

ÁREA: CÁNCER

Grupos:

Grupo de Anatomía Patológica

Responsables: Federico Rojo Todo
Miguel Ángel Piris Pinilla (hasta 31/01/2023)
María Socorro Rodríguez Pinilla

IPs: Luis Requena Caballero
Laura Úrsula Tomás Roca

Investigación: Básica, Traslacional y Clínica

Grupo de Oncología Médica

Responsables: Manuel Dómine Gómez
Jesús García-Foncillas
Javier Zenón Martín Broto

IPs: María Arantzazu Cebrián Aranda (Co-IP)

Investigación: Básica y Clínica

Grupo de Hematología

Responsable: M^a Pilar Llamas Sillero

IPs: Raul Córdoba Mascuñano
Araceli Beatriz Martín Antonio

Investigación: Básica y Clínica

Grupos Asociados

Grupo de Cirugía General, Torácica, Neurocirugía y otras

Responsables: Ángel Celdrán Uriarte
Ricardo Díez Valle
Ignacio Muguruza Trueba
José Julio Zapatero Gaviria

Investigación: Clínica

Grupo de Oncología Radioterápica

Responsable: Ignacio Azinovic Gamo

Investigación: Clínica

VI REUNIÓN ANUAL DEL ÁREA DE CÁNCER DEL IIS-FJD
19 de junio del 2024

Preclinical rationale for the development of new therapeutic opportunities for sarcoma patients

David S. Moura

**Javier Martin-Broto laboratory
(ATBSarc)**

**Instituto de Investigación Sanitaria
de la Fundación Jimenez Diaz
(IIS-FJD)**

dmoura@atbsarc.org

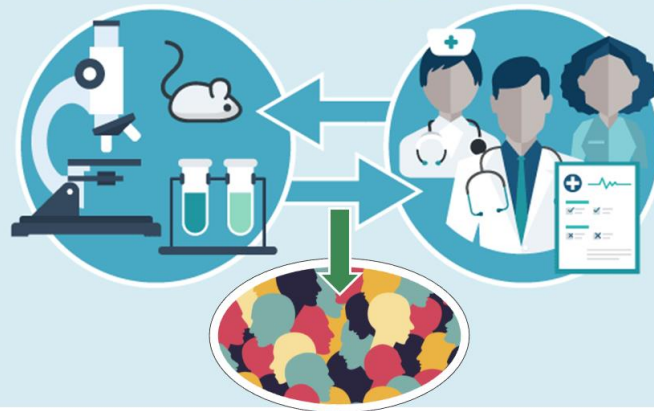
TRANSLATIONAL RESEARCH APPLIED TO MEDICINE

Laboratory:

- New drugs
- Drug combinations
- Predictive biomarkers
- Diagnostic tools
- Follow-up markers
- Etc.

