

### General Information

**Project title**

Sarcoma subtyping and stratification using genome-wide epigenetic profiling

**Project acronym**

EpiNanSarc

**Duration of project (months)**

36

**List of Partners:**

Silvestro Conticello, Italy  
Andrea De Vita, Italy  
Aviad Zick, Israel  
Atocha Romero, Spain  
Anca Zgura, Romania  
Kazim Yalçın Arga, Turkiye

**Publishable Project Abstract**

Background, rationale

Sarcoma subtyping is crucial for determining the prognosis of the disease, as it helps predict how rapidly the cancer will grow and spread. While several diagnostic tools exist to support subtyping and patient classification, a high inter-observer variability makes their classification harder, with 15-20% of cases remaining unclassified.

Molecular analyses greatly improve classification by detecting typical genetic alterations and, recently, a methylation-based classifier has been shown to be capable of reliably classifying most sarcoma subtypes. Yet, this approach cannot be easily translated into routine diagnostics and comprehensive molecular analysis requires access to several analytical tools - not always available, especially in smaller hospitals.

Oxford Nanopore Technologies (ONT) sequencing is a competitive platform in terms of sample handling and instrumental costs. We have shown that ONT sequencing can detect multiple genome-wide genetic/epigenetic tumor DNA features from a single assay.

Hypothesis

Our hypothesis is that comprehensive genome-wide characterization of sarcomas using ONT sequencing will result in enhanced patient stratification.

Aims

Main aim of the project is to validate methylation-profiling by ONT sequencing as a viable alternative to more complex approaches. Additionally, we will develop multi-modal analysis to correlate epigenetic (methylation levels, specific alterations), genetic (CNAs, structural variants, signatures of CNAs, mutational signatures), and clinical features with treatment outcomes and evolution of the disease.

Methods

A retrospective and a prospective study will be carried out on tumor tissues (WP1), tumor-derived cell lines (WP2), and liquid biopsy (WP3). ONT sequencing will be performed on the various samples to extract genome-wide methylation profiles. Additional epigenetic/genetic features will be extracted as well. A multi-modal Machine Learning model will be trained based on all these features for sarcoma subtype classification and patient stratification.

Expected results and potential impact

We expect that our methylation profiling via ONT sequencing will match or improve other subtyping approaches, and that this novel approach will facilitate more effective and streamlined diagnostic management for sarcoma patients, ultimately leading to improved outcomes.

