 12:00 – 12:15: Q/A with both speakers
- 12:15 – 13:45: **Lunch**
- 13:45 – 15:00: **Phenotype definition in monogenic & complex diseases**
Chair: Barbara Obermayer-Pietsch
- 13:45: Phenotypic landscape of patients with fragility fractures: past & future (Outi Mäkitie)
 - 14:15: Findings from GWAs in the era of large biobanks: Have we reached a plateau yet? (Vangelis Evangelou)
 - 14:45 – 15:00: Q/A with both speakers

Wednesday 27-11-2019 (cont.)

- 15:00 – 15:45: **Back to the future of GEMSTONE in 2020 – Current challenges**
Chair: Evangelia Ntzani
- 15:00: Machine learning approaches in biomedical research (AI) (Gennady Roshchupkin)
 - 15:30: From GWAS signals to gene and function (Vincenzo Forgetta)
 - 16:00 – 16:15: Q/A with both speakers
- 16:15 – 16:30: **Coffee break**
- 16:30 – 18:15: **Translational outreach of genomic discoveries – Perspectives**
Chair: Maria Luisa Brandi
- 16:30: Needs and expectations of patients (Ines Alvês)
 - 17:00: Translational approach to identify novel targets for cortical bone (Claes Ohlsson)
 - 17:30: Tailoring treatments and novel indications (repositioning) (Karol Estrada)
 - 18:00 – 18:15: Q/A with all three speakers
- 18:15 – 18:30: **Closing**
- 18:40 – 22:00: **Social Event**
Guided Tour of Valletta, Capital City, Malta (Duration: 1 hour)
Dinner on own
Transport to be provided to & from Valletta



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Thursday 28-11-2019

GEMSTONE Training School

8:30 – 09:30: **Managing Big Data** (Fjorda Koromani)

Overview: The field of complex traits has been revolutionized by the advent of genome-wide association studies (GWAS). The musculoskeletal field is no exception, with the discovery of several hundreds of loci influencing BMD and other musculoskeletal traits. An increasing number of GWAS with huge sample sizes (hundreds of thousands) are emerging, making their meta-analysis results publicly available. This means that: 1) the number of discoveries will increase dramatically; 2) these data will be widely and readily available to researchers for performing functional follow-up evaluations. In this practical, we will use real GWAS results as an example of the wealth of data-mining possibilities able to be applied across selected candidate genomic regions.

Learning Objective: Learn how to manage large files and grasp the use of Linux commands to browse, lookup and filter results.

Target Audience: Researchers working with large data files.

Requirements: Each participant should bring their own laptop, as the session will be hands-on.

09:30 – 09:45: **Coffee Break**

09:45 – 11:30: **FUMA, GWAS ATLAS & the Musculoskeletal Knowledge Portal** (Katerina Trajanoska)

Overview: After performing a genome-wide association study (GWAS), we would like to link the identified SNPs to biological pathways or druggable genes. However, the significant disease-associated SNPs are often not necessarily causal. Nevertheless, we can pinpoint the potential causal gene(s) in the identified loci by combining functional information across several tools, resources and repositories such as, the 1000 Genomes, ANNOVAR, CAAD, Genotype-Tissue Expression (GTEx), Encyclopedia of DNA Elements (ENCODE), Roadmap Epigenomics Project, or chromatin interaction information. This workshop will show tools to browse, screen, annotate and visualize GWAS summary statistics.

Learning objectives: Provide an oversight of the different possibilities offered by:

- a) FUMA: which integrates different web-resources to annotate, prioritize, visualize and interpret GWAS results.
- b) GWAS atlas: which contains summary statistics of hundreds of GWASs and provides information on SNP-based heritability and genetic correlation.
- c) Musculoskeletal Knowledge Portal: which enables browsing, searching, and analysis of human genetic and genomic information linked to musculoskeletal traits and diseases.

Target Audience: The workshop is recommended for students, scientists, and clinicians interested in data mining and database use.

Requirements: Participants are required to bring their own laptops for the practical hands-on portions of the workshop. FUMA account is highly recommended (<https://fuma.ctglab.nl/>).

11:30 – 12:45: **How do I know if my variant is pathogenic? – An overview of variant annotation databases (including GeneMatcher and VariantMatcher)**
(Anders Kampe)

Overview: Next generation sequencing has exploded in recent years, it is now both quick and cheap (at least relatively cheap) to sequence a whole genome or whole exome in a patient. At Karolinska Hospital, Stockholm, Sweden, whole genome sequencing has now also moved into the clinic and can almost be considered a routine analysis. However, we still lack knowledge how to interpret all these sequenced variants. The workshop aims to present some of the tools and databases that can be of help, both in a research setting and in a clinical setting.

Content: The workshop will feature two parts: Part 1 will be a regular “PowerPoint introduction” and aims to give the attendants an introduction to the topic. Part 2 will be an interactive session. The idea is to have a few cases for the attendants to solve / that we will solve together.

Target Audience: Individuals both in the research field and in the clinical field. The hope for this workshop is that it will be interesting for anyone with an interest in human genetics and monogenic disorders.

Requirements: Participants should bring their own computers. No special skills / computer knowledge are required.

12:45 – 13:30: **LUNCH**

13:30 – 15:00: **Advancing the Use of Zebrafish for Skeletal Genetic Research**
(David Karasik & Erika Kague)

Content overview: GWAS have identified a high number of genetic variants associated with skeletal conditions. The functional evaluation of these variants is laborious and time-consuming. The zebrafish has emerged as a powerful model system for the study of vertebrate development and disease, drug and genetic screening. This workshop will introduce zebrafish as a model system with focus in bone and cartilage and the most common techniques used to address gene expression and function in zebrafish. Examples of zebrafish mutants for osteoporosis candidate genes will be demonstrated at the practical sections. Finally, this workshop will show tools that could serve as a rapid functional screening of candidate genes.