Bench to the bedside

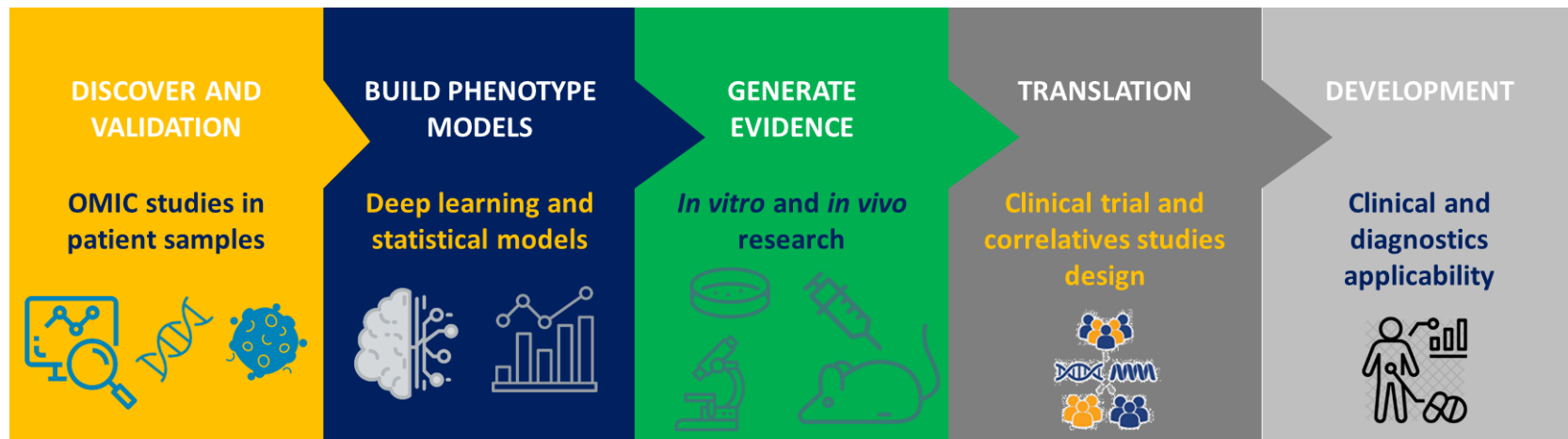
Bedside to the bench



Clinic

- Observations taken by the physician
- Omic studies applied to human samples
- Etc.

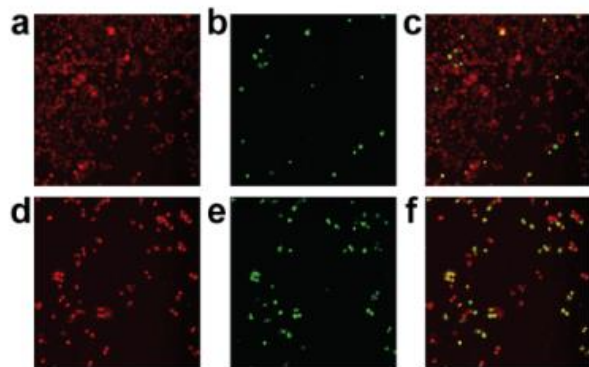
KEY STEPS IN DEVELOPING NEW THERAPIES AND PREDICTIVE BIOMARKERS FOR SARCOMA PATIENTS



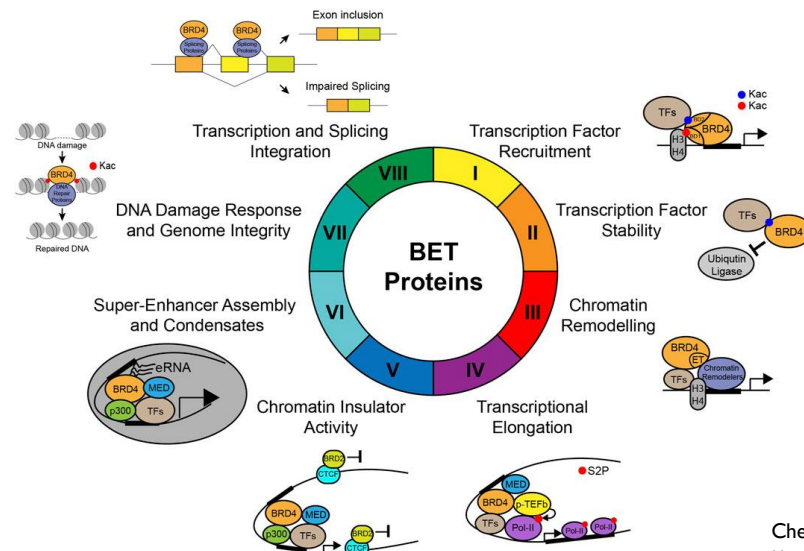
FROM BENCH TO BEDSIDE

Primary High-Throughput Screen (HTS)*

- 2,600 known and experimental drugs



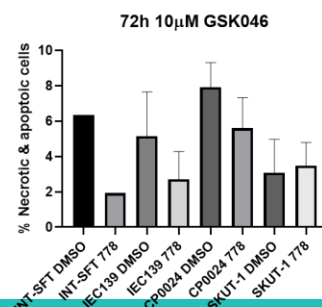
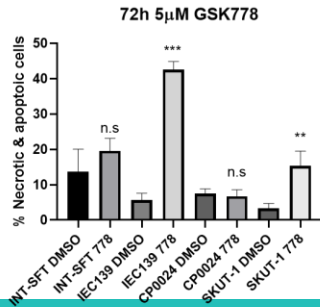
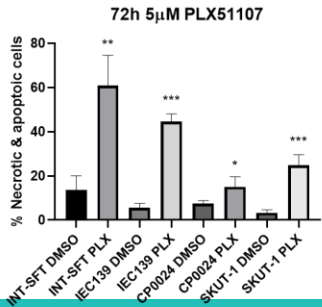
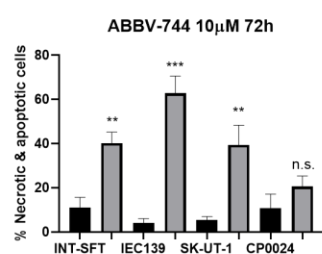
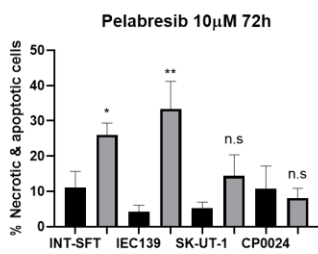
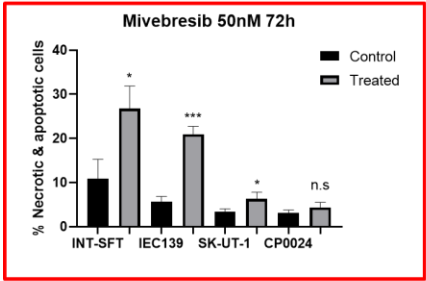
The bromodomain and extraterminal domain (BET) family of proteins consists of four conserved mammalian members (BRD2, BRD3, BRD4, and BRDT) that regulate the expression of many genes and pathways at epigenetic level.



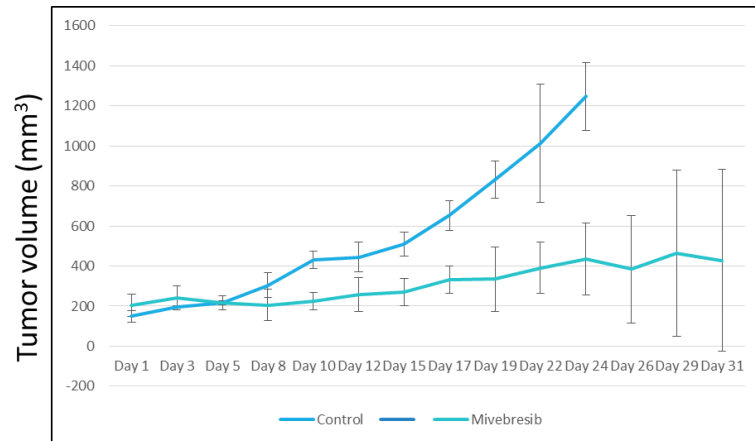
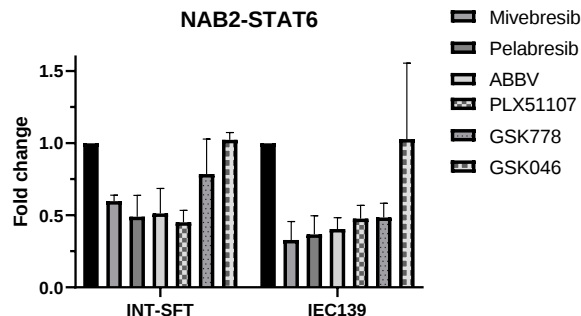
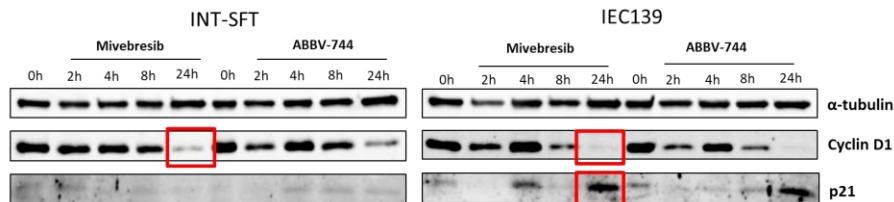
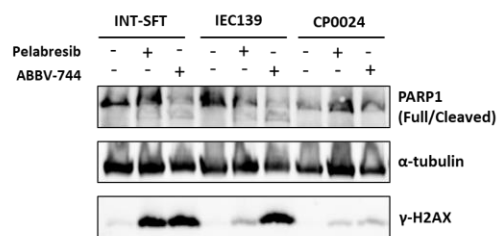
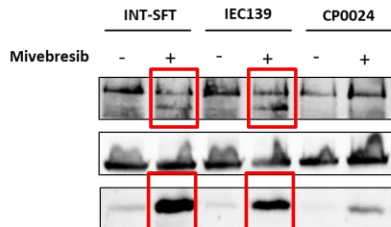
Cheung KL et al. (2021)
Hayenga et al.

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	Pan-BET	Inh BRD2/4	Inh BD2	Pan-BET	Inh BD1	Inh BD2
IC50 (uM)	Mivebresib	Pelabresib	ABBV-744	PLX51107	GSK778	GSK046
INT-SFT	0.00052	1.033	27.57	0.7292	20.71	NC
IEC139	0.00191	2.306	7.514	1.203	24.93	NC
SKUT-1	0.0286	2.576	33.74	0.800	12.72	NC
CP0024	0.1235	NC	NC	27.82	15.99	NC



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BDR4-BD1 / BDR4-BD2

	ΔGprediction Kcal/mol
BD1_BMS	-8,24
BD1_MIV	-6,50
BD1_MM1	-8,02
BD1_MM2	-8,72
BD2_BMS	-8,10
BD2_MIV	-6,50
BD2_MM1	-7,98
BD2_MM2	-8,54

 "la Caixa" Foundation

CaixaImpulse
Health Innovation Call 2024

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 Universidad Autónoma de Madrid

 Hospital Universitario Fundación Jiménez Díaz
Grupo Quirónsalud

 INSTITUTO DE INVESTIGACIÓN SANITARIA FUNDACIÓN JIMÉNEZ DÍAZ

Cancer Letters 473 (2020) 186–197



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journal homepage: www.elsevier.com/locate/canlet



Original Articles

The CLK inhibitor SM08502 induces anti-tumor activity and reduces Wnt pathway gene expression in gastrointestinal cancer models

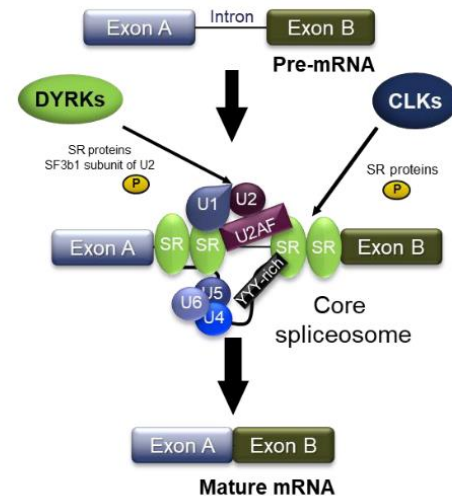
Betty Y. Tam^a, Kevin Chiu^b, Heekyung Chung^b, Carine Bossard^b, John Duc Nguyen^a, Emily Creger^b, Brian W. Eastman^b, Chi Ching Mak^b, Maureen Ibanez^b, Abdullah Ghias^b, Joseph Cahiwat^b, Long Do^b, Shawn Cho^b, Jackie Nguyen^b, Vishal Deshmukh^b, Josh Stewart^b, Chiao-Wen Chen^b, Charlene Barroga^b, Luis Dellamary^a, Sunil K. KC^b, Timothy J. Phalen^b, John Hood^a, Steven Cha^b, Yusuf Yazici^{b,*}

^a Formerly Samumed, LLC, CA, USA

^b Samumed, LLC, San Diego, CA, USA



Alternative Splicing (AS)



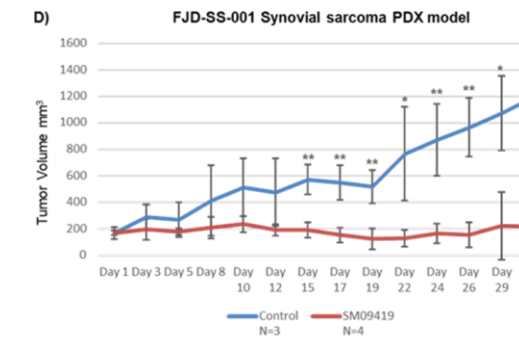
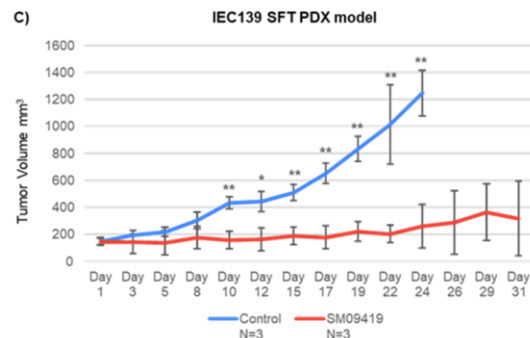
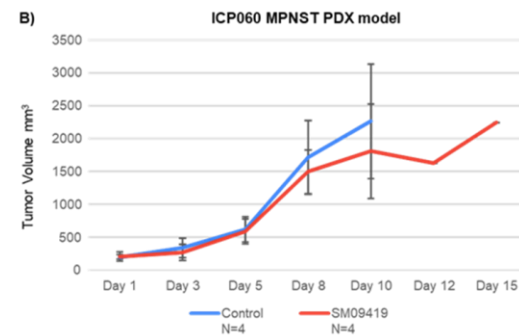
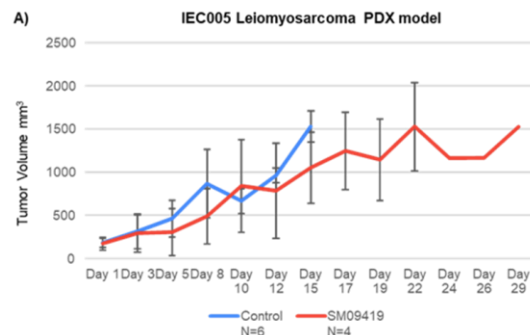
Adapted from Biamonti, et al. 2019.

SR: SRSF (serine/arginine-rich splicing factor)

*CLK: cdc2-like kinase

ÁREA: CÁNCER

Cell Line	Subtype	SM09419 IC ₅₀ (nM)
AA	Leiomyosarcoma	247.7
CP0024	Leiomyosarcoma	175.2
IEC005	Leiomyosarcoma	190.2
SK-UT-1	Leiomyosarcoma	29.8
93T449	Liposarcoma	116.3
IEC139	Solitary fibrous tumor	313.1
INT-SFT	Solitary fibrous tumor	407.9
MCP037	Synovial sarcoma	9000 (9.0 µM)
SW982	Synovial sarcoma	80.5
MCP016	UPS	2120 (21.2 µM)
MCP021	UPS	1700 (1.7 µM)
MCP025	UPS	5000 (5.0 µM)
A4573	Ewing sarcoma	58.7
A673	Ewing sarcoma	41.8
CADO-ESI	Ewing sarcoma	88.2
MHH-ESI	Ewing sarcoma	88.3
RDES	Ewing sarcoma	69.4
SK-PN-DW	Ewing sarcoma	81.7
SKES	Ewing sarcoma	68.7
SKNMC	Ewing sarcoma	70.7
TC71	Ewing sarcoma	103.4
1765-92	Myxoid liposarcoma	141.5
402-91	Myxoid liposarcoma	106.1
SAOS	Osteosarcoma	77.47
U2OS	Osteosarcoma	116.1
MG63	Osteosarcoma	178.3
IEC036	Osteosarcoma	452.2



SELNET-07-02: PHASE II CLINICAL TRIAL OF CIRTUVIVINT IN SECOND LINES OF
SELECTED ADVANCED SOFT-TISSUE SARCOMAS



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19 de junio del 2024

UAM Universidad Autónoma de Madrid

Fundación Jiménez Díaz
Grupo Quirónsalud

IIS FJD
INSTITUTO DE INVESTIGACIÓN SANITARIA FUNDACIÓN JIMÉNEZ DÍAZ

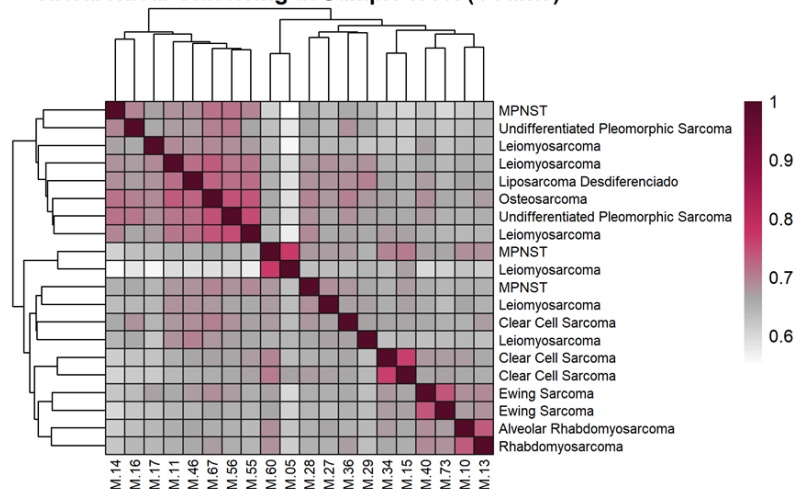
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Subtype	N=34
Adamantinoma	1
Alveolar soft-part sarcoma	2
Chondrosarcoma	1
Clear Cell Sarcoma	2
DD Liposarcoma	1
Epithelioid Sarcoma	1
Ewing Sarcoma	4
GIST	2
Leiomyosarcoma	5
MPNST	2
Myxoid Liposarcoma	1
Myxofibrosarcoma	2
Osteosarcoma	2
Rhabdomyosarcoma	3
Sclerosing Epithelioid Fibrosarcoma	1
Solitary Fibrous Tumor	1
Synovial Sarcoma	1
Undifferentiated pleomorphic sarcoma	2

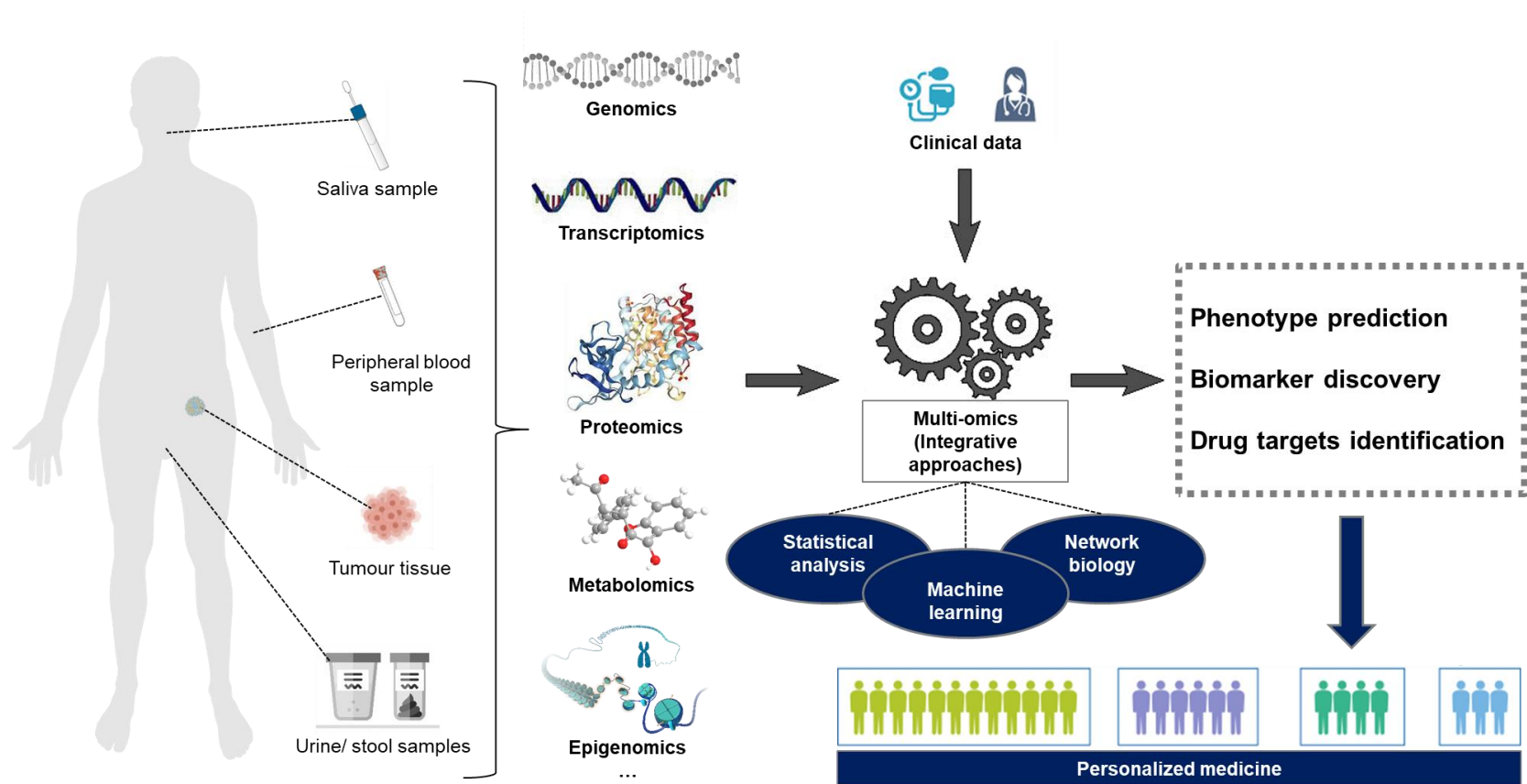
Characterization (18/34):

1. RNA-Seq
2. Whole exome sequencing

Hierarchical Clustering at Sample-level (Counts)



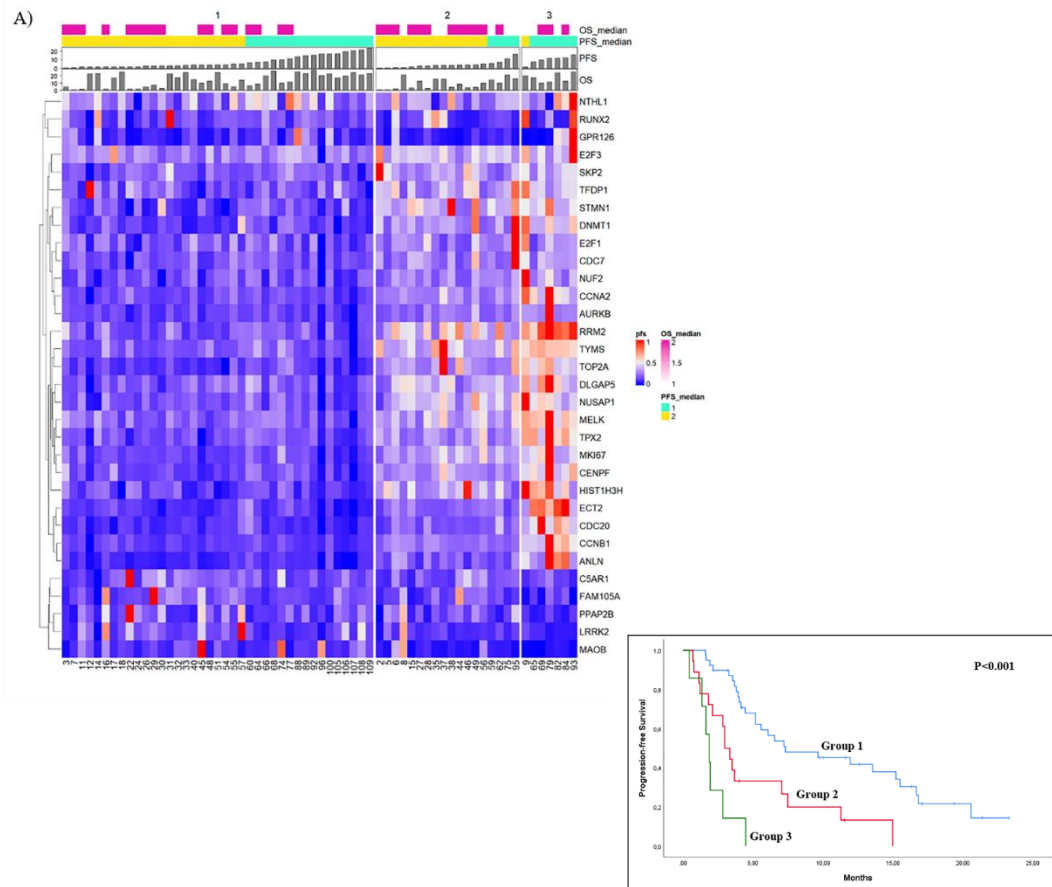
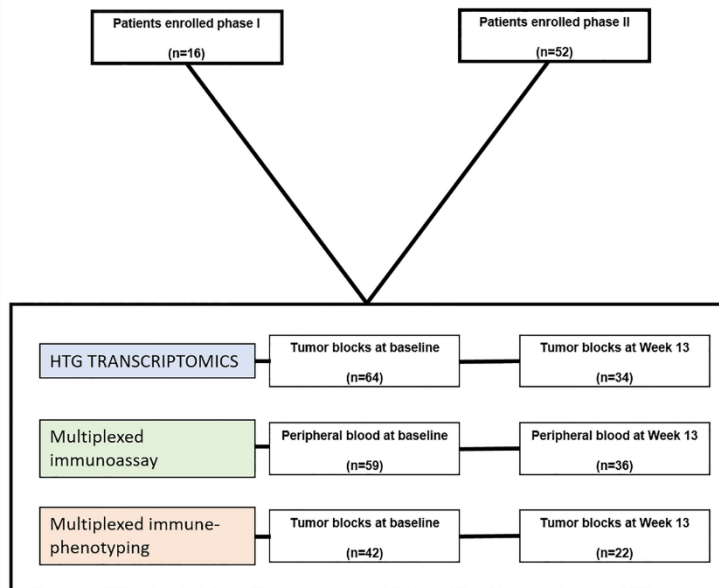
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ÁREA: CÁNCER

IMMUNOSARC TRIAL: Sunitinib plus Nivolumab



ÁREA: CÁNCER

Gene

CD86

CHI3L1

CXCL10

CXCL9

LAG3

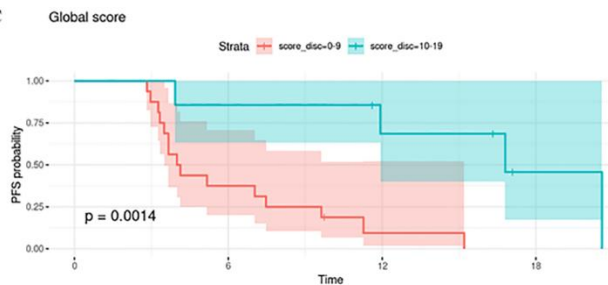
NR4A1

VCAM1

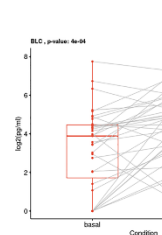
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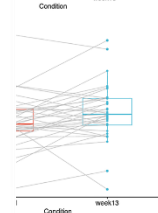
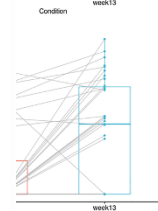
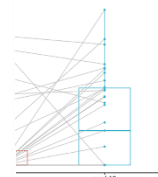
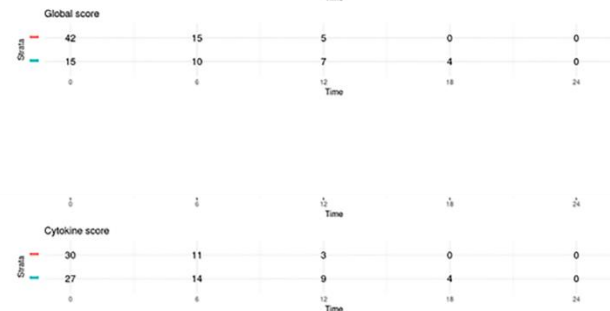
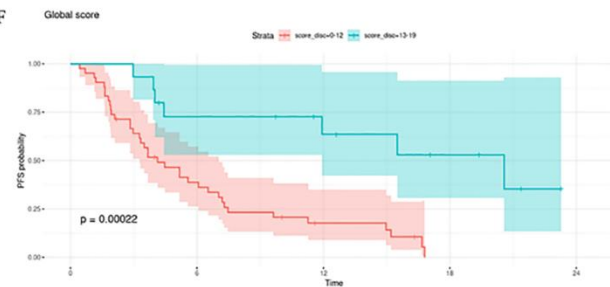
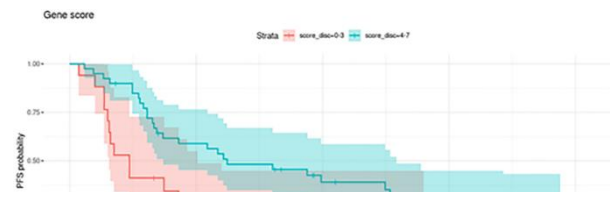
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Grupo Quironsalud

COLLABORATION

1. Expertise: Drug testing in vitro and in vivo, drug development, High-throughput multi-omics, PDX modelling, human sample processing, etc.

2. Work in progress: Expertise in epigenomics (i.e. ChIP-Seq, ATAC-Seq, PRO-Seq, etc).

THANK YOU

ATBSarc group:

Javier Martin Broto

Nadia Hindi

Jose L. Mondaza Hernandez

Marta Martin Ruiz

Pablo Romero Gonzalez

Marta Renshaw Calderon

Isabel Marin

Antonio Rubio Reyes

Jaime Carrillo Garcia



EUROPEAN COMMISSION



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Instituto de Salud Carlos III

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University of Texas:

Dr. Heather Hayenga

Dr. Leonidas Bleris

Dr. Yi Li



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