**Project Coordinator**

**Last name**  
Conticello

**Sex**  
male

**Date of birth**  
14-08-1971

**Institute**  
Istituto per lo Studio, la Prevenzione e la Rete Oncologica (ISPRO)

**Department**  
Core Research Laboratory

**Zip code**  
50139

**Phone number**  
+39 055 7944565

**Country**  
Italy

**Personnel €**  
90,000

**Equipment €**  
-

**Travel €**  
6,000

**Other direct costs €**  
6,000

**Total requested budget €**  
299,992

**First name**  
Silvestro

**Title**  
Dr

**Organisation legal name**  
Istituto per lo Studio, la Prevenzione e la Rete Oncologica (ISPRO)

**Type of entity (tick as appropriate)**  
Clinical or Public Health

**Street, No.**  
Via Cosimo il Vecchio 2

**City**  
Firenze

**eMail**  
s.conticello@ispro.toscana.it

**Funding organization to which you apply**  
Tuscany Region (TuscReg), Tuscany, Italy

**Consumables €**  
164,720

**Study/Clinical trial €**  
-

**Capacity building €**  
6,000

**Overheads €**  
27,272

**Project Partners (1/5)**

<b>Last name</b> De Vita	<b>First name</b> Alessandro
<b>Sex</b> male	<b>Title</b> Dr
<b>Date of birth</b> 14-11-1985	<b>Organisation legal name</b> IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori"
<b>Institute</b> IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori"	<b>Type of entity</b> Clinical or Public Health
<b>Department</b> Preclinic and Osteoncology Unit, Biosciences Laboratory	<b>Street, No.</b> Via Piero Maroncelli, 40
<b>Zip code</b> 47014	<b>City</b> Meldola
<b>Phone number</b> +39 0543 739239	<b>eMail</b> alessandro.devita@irst.emr.it
<b>Country</b> Italy	<b>Funding organization to which the partner applies</b> Ministry of Health (IT-MOH), Italy
<b>Personnel €</b> 200,000	<b>Consumables €</b> 148,000
<b>Equipment €</b> -	<b>Study/Clinical trial €</b> -
<b>Travel €</b> 12,000	<b>Capacity building €</b> -
<b>Other direct costs €</b> -	<b>Overheads €</b> 40,000
<b>Total requested budget €</b> 400,000	

**Project Partners (2/5)**

<b>Last name</b> Zick	<b>First name</b> Aviad
<b>Sex</b> male	<b>Title</b> Dr
<b>Date of birth</b> 21-01-1974	<b>Organisation legal name</b> Hebrew University, Hadassah Medical Center
<b>Institute</b> Sharett institute	<b>Type of entity</b> Academia Clinical or Public Health
<b>Department</b> Oncology Department	<b>Street, No.</b> ,Kalman Ya'akov Man St, Jerusalem,1
<b>Zip code</b> 91120	<b>City</b> Jerusalem
<b>Phone number</b> +972 50 404-8024	<b>eMail</b> aviadz@hadassah.org.il
<b>Country</b> Israel	<b>Funding organization to which the partner applies</b> The Chief Scientist Office of the Ministry of Health (CSO-MOH), Israel
<b>Personnel €</b> 97,750	<b>Consumables €</b> 27,023
<b>Equipment €</b> -	<b>Study/Clinical trial €</b> -
<b>Travel €</b> 2,500	<b>Capacity building €</b> -
<b>Other direct costs €</b> -	<b>Overheads €</b> 12,727
<b>Total requested budget €</b> 140,000	

**Project Partners (3/5)**

<p><b>Last name</b> Romero</p> <p><b>Sex</b> female</p> <p><b>Date of birth</b> 05-01-1979</p> <p><b>Institute</b> FUNDACION DE INVESTIGACION HOSPITAL UNIVERSITARIO PUERTA DE HIERRO</p> <p><b>Department</b> FUNDACION DE INVESTIGACION HOSPITAL UNIVERSITARIO PUERTA DE HIERRO</p> <p><b>Zip code</b> 28222</p> <p><b>Phone number</b> +3463452 4396</p> <p><b>Country</b> Spain</p> <p><b>Personnel €</b> 62,000</p> <p><b>Equipment €</b> -</p> <p><b>Travel €</b> 3,000</p> <p><b>Other direct costs €</b> -</p> <p><b>Total requested budget €</b> 174,820</p>	<p><b>First name</b> Atocha</p> <p><b>Title</b> Dr</p> <p><b>Organisation legal name</b> Hospital Universitario Puerta del Hierro</p> <p><b>Type of entity</b> Academia Clinical or Public Health</p> <p><b>Street, No.</b> Joaquín Rodrigo 1</p> <p><b>City</b> Madrid</p> <p><b>eMail</b> atocha10@hotmail.com</p> <p><b>Funding organization to which the partner applies</b> National Institute of Health Carlos III (ISCIII) AND The Scientific Foundation of the Spanish Association Against Cancer (FCAECC), Spain</p> <p><b>Consumables €</b> 80,000</p> <p><b>Study/Clinical trial €</b> -</p> <p><b>Capacity building €</b> -</p> <p><b>Overheads €</b> 29,820</p>
-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