The mission of GEMSTONE WG₄ is to bring clinically-oriented researchers together with skeletal biologists to solve the mechanistic aspects of the recent genomics discoveries relevant to skeletal diseases. Through this workshop, researchers will have the opportunity to discuss foundations and the possibility of using zebrafish to meet their current research goals.

Target audience: This workshop is suggested to anyone interested in learning about zebrafish as an animal model for functional skeletal studies. Clinicians, biologists and geneticists at any level of their career are welcome.

Objectives: Participants should get

- A overview of the advantages/limitations to using fish for modelling skeletal diseases
- A better knowledge of the possibility to use fish in preclinical/translational studies
- Familiarization with zebrafish genome editing techniques and available tools for musculoskeletal characterization (including bone regeneration)

15:00 – 16:00: **Understanding patient phenotyping in musculoskeletal diseases**
(Barbara Obermayer-Pietsch)

Overview: Patient cohorts are indispensable components of translational musculoskeletal research. Many technical approaches are used, including patient medical history and examination, imaging techniques from dual-energy-X-ray-absorptiometry (DXA), magnetic resonance imaging (MRI) to bone ultrasound, bone scintigraphy and computed tomography (CT, including high-resolution peripheral quantitative CT (HRpQCT)) to bone biopsies (histology, static and dynamic histomorphometry, immunohistochemistry and gene expression patterns) and a large panel of systemic biochemical measurements in serum and urine, including parameters of bone formation and resorption and calciotropic hormones, genetic and epigenetic measurements.

The mission of GEMSTONE WG2 is to support and harmonize patient-oriented phenotyping approaches, data mining and protection, general musculoskeletal health issues and health economy topics, research agendas and prospective data generation. We expect an increased understanding of either patient-related research issues or a comprehensive networking of clinical and non-clinical researchers in this area.

Target audience: This workshop is mandatory for clinical researchers, but also for non-clinical scientists to understand approaches in patient phenotyping and research.

Objectives: Participants should get:

- An overview of current examination and testing techniques in clinical patients, and their follow-up
- An involvement in strengths and limitations of patient-derived data for translational research as well as patient data protection
- A better understanding of areas of standardisation and harmonisation in patient phenotyping
- Potential links to and networking with other important areas of musculoskeletal research

16:00 – 16:15: **Coffee break**

16:15 – 17:30: **Machine learning and deep learning algorithms in biomedicine**
(Gennady Roshchupkin)

Overview: Comprehensive molecular and clinical datasets including complete human genomes, gene expression profiles, high-resolution imaging, metabolomics, electronic medical records increased the mechanistic understanding of genome biology to an incredible degree. Connecting genotype to phenotype, predicting regulatory function and linking together multi-omics datasets are all areas in which harnessing the vast information from a large number of individuals can lead to new insights. However, working with large datasets is challenging from data analysis as well as from methodological point of views. Therefore, new and innovative approaches are needed to enrich understanding of basic biology and connections to disease. Machine learning and deep learning approaches become more and more popular for mining relevant information from large datasets. The aim of this workshop is to introduce these methods to the participants and teach them how they can apply them in their own research practice.

Objectives:

- Introduce machine learning algorithms
- Teach how to build simple neural networks
- Apply neural networks to genomics data

Requirements: Basic knowledge of python, a laptop, and a gmail account.

17:30 – 18:30: **What's a polygenic risk score and how it's made**
(Vincenzo Forgetta)

Overview: Polygenic risk scores are risk scores that capture information from natural variation in our entire genome. They study nearly all common genetic variation in the human genome extracting information on genetic variants which are associated with diseases, through two steps:

- First, they identify variation in the genome that is associated with risk of disease.
- Second, they combine information across all the associated genomic regions to generate a summary risk score per individual. This risk score is then tested to see if it can predict risk of diseases.

However, in addition to predicting diseases, polygenic risk scores can also predict medically relevant risk factors such as plasma cholesterol levels and bone density measurements. Predicting medically relevant risk factors can be useful in the clinic because it can highlight individuals who should undergo further testing—but they can also identify individuals who may not need further testing, because their genetic risk is low.

Objectives:

- Describe the motivation for, and design of, a polygenic risk score for bone-density.
- Demonstrate how to design a polygenic risk score for bone-density using UK Biobank.

Target Audience: Introductory level. Analysis details will be provided in slides as guidance for trainees to use in their own research.

Thursday 28-11-2019 (cont.)

18:45 – 23:00:

Social Event

Guided Tour of Mdina (Duration 1 hour) followed by dinner at Palazzo de Piro

Dinner at 20.15

Price €35

Transport to be provided to & from Mdina



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Friday 29-11-2019

Management Committee & Working Group Meetings

(N.B. Concurrent sessions to be held in different rooms)

08:30 – 10:30:	Management Committee meeting (Mistral Conference Room; Marina Hotel Corinthia)
10:30 – 11:00:	Coffee break
11:00 – 12:30:	WG2 (Mistral Conference Room; Marina Hotel Corinthia) WG3 (Gardjola I; Corinthia St George's Bay Hotel) WG5 (Gardjola II; Corinthia St George's Bay Hotel)
12:30 – 13:30:	LUNCH
13:30 – 15:00:	WG1 (Mistral Conference Room; Marina Hotel Corinthia) WG4 (Gardjola I; Corinthia St George's Bay Hotel) WG6 (Gardjola II; Corinthia St George's Bay Hotel)
15:00:	Closing



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