

RAGMA
23 16ª Revisión Anual
GEICAM de Avances
en Cáncer de Mama

Realidades y esperanzas

Avances en metodología de la investigación. Nuevos diseños

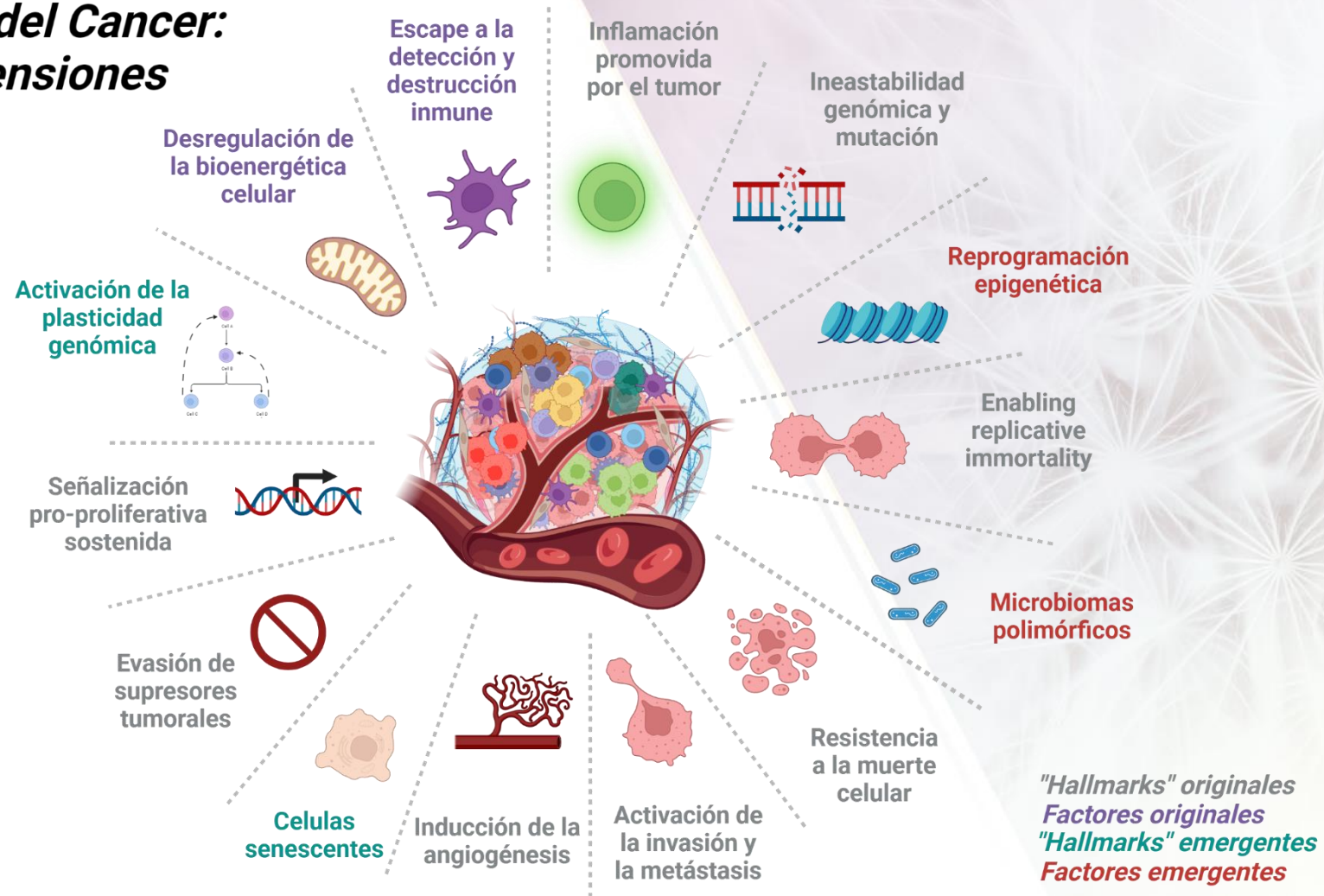
Dra. Laura Vera Ramírez
Área de Medicina Genómica (GENYO). Universidad de Granada

Organizado por:

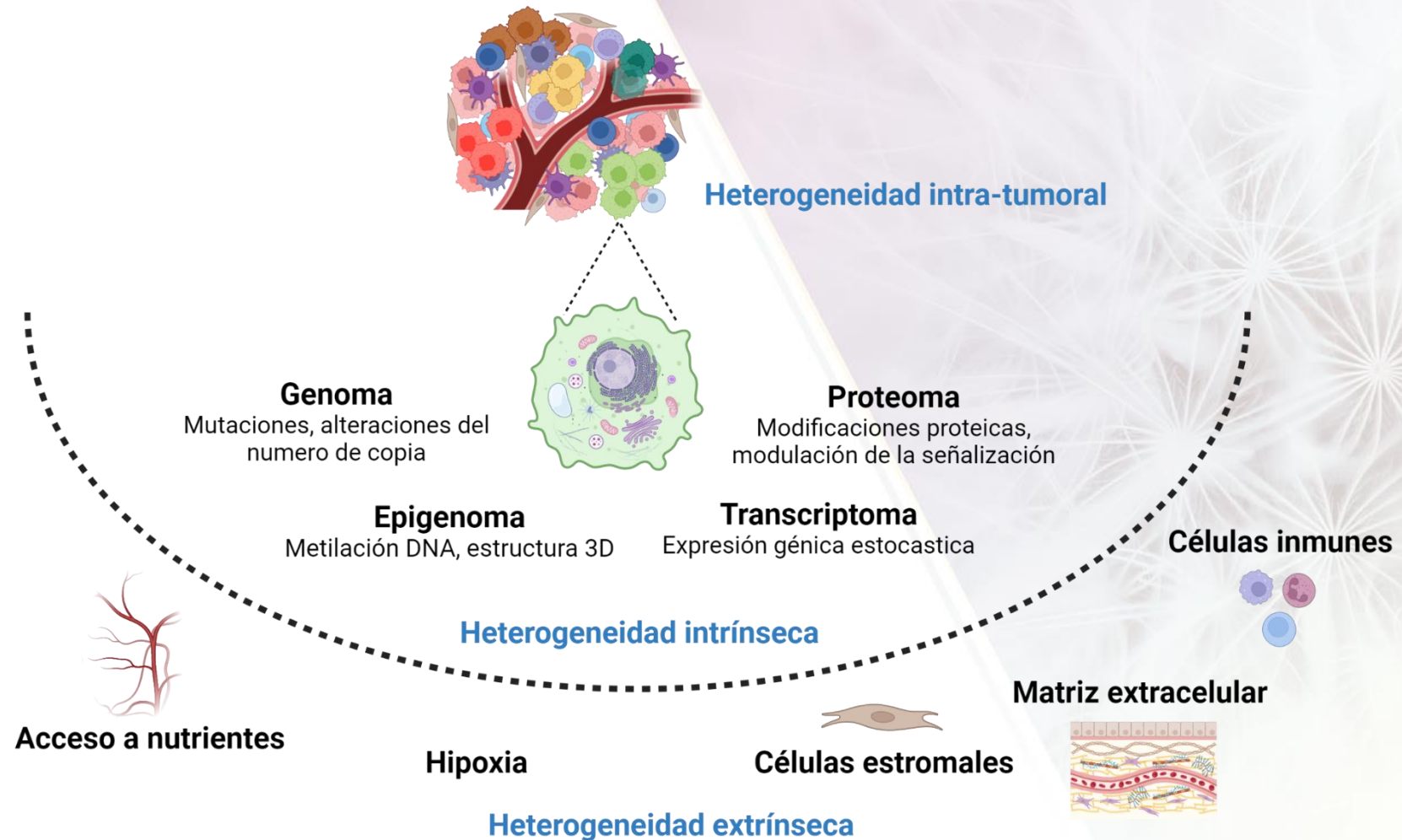
GEICAM
investigación en
cáncer de mama

La variedad de características distintivas del cáncer ilustra su complejidad

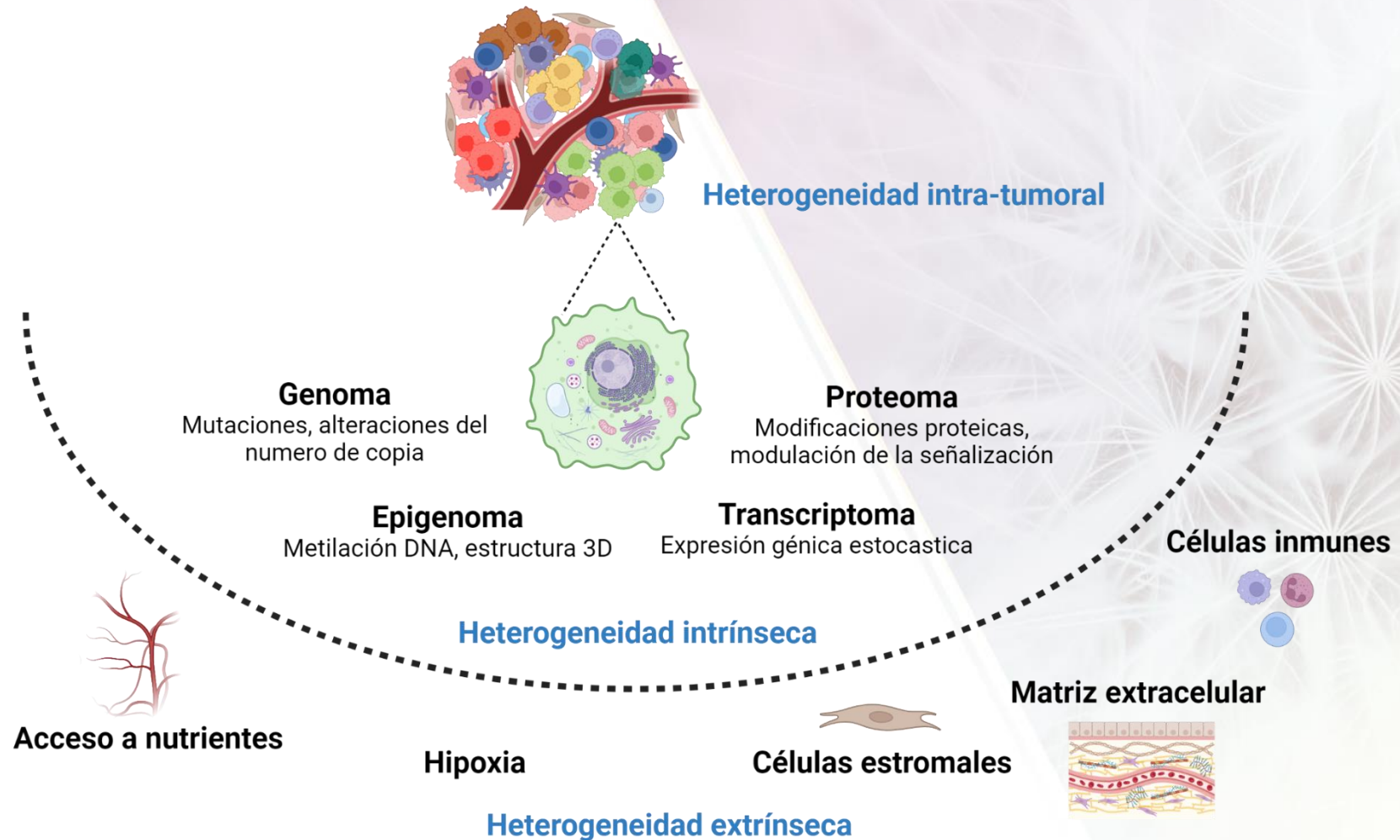
Características distintivas (hallmarks) del Cáncer: nuevas dimensiones



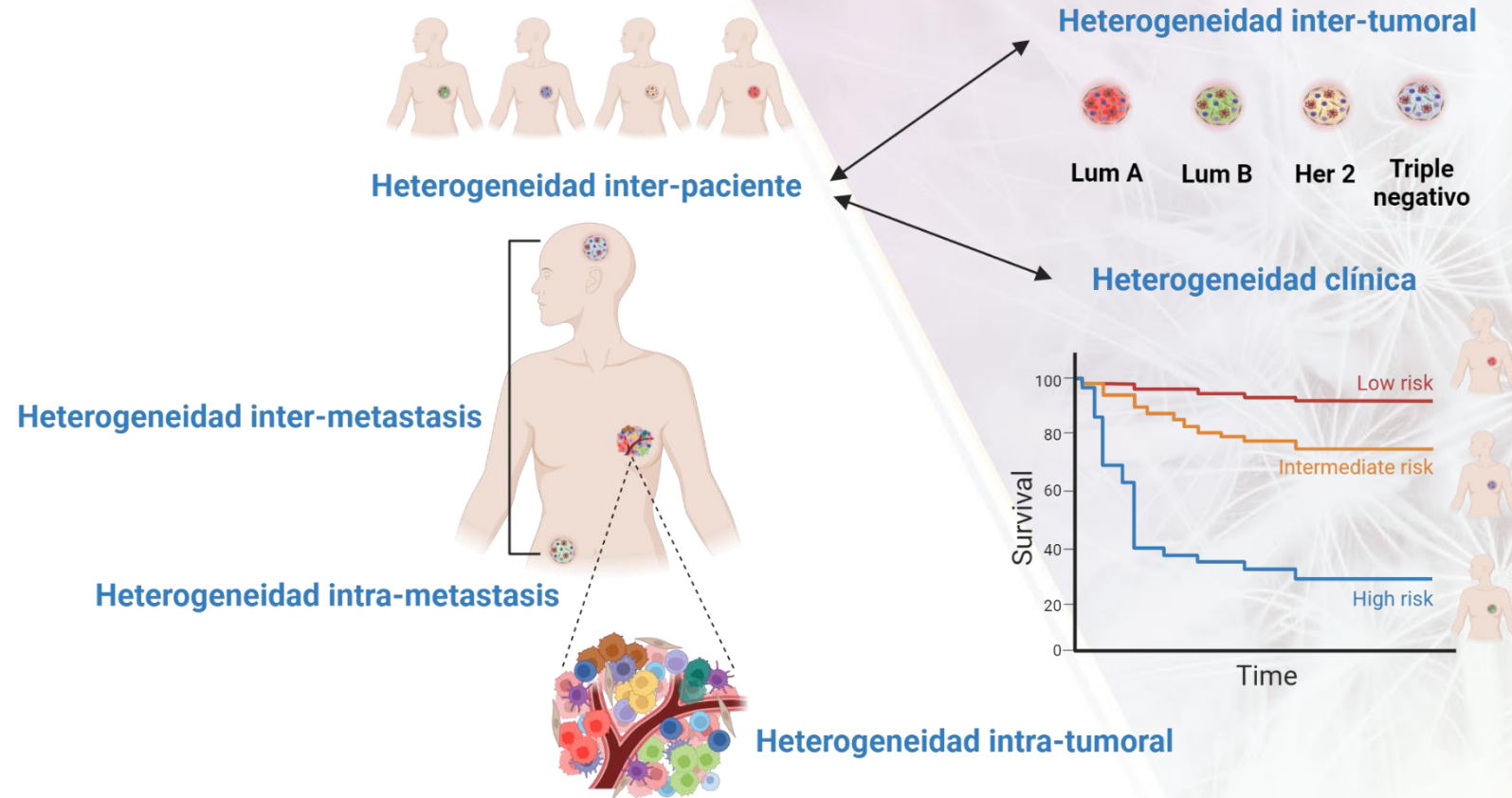
La complejidad del cáncer es fuente de heterogeneidad



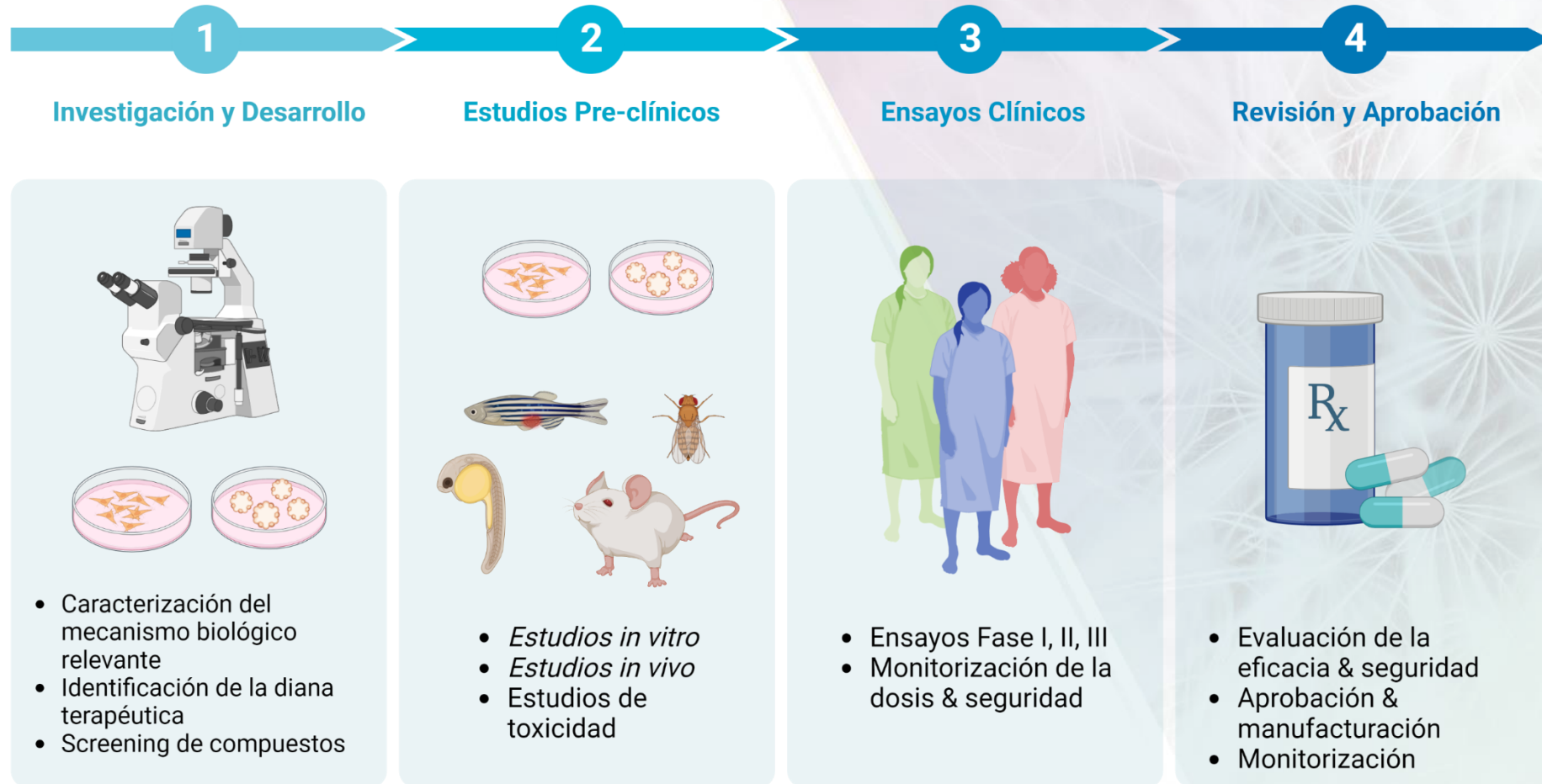
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La heterogeneidad tumoral genera heterogeneidad clínica



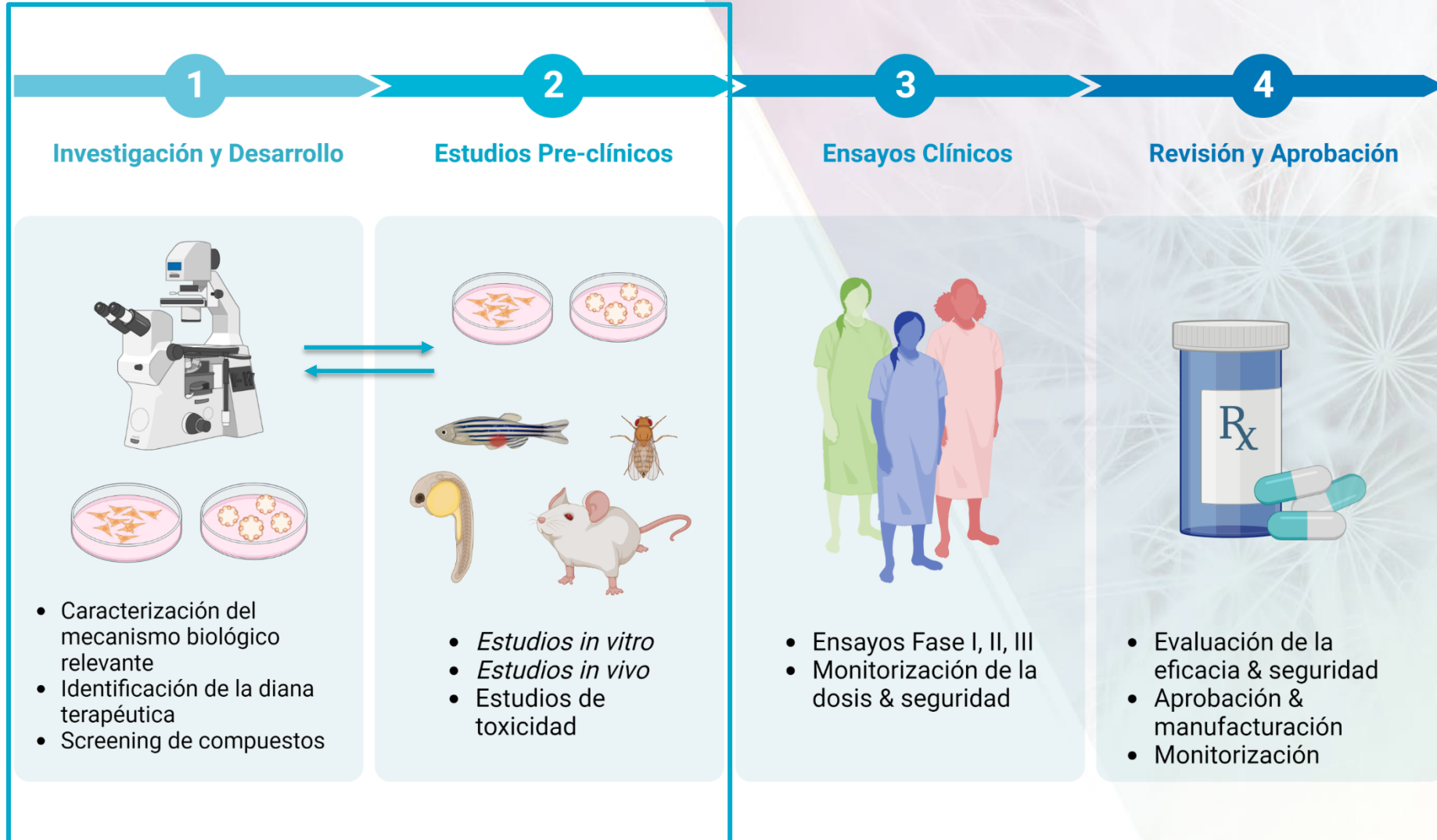
Modelos preclínicos de cáncer



Modelos preclínicos de cáncer



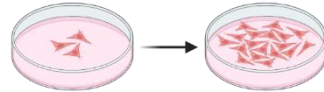
Modelos preclínicos de cáncer



Los modelos in vitro 3D incorporan elementos del microambiente tumoral y proporcionan resultados preclínicos significativos

In vitro

Cultivos 2D de **líneas celulares establecidas**



Cultivos 3D:

Cultivos en suspensión

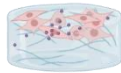


Superficies de baja adherencia

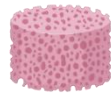


Hanging drop

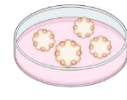
Matrices 3D/bioplataformas



BME/hydrogel



Bio-plataformas



Organoides

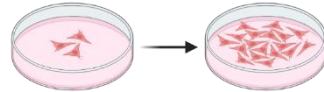


Órganos decelularizados

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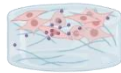


Superficies de baja adherencia



Hanging drop

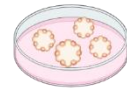
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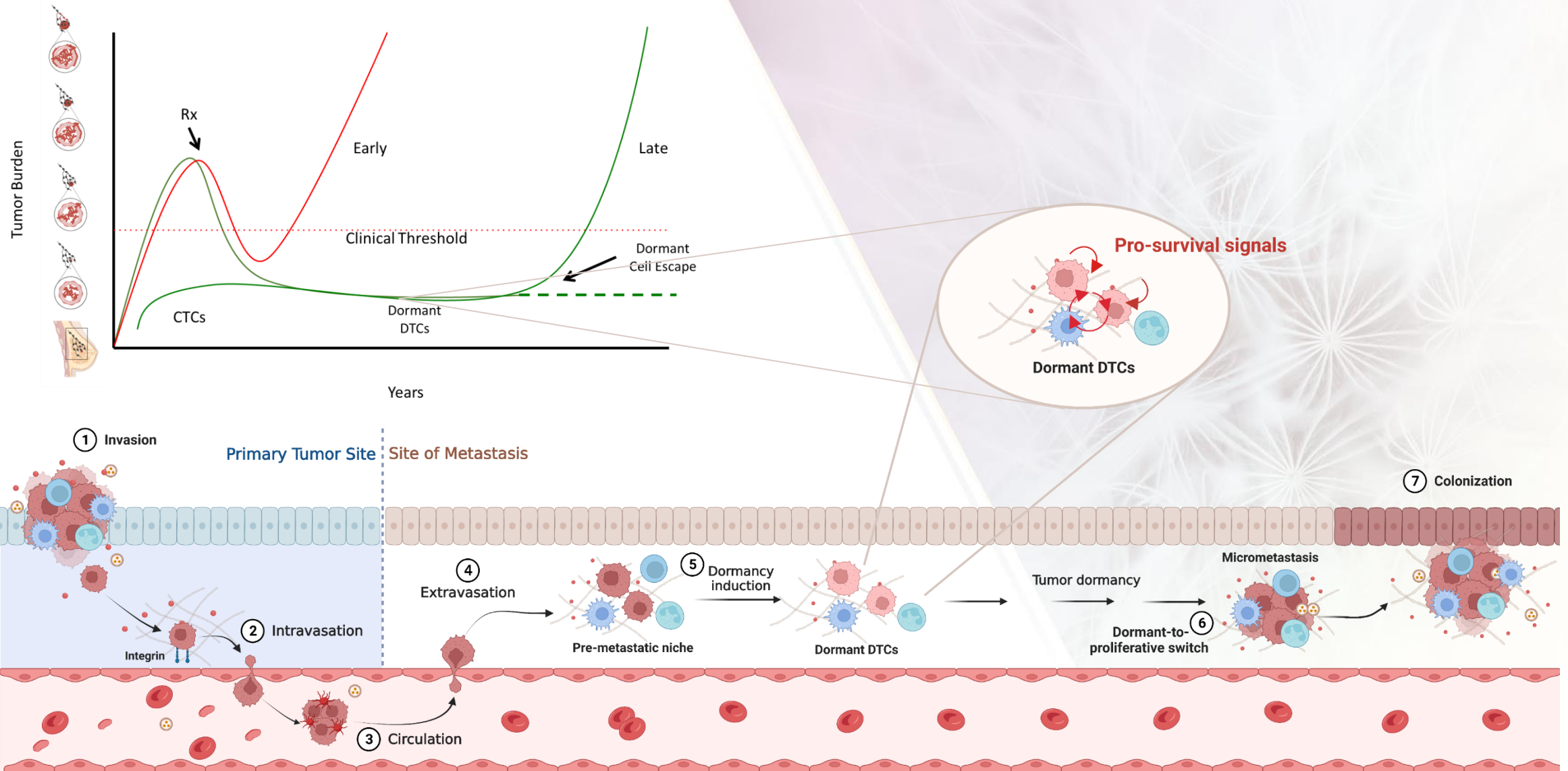


Organoides



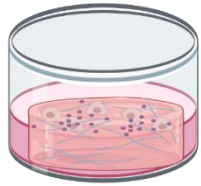
Órganos decelularizados

Las células tumorales diseminadas en estado durmiente dependen de señales pro-supervivencia intrínsecas y microambientales

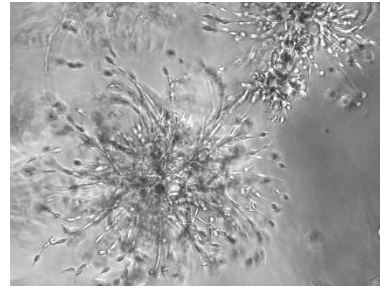


Los sistemas *in vitro* 3D son una herramienta útil para el estudio de la dormancia tumoral

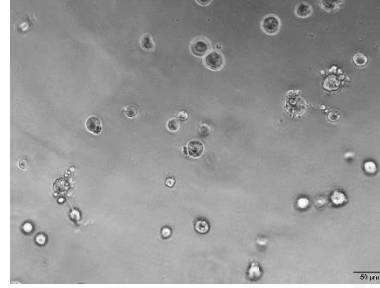
Cultivo 3D
sobre BME



D2A1

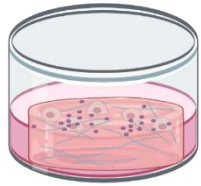


D2.0R

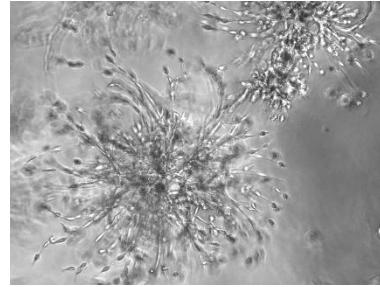


Los sistemas *in vitro* 3D son predictivos del comportamiento de las células tumorales *in vivo*

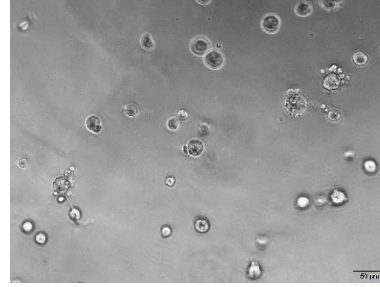
Cultivo 3D sobre BME



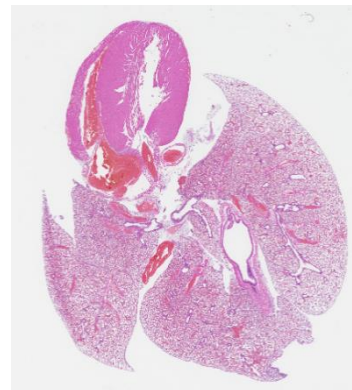
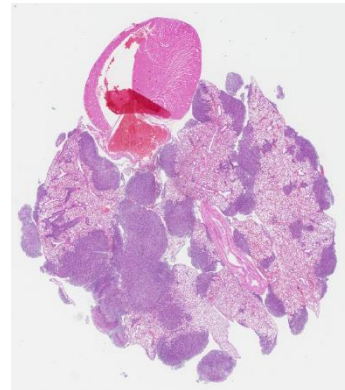
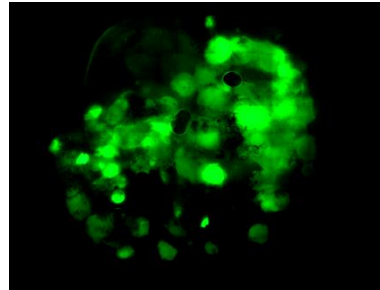
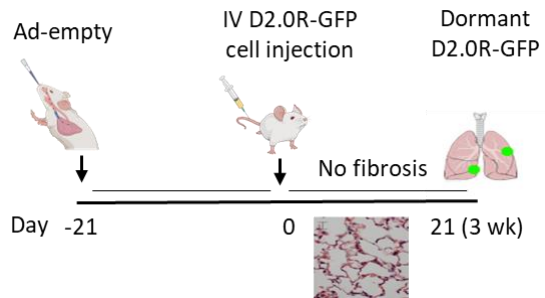
D2A1



D2.0R

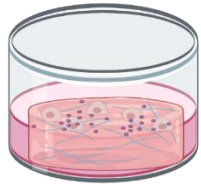


Ensayo de metástasis *in vivo*

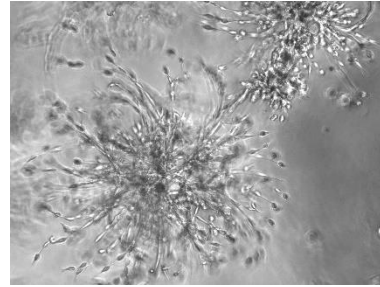


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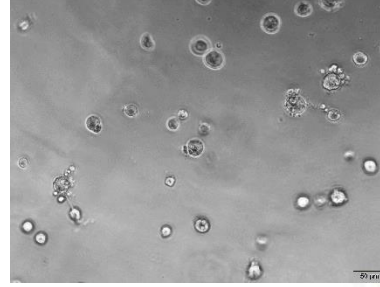
Cultivo 3D sobre BME



D2A1

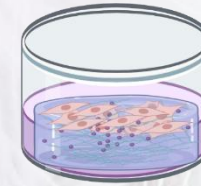


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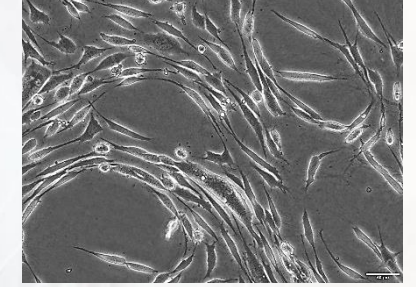


Modificación de la MEC *in vitro*

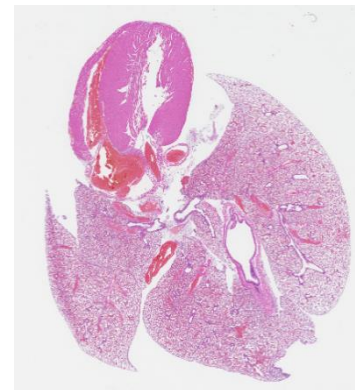
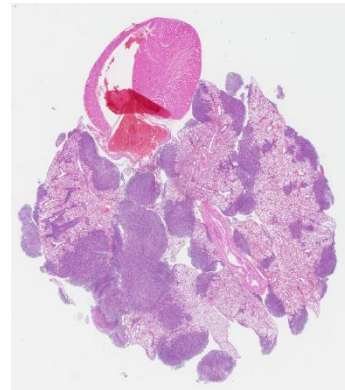
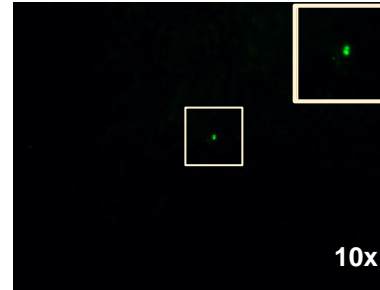
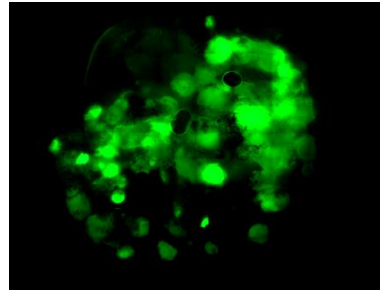
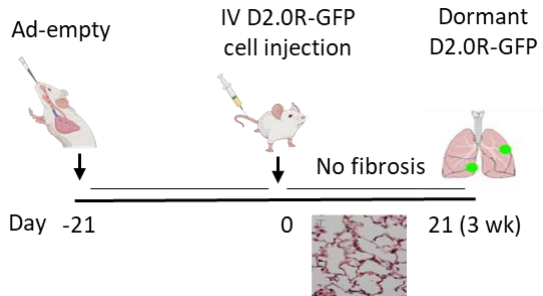
Cultivo 3D sobre BME + COL1



D2.0R

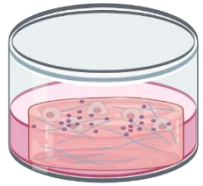


Ensayo de metástasis *in vivo*

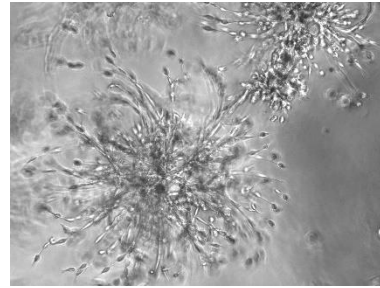


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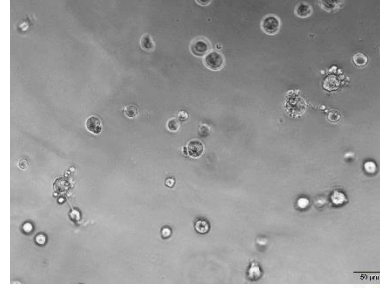
Cultivo 3D sobre BME



D2A1

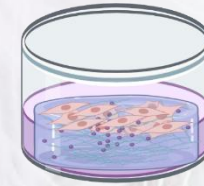


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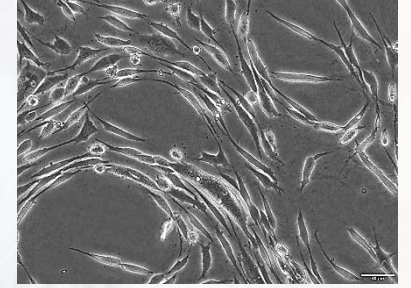


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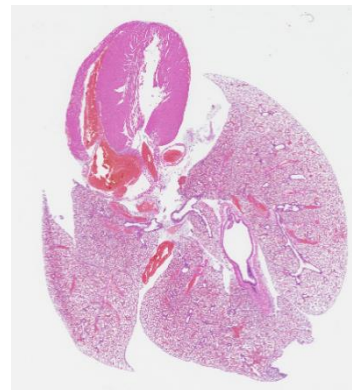
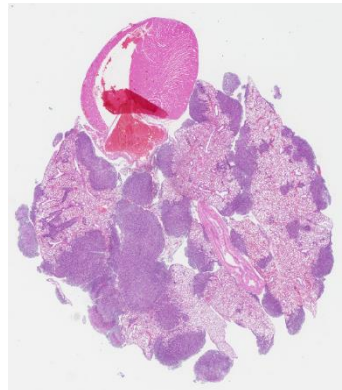
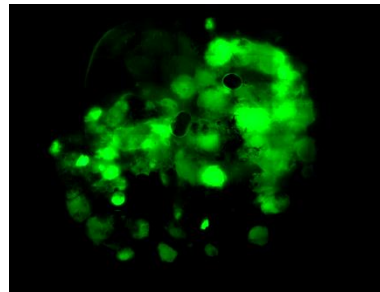
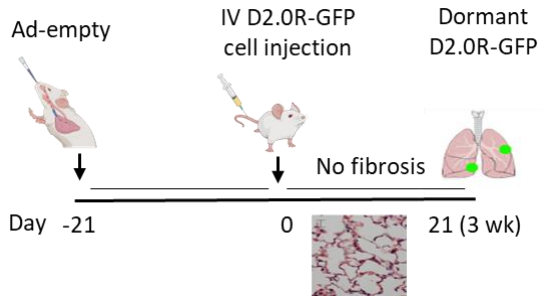
Cultivo 3D sobre BME + COL1



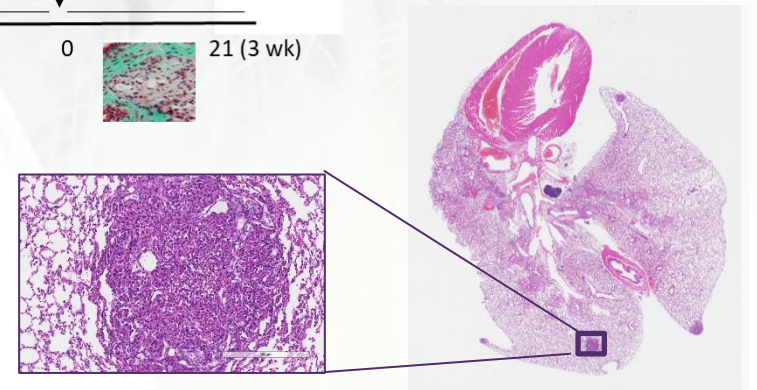
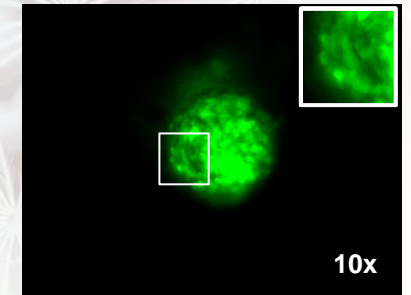
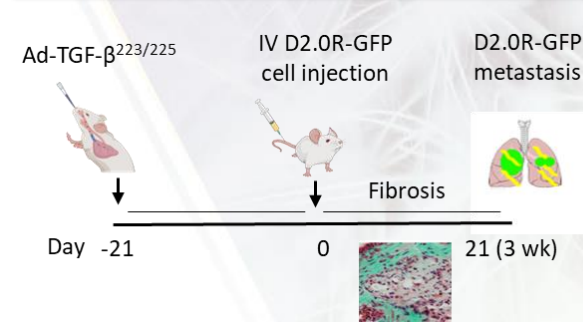
D2.0R



Ensayo de metástasis *in vivo*

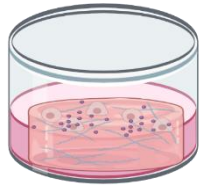


Modificación de la MEC *in vivo*

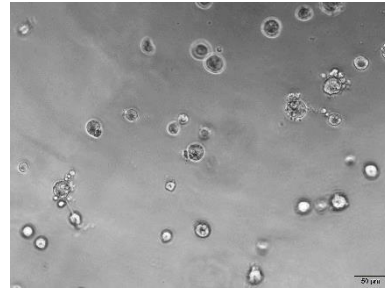


Los modelos 3D in vitro permiten llevar a cabo estudios mecanísticos

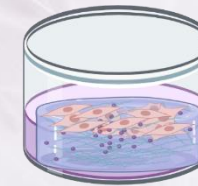
Cultivo 3D sobre BME



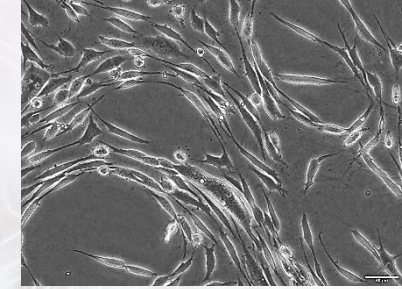
D2.0R



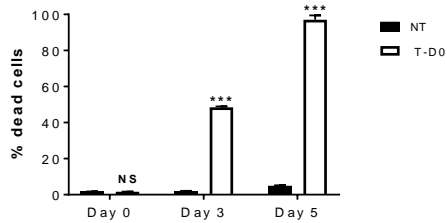
Cultivo 3D sobre BME + COL1



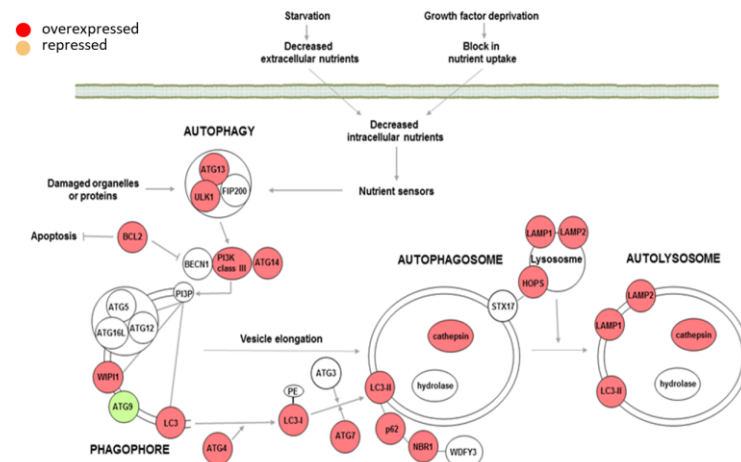
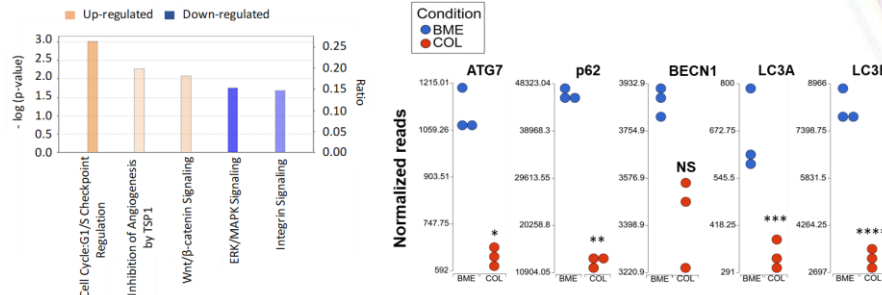
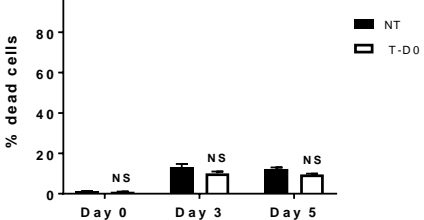
D2.0R



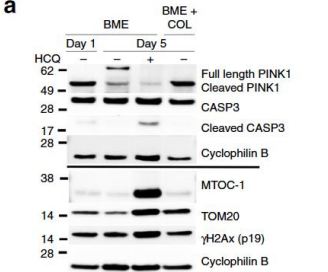
D2.0R cells on BME Cytotoxicity assay



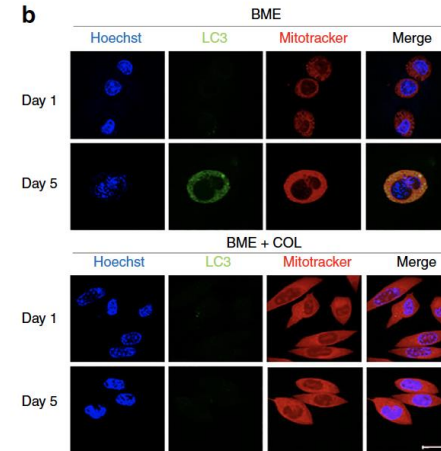
D2.0R cells on BME + COL1 Cytotoxicity assay



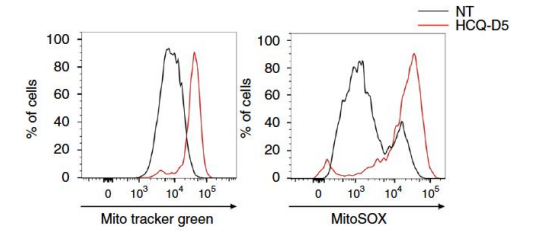
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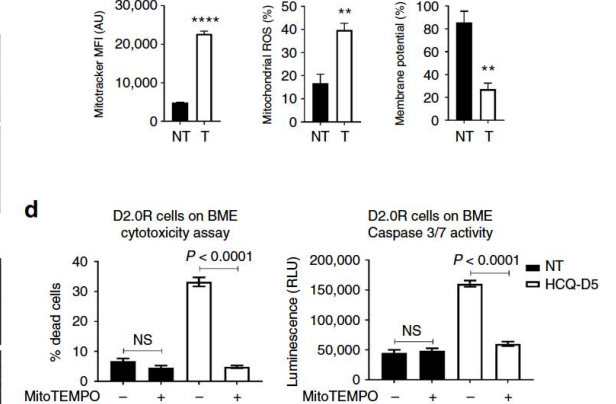
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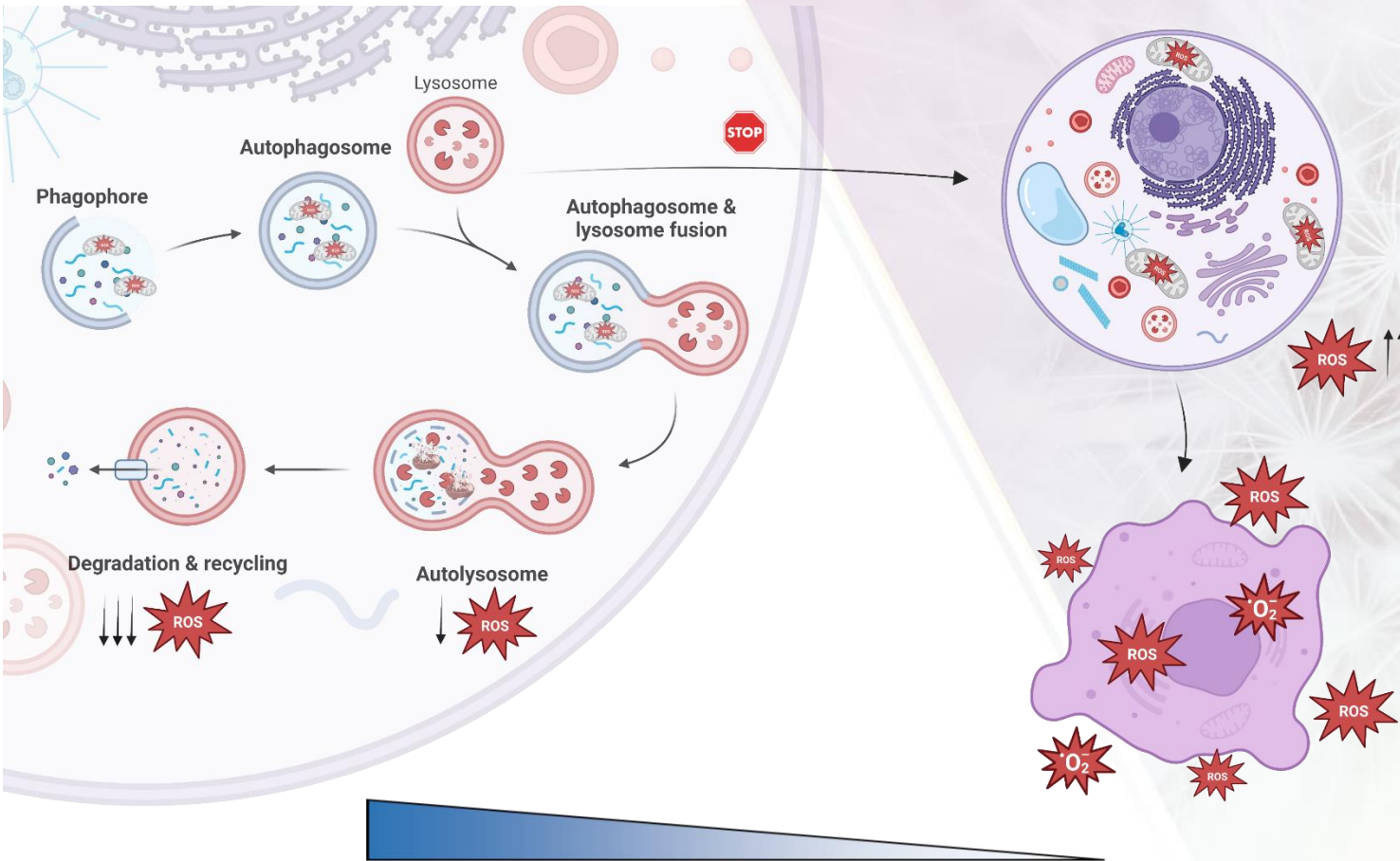
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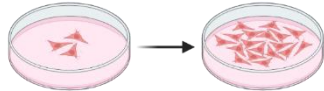
La supervivencia de células de cáncer de mama en estado durmiente y la progresión metastásica depende de la activación de la autofagia



Los dispositivos “Organ on a chip” modelan las distintas fases de la progresión tumoral.

In vitro

Cultivos 2D de **líneas celulares establecidas**



Cultivos 3D:

Cultivos en suspensión

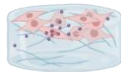


Superficies de baja adherencia



Hanging drop

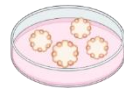
Matrices 3D/bioplataformas



BME/hydrogel



Bio-plataformas

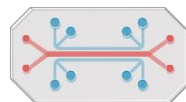


Organoides

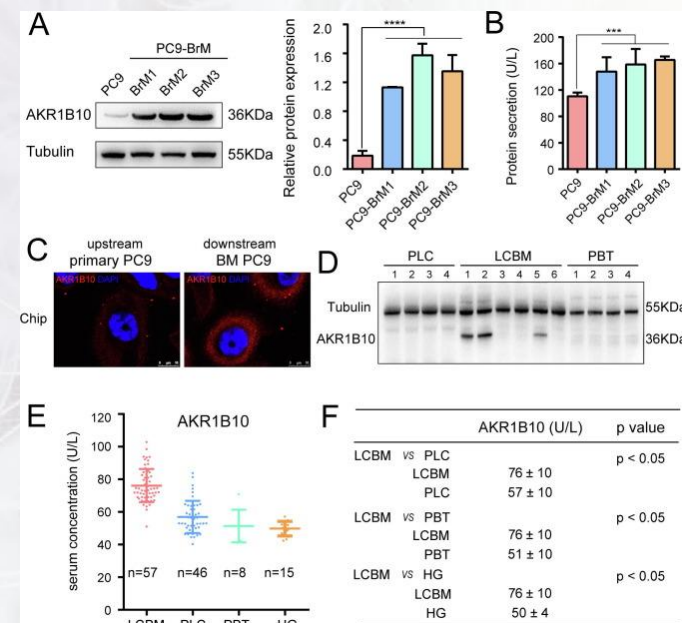
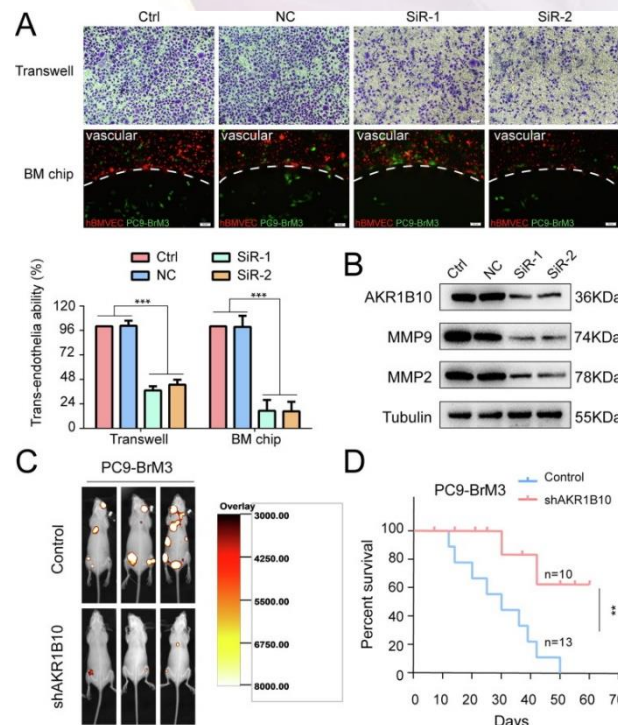
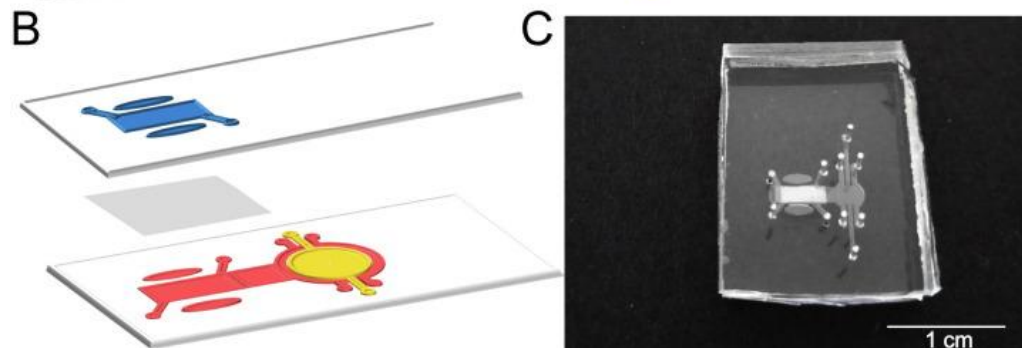
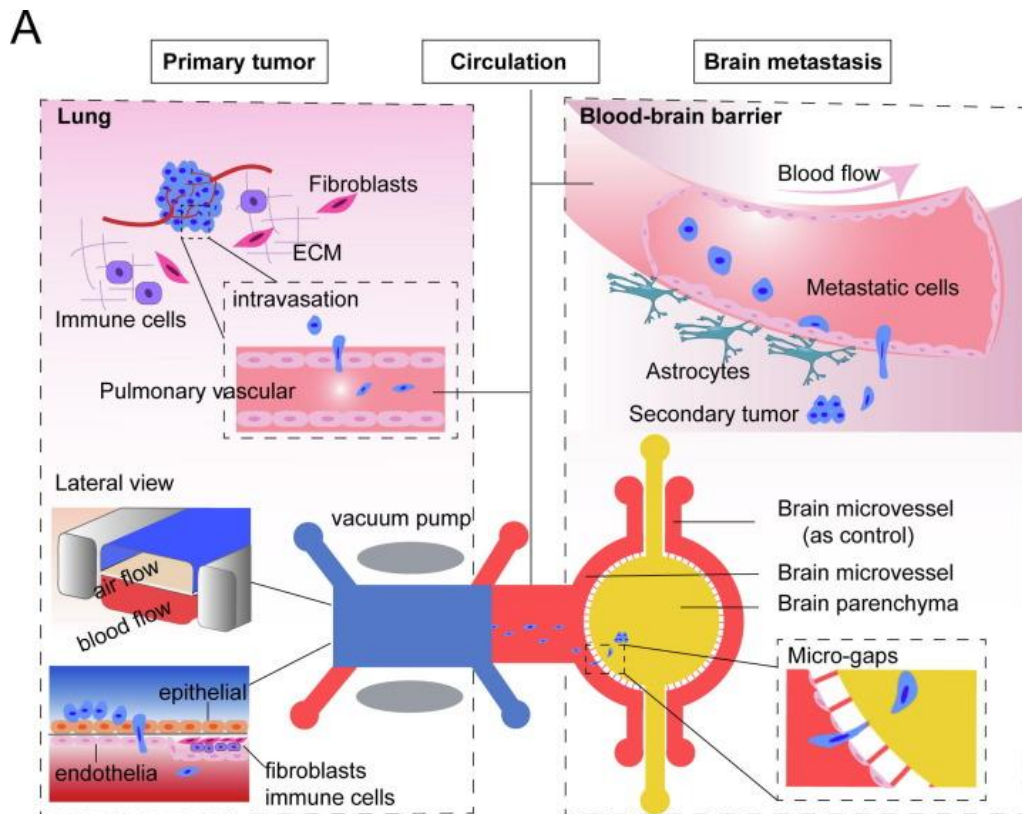


Órganos decelularizados

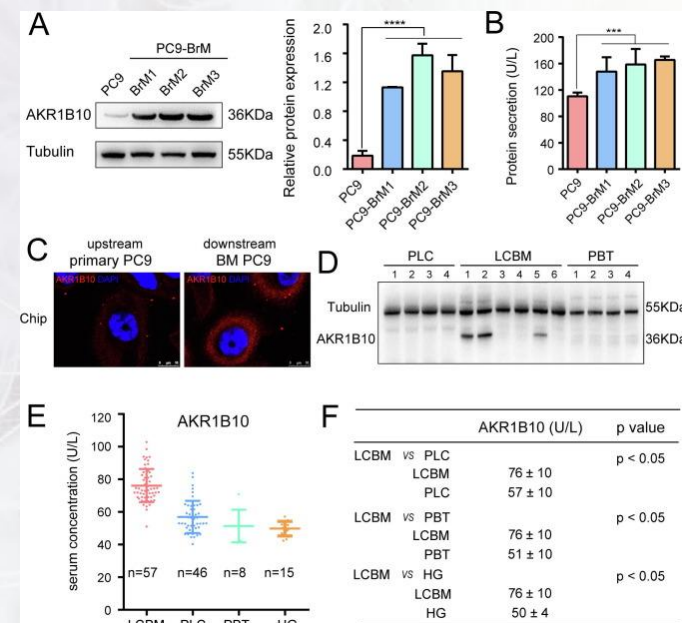
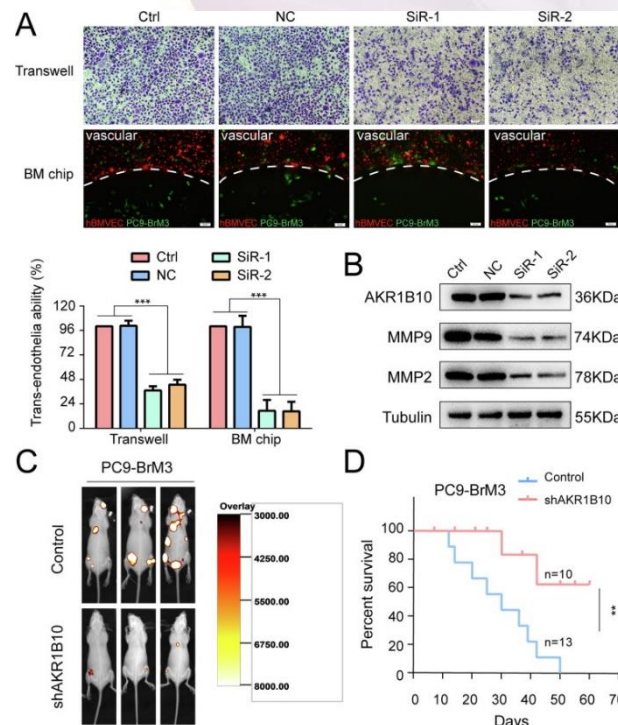
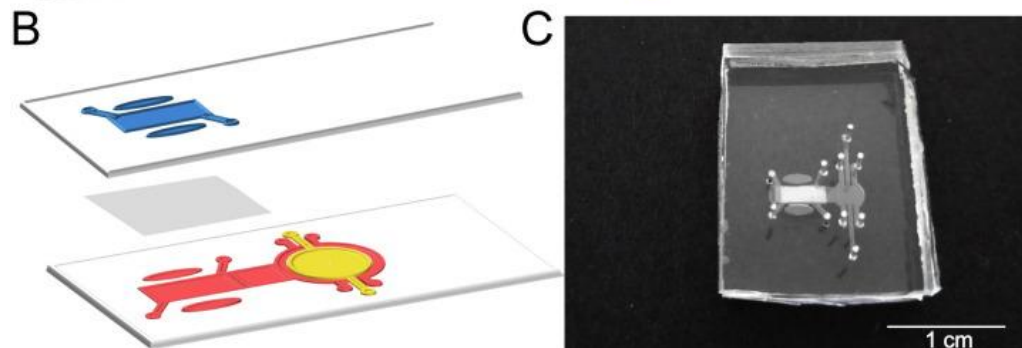
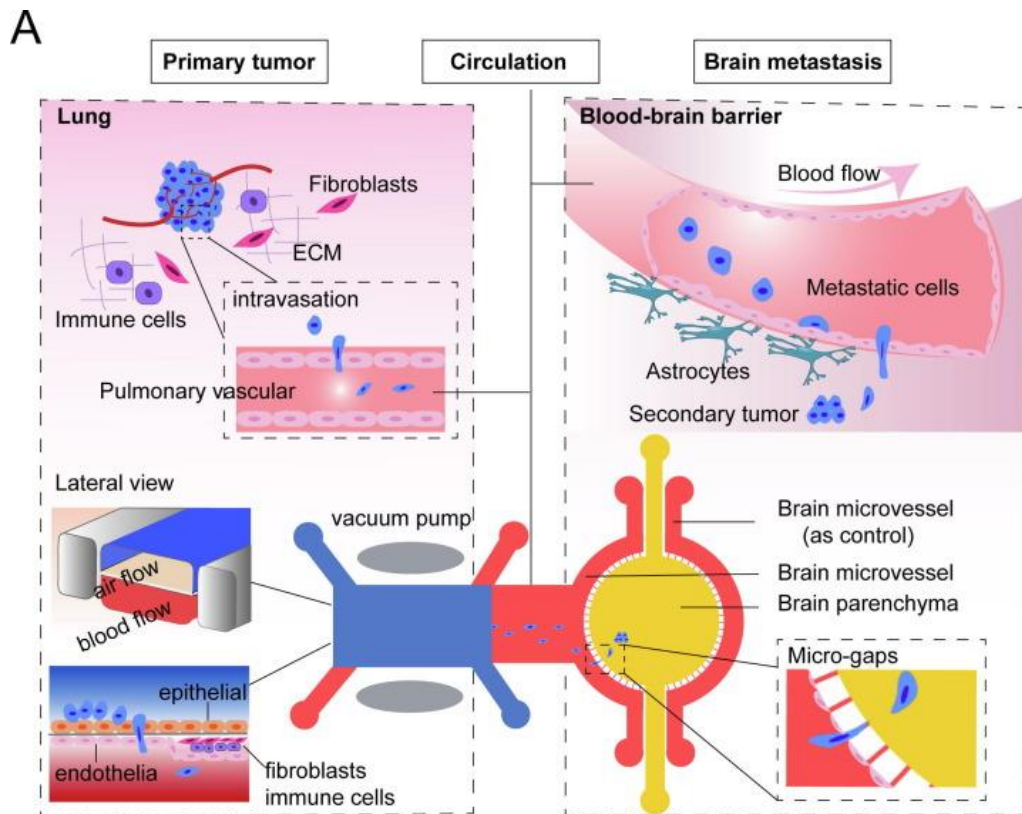
"Organ on a chip"



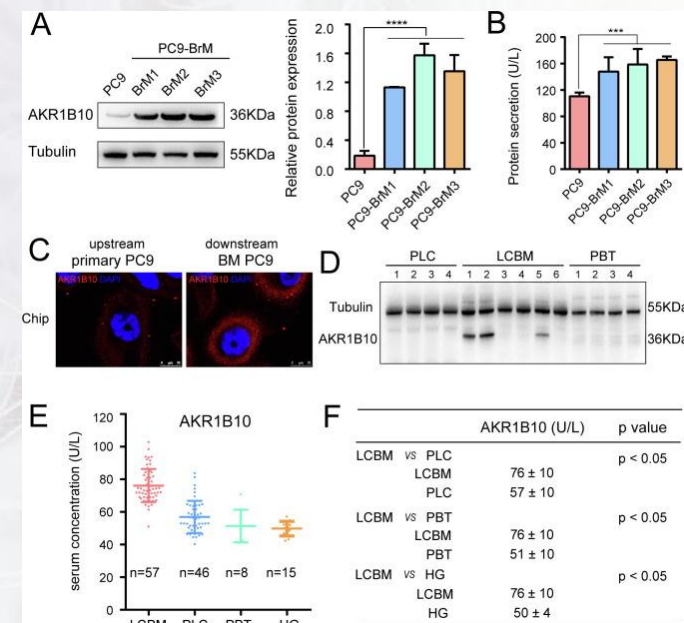
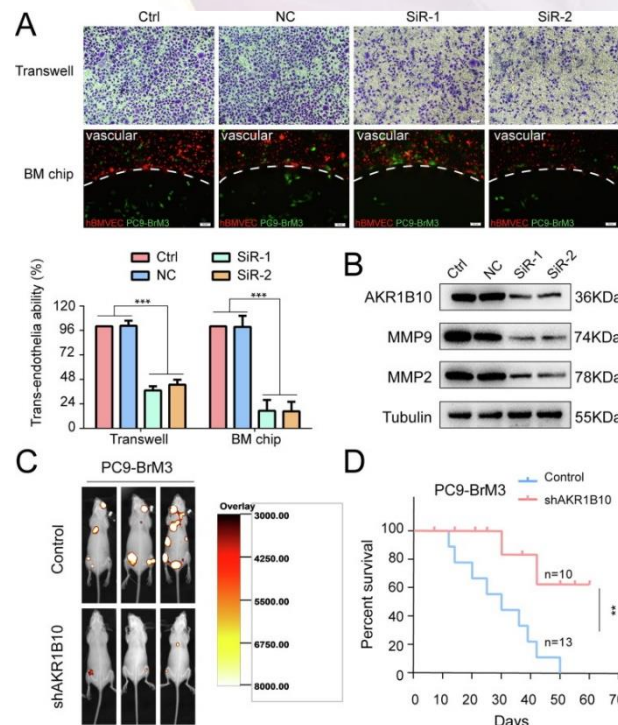
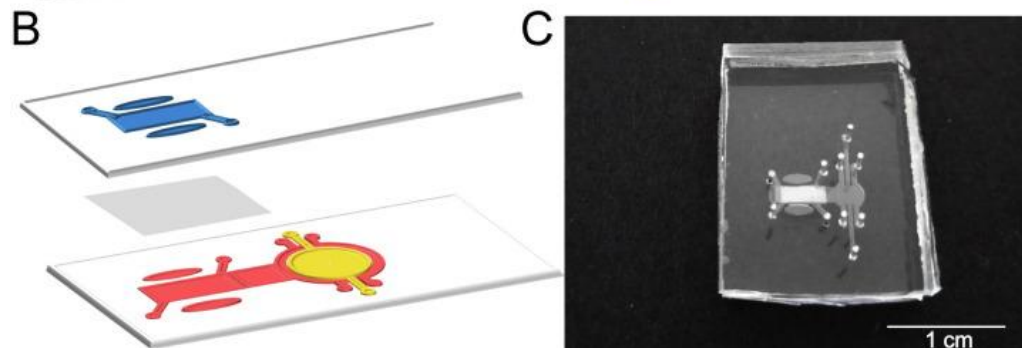
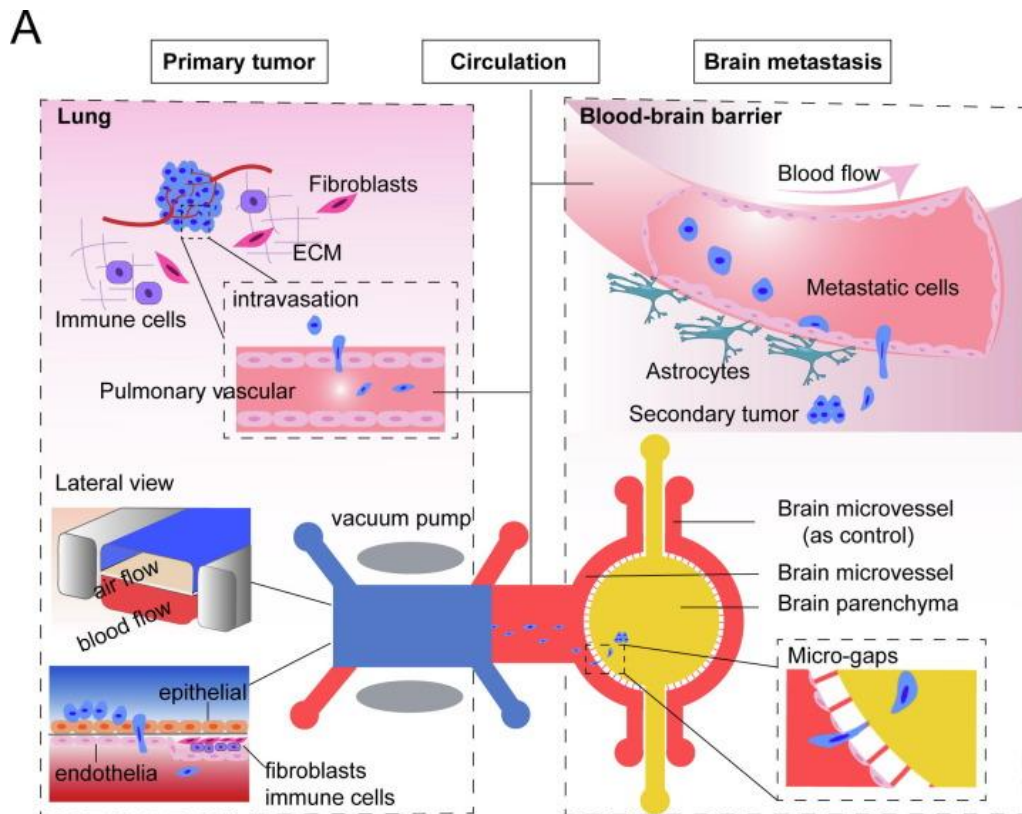
El empleo de los dispositivos MOC generan datos con elevado potencial traslacional



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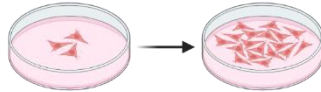
El empleo de los dispositivos MOC generan datos con elevado potencial traslacional



El pez cebra es un excelente modelo para el estudio de la diseminación tumoral

In vitro

Cultivos 2D de **líneas celulares establecidas**



Cultivos 3D:

Cultivos en suspensión

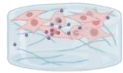


Superficies de baja adherencia



Hanging drop

Matrices 3D/bioplataformas



BME/hydrogel



Bio-plataformas

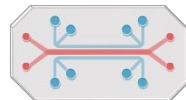


Organoides



Órganos decelularizados

"Organ on a chip"



In vivo

Organismos inferiores



Drosophila



Pez cebra



Pez killi



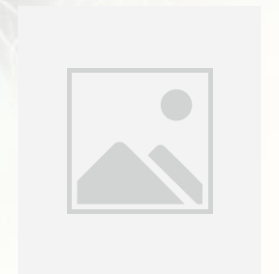
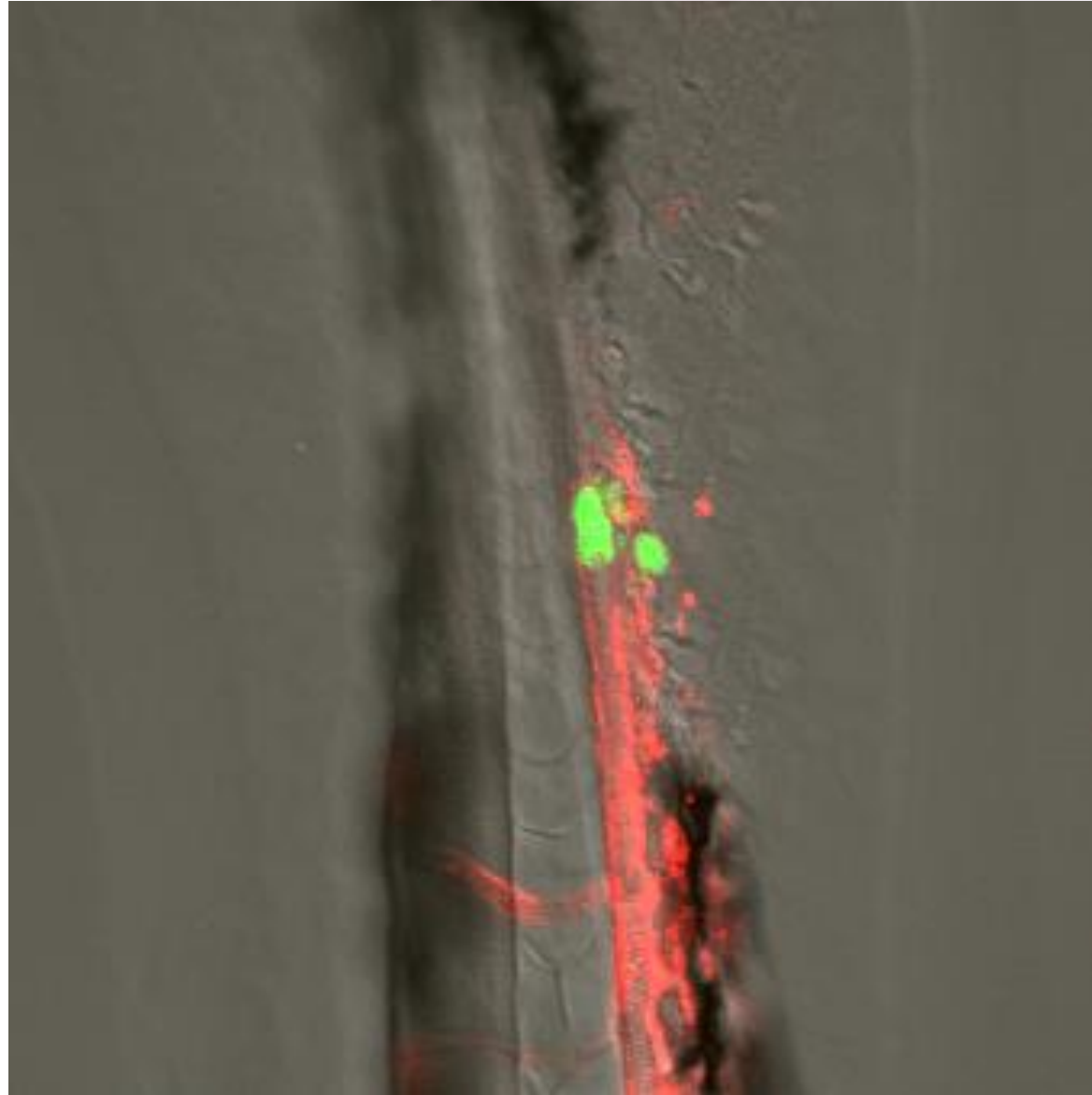
Membrana corioalantoidea del huevo

El pez cebra es un excelente modelo para el estudio de la diseminación tumoral



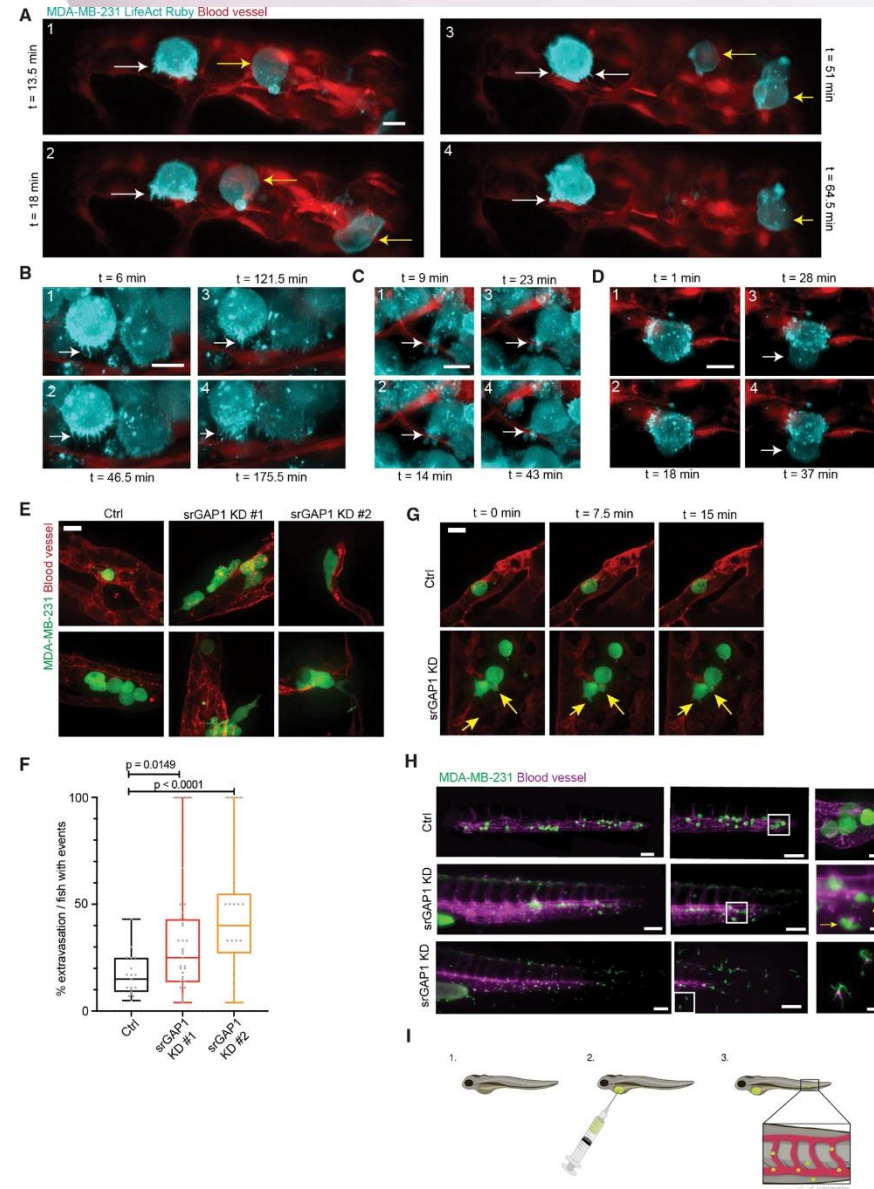
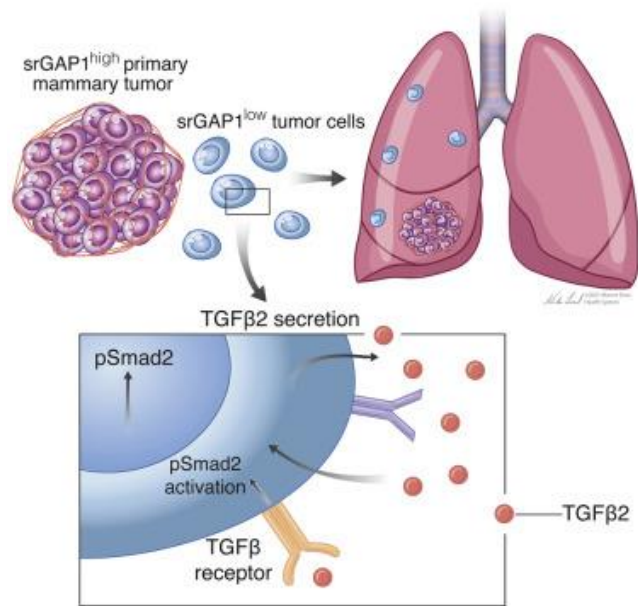
Thomas Widmann
Genyo

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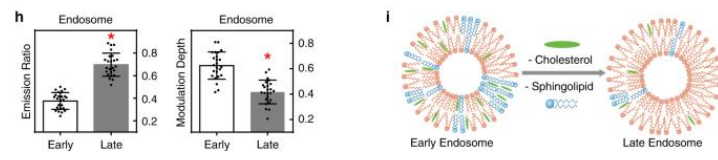
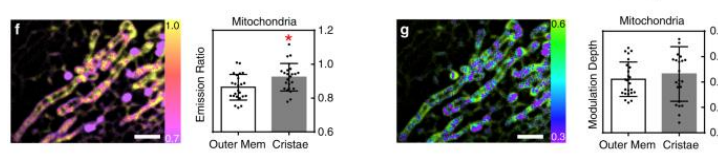
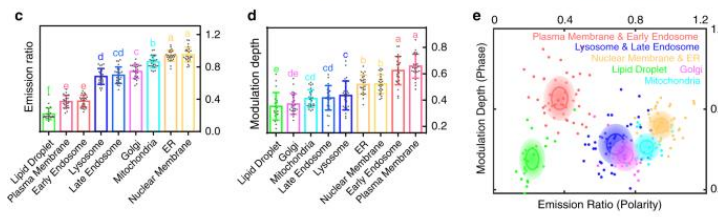
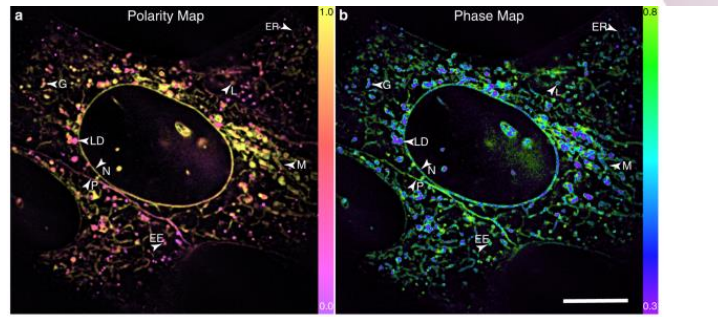
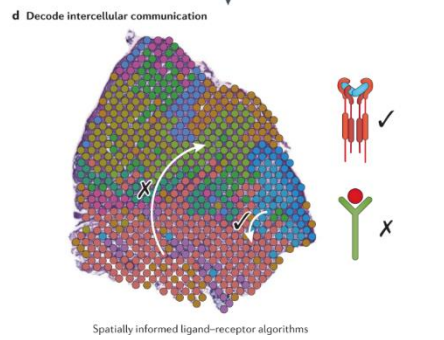
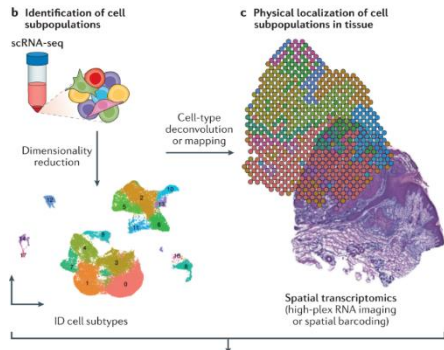
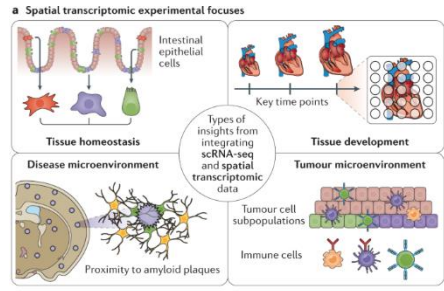


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Genyo

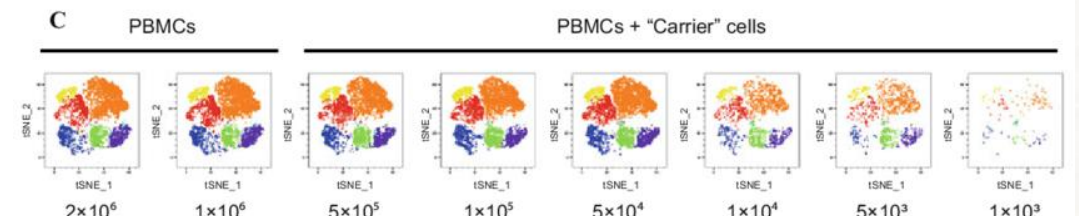
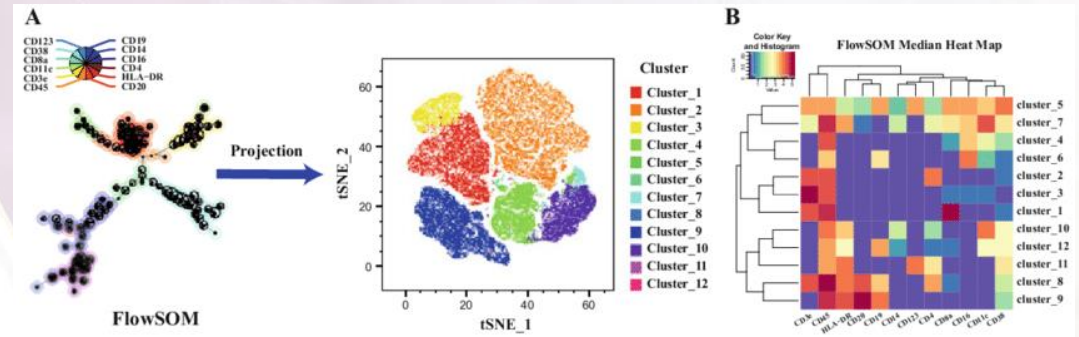
A proliferative to invasive switch is mediated by srGAP1 downregulation through the activation of TGF- β 2 signaling



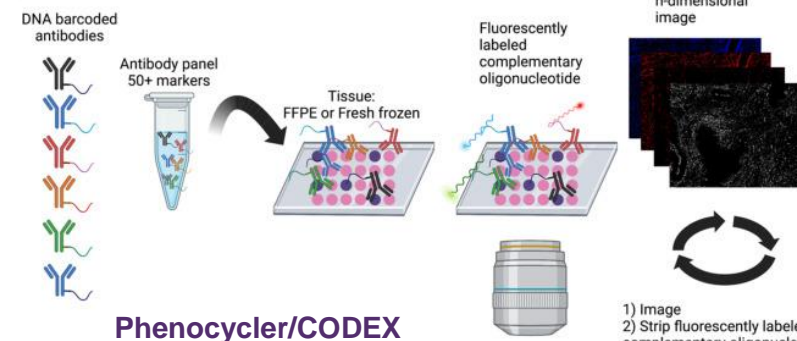
Los modelos basados en organismos inferiores permiten la aplicación de técnicas de análisis multidimensionales y de alto rendimiento



High dimensional imaging



citometría por tiempo de vuelo (CyTOF)



- 1) Image
- 2) Strip fluorescently labeled complementary oligonucleotide
- 3) Add next set and repeat until all antibodies are imaged

Transcriptómica espacial

Zanghao K et al., Nat. Comm. 11: 5890 (2020)

Longo SK et al., Nat. Rev Genet 22: 627–644 (2021)

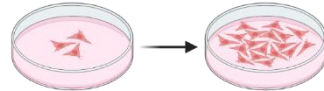
Jia X et al., Meth Mol Biol, 2111:21-33 (2020)

Kuswanto W. et al., Semin Immunopathol. 45(1): 145–157 (2023)

Los modelos murinos son considerados el estándar de excelencia

In vitro

Cultivos 2D de **líneas celulares establecidas**



Cultivos 3D:

Cultivos en suspensión

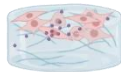


Superficies de baja adherencia



Hanging drop

Matrices 3D/bioplataformas



BME/hydrogel



Bio-plataformas

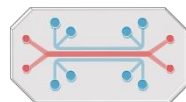


Organoides



Órganos decelularizados

"Organ on a chip"



In vivo

Organismos inferiores



Drosophila



Pez cebra



Pez killi



Membrana corioalantoidea del huevo

Modelos murinos

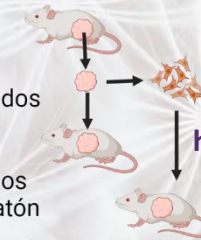
Autóctonos

- Modelos iniciados por carcinógeno
- Modelos murinos modificados genéticamente (GEMMs)



Transplante

- Alotransplantes derivados de GEM (GDAs)
- Alotransplantes derivados de líneas celulares de ratón (CellDAs)

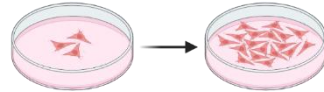


<https://mubase.crownbio.com>

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Cultivos en suspensión

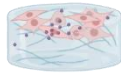


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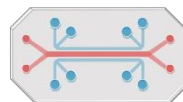


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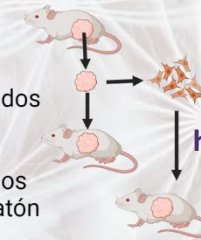
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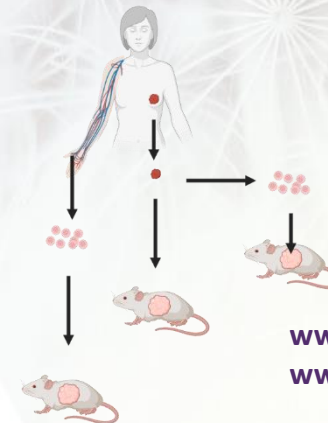
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- Alotransplantes derivados de líneas celulares de ratón (CellDAs)



<https://mubase.crownbio.com>

"Human-in-mouse"

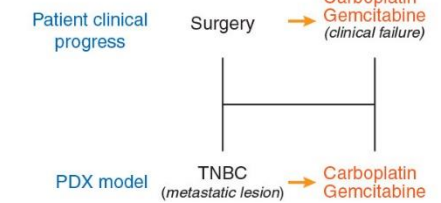
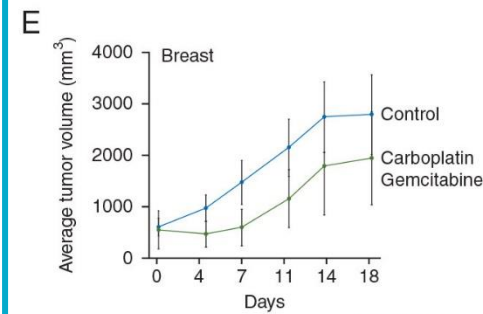
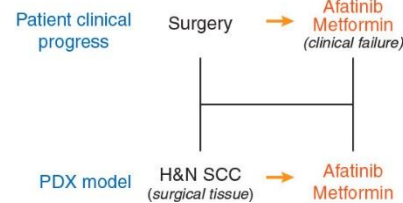
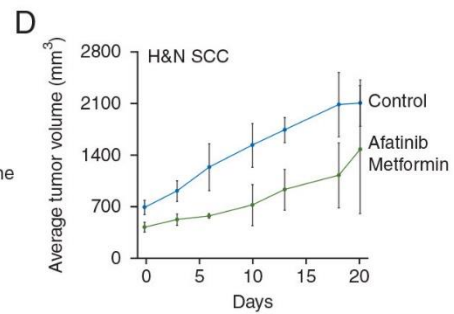
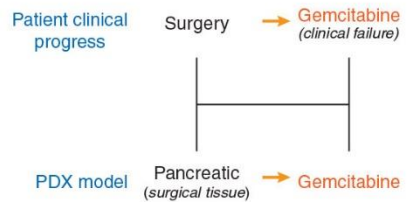
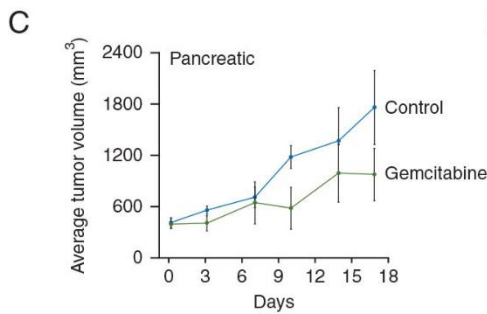
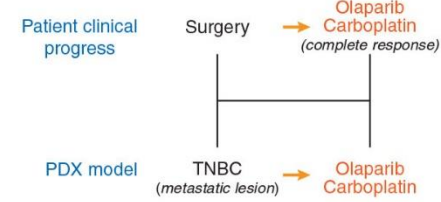
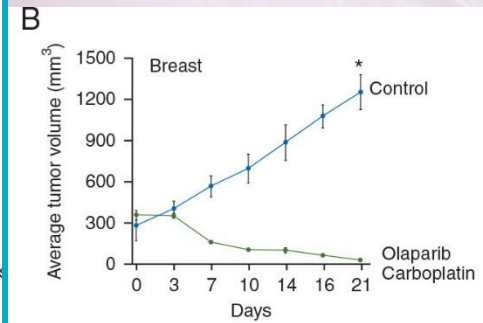
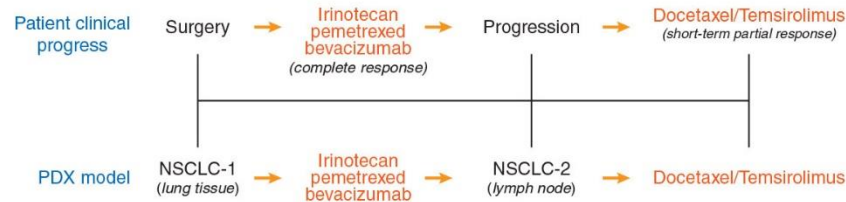
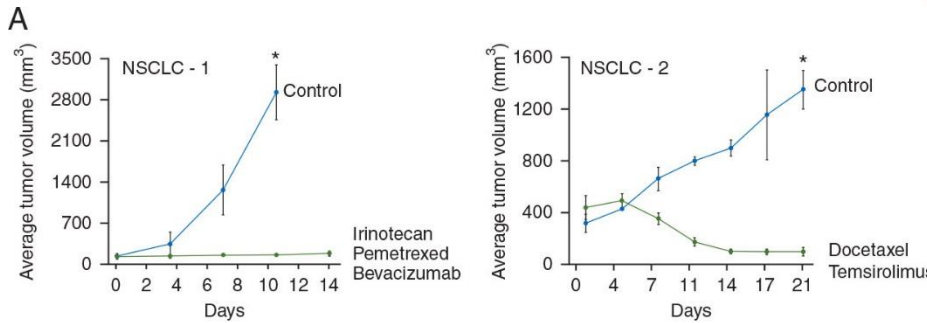
- Xenotransplantes derivados de líneas celulares humanas (CellDXs)
- Xenotransplantes derivados de pacientes (PDXs)
- Xenotransplantes de CTCs derivadas de pacientes (CDXs)



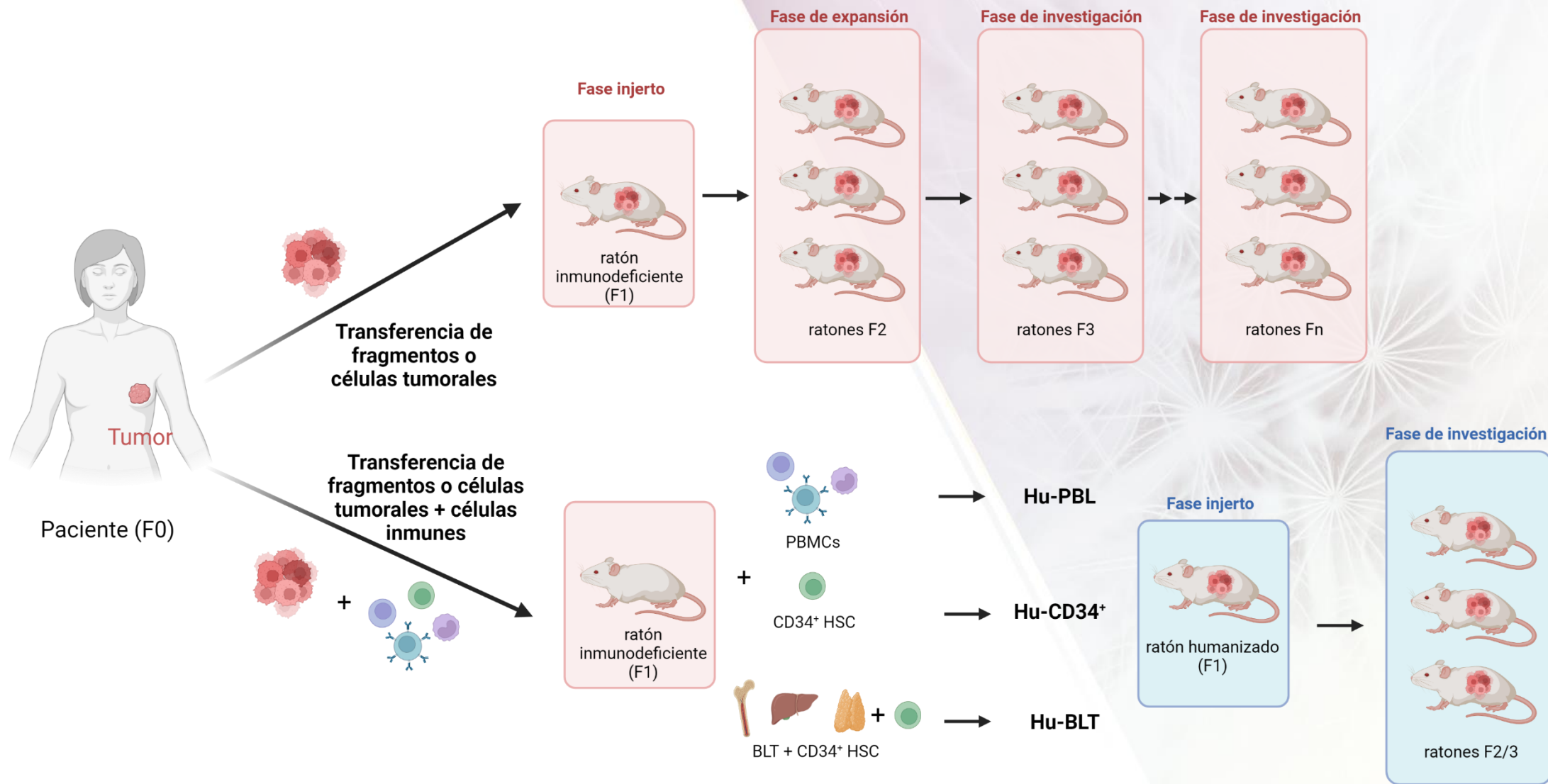
www.europdx.eu
www.pdxnetwork.org

Imagen elaborada usando <https://Biorender.com>

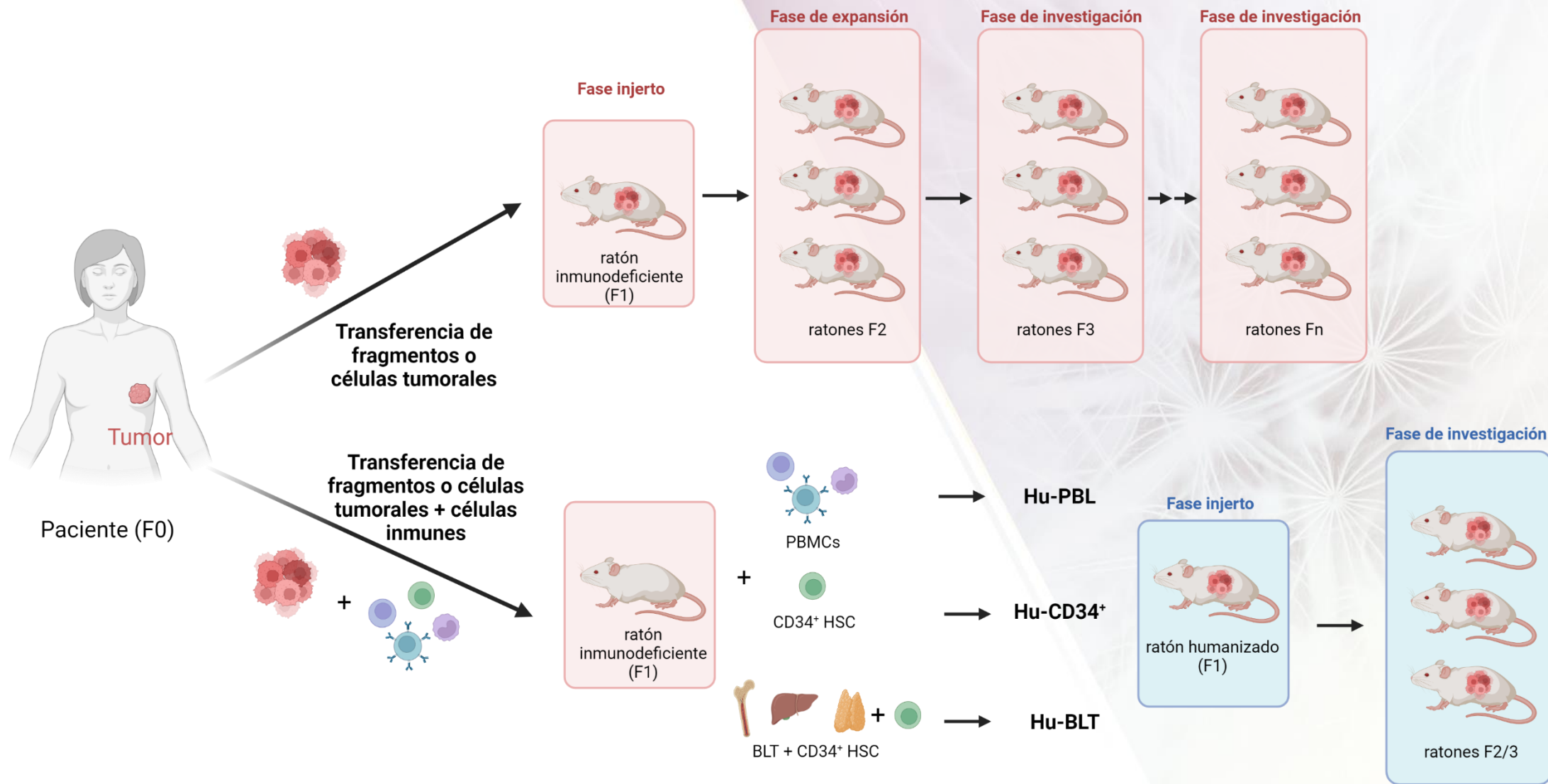
Patient-derived xenografts effectively capture responses to oncology therapy in a heterogeneous cohort of patients with solid tumors



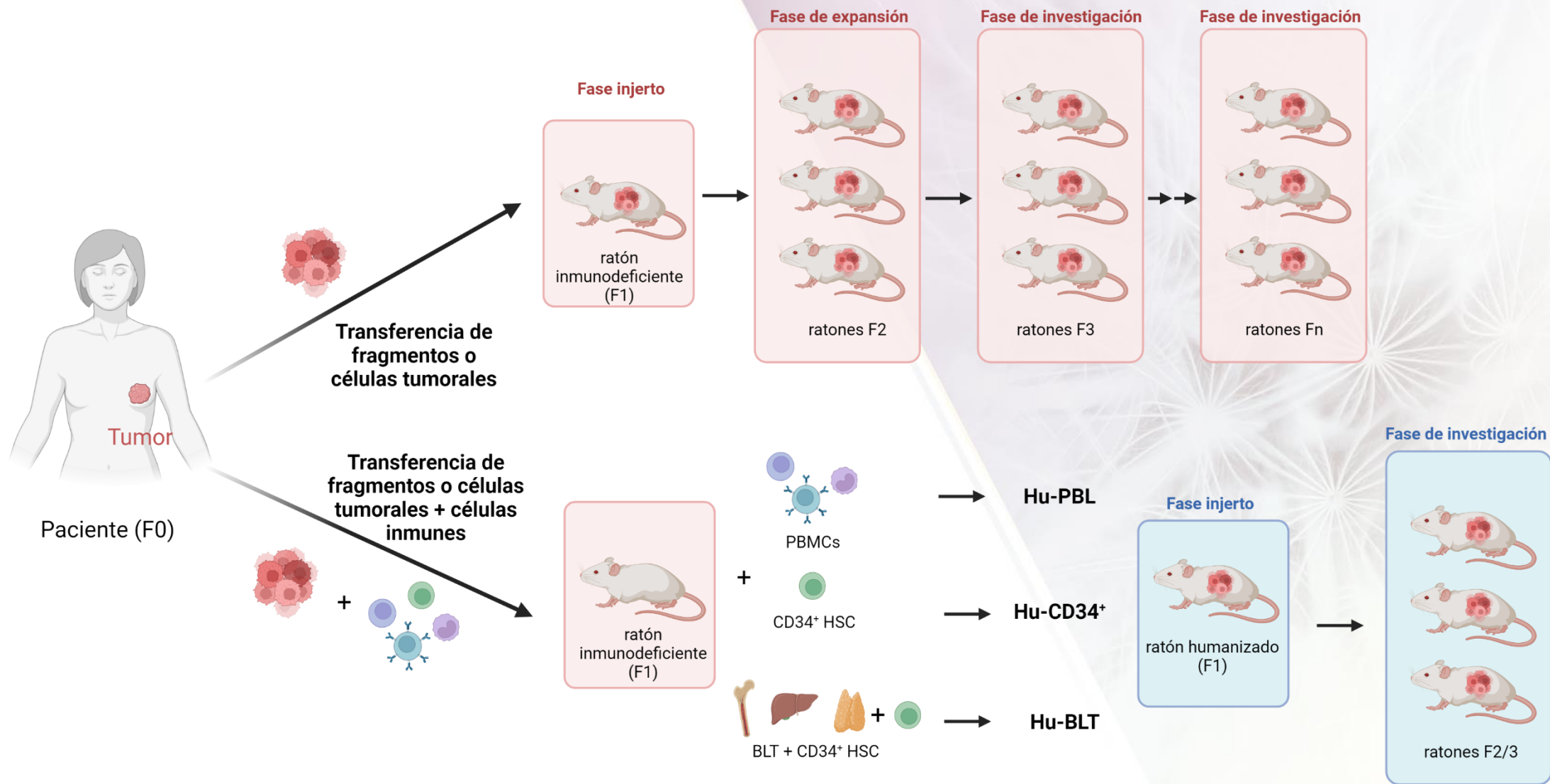
El cáncer de mama puede ser modelado en ratones inmunocompetentes humanizados



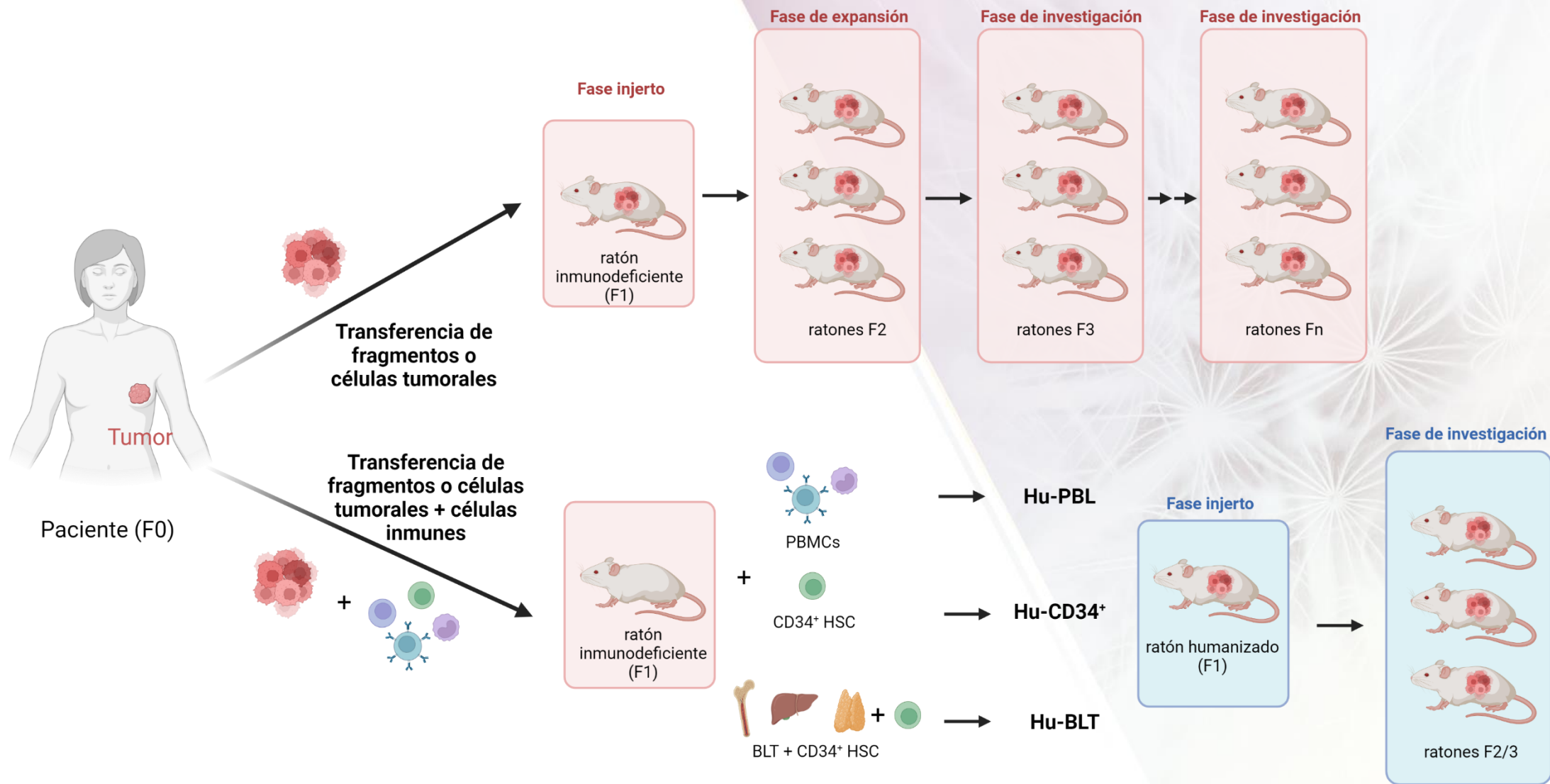
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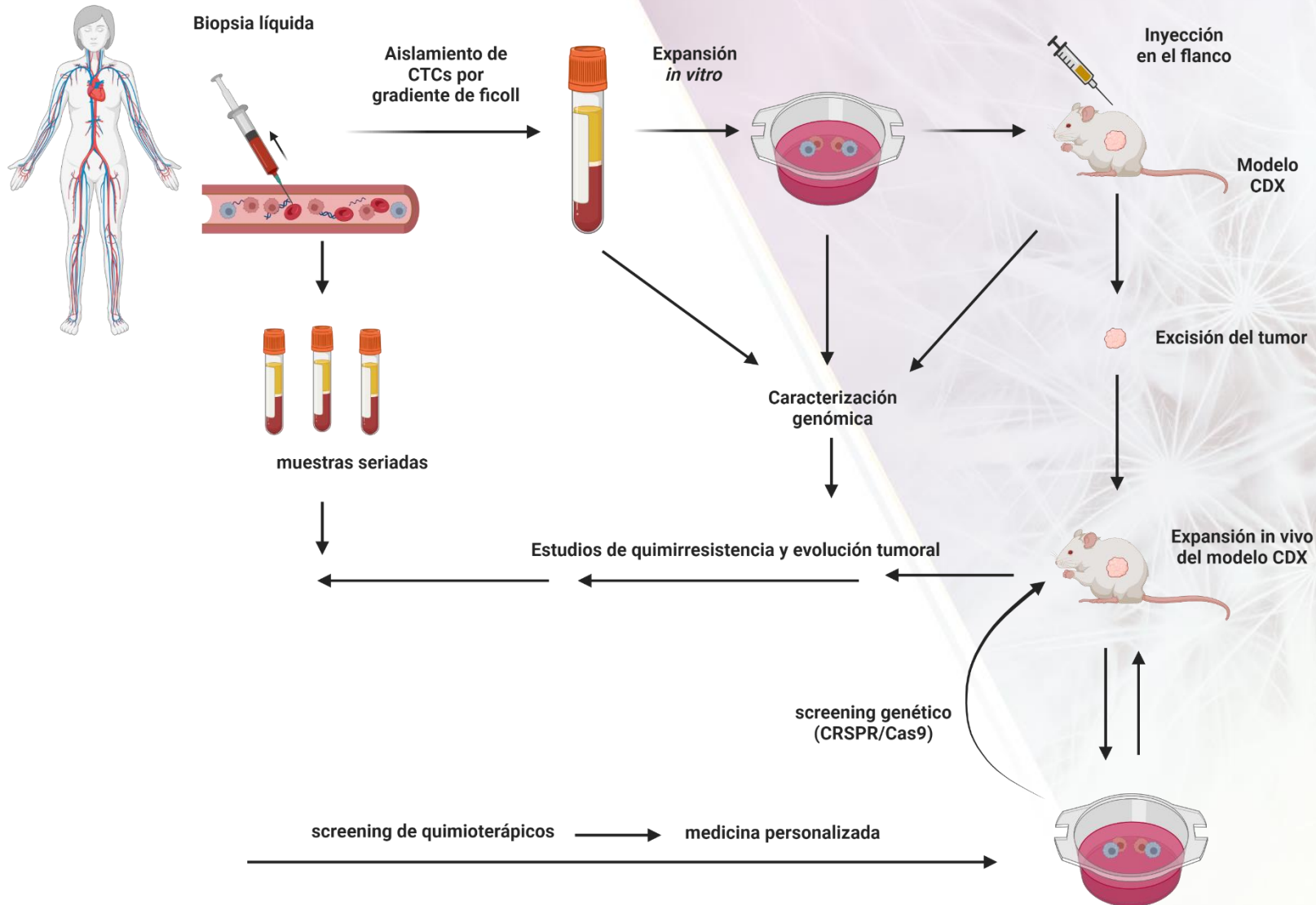
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