**Project Partners (4/5)**

<b>Last name</b> Zgura	<b>First name</b> Anca Florina
<b>Sex</b> female	<b>Title</b> Dr
<b>Date of birth</b> 28-11-1985	<b>Organisation legal name</b> Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
<b>Institute</b> Faculty of General Medicine Oncofort	<b>Type of entity</b> Academia Clinical or Public Health
<b>Department</b> Department of Oncology-Radiotherapy, Prof. Dr. Alexandru Trestioreanu Institute of Oncology	<b>Street, No.</b> Dionisie Lupu Street, no. 37, Sector 2
<b>Zip code</b> 077190	<b>City</b> Bucharest
<b>Phone number</b> +40751110005	<b>eMail</b> medianca@gmail.com
<b>Country</b> Romania	<b>Funding organization to which the partner applies</b> Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI), Romania
<b>Personnel €</b> 132,300	<b>Consumables €</b> 42,840
<b>Equipment €</b> -	<b>Study/Clinical trial €</b> -
<b>Travel €</b> 11,900	<b>Capacity building €</b> -
<b>Other direct costs €</b> 12,959	<b>Overheads €</b> -
<b>Total requested budget €</b> 199,999	

**Project Partners (5/5)**

<b>Last name</b> Yalçın Arga	<b>First name</b> Kazım
<b>Sex</b> male	<b>Title</b> Prof
<b>Date of birth</b> 19-01-1980	<b>Organisation legal name</b> Marmara University
<b>Institute</b> Marmara University	<b>Type of entity</b> Academia
<b>Department</b> Department of Bioengineering	<b>Street, No.</b> Aydınevler Mah
<b>Zip code</b> 34854	<b>City</b> Maltepe
<b>Phone number</b> 0090 216 7773570	<b>eMail</b> kazim.arga@marmara.edu.tr
<b>Country</b> Türkiye	<b>Funding organization to which the partner applies</b> The Scientific and Technological Research Council of Türkiye (TÜBİTAK), Türkiye
<b>Personnel €</b> 28,000	<b>Consumables €</b> -
<b>Equipment €</b> -	<b>Study/Clinical trial €</b> -
<b>Travel €</b> 5,350	<b>Capacity building €</b> -
<b>Other direct costs €</b> -	<b>Overheads €</b> 20,545
<b>Total requested budget €</b> 53,895	

### Financial plan

**Project Coordinator**

	Personnel €	Consumables €	Equipment €	Study/Clinical trial €	Travel €	Capacity building €	Other direct costs €	Overheads €	Total costs (EUR)	Requested funds (EUR)
Istituto per lo Studio, la Prevenzione e la Rete Oncologica (ISPRO)	90,000	164,720	0	0	6,000	6,000	6,000	27,272	299,992	299,992
	<b>90,000</b>	<b>164,720</b>	<b>0</b>	<b>0</b>	<b>6,000</b>	<b>6,000</b>	<b>6,000</b>	<b>27,272</b>	<b>299,992</b>	<b>299,992</b>

**Project Partners**

	Personnel €	Consumables €	Equipment €	Study/Clinical trial €	Travel €	Capacity building €	Other direct costs €	Overheads €	Total costs (EUR)	Requested funds (EUR)
IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori"	200,000	148,000	0	0	12,000	0	0	40,000	400,000	400,000
Hebrew University, Hadassah Medical Center	97,750	27,023	0	0	2,500	0	0	12,727	140,000	140,000
Hospital Universitario Puerta del Hierro	62,000	80,000	0	0	3,000	0	0	29,820	174,820	174,820
Carol Davila University of Medicine and Pharmacy, Bucharest, Romania	132,300	42,840	0	0	11,900	0	12,959	0	199,999	199,999
Marmara University	28,000	0	0	0	5,350	0	0	20,545	53,895	53,895
	<b>520,050</b>	<b>297,863</b>	<b>0</b>	<b>0</b>	<b>34,750</b>	<b>0</b>	<b>12,959</b>	<b>103,092</b>	<b>968,714</b>	<b>968,714</b>

Total costs	Requested funds
1,268,706 €	1,268,706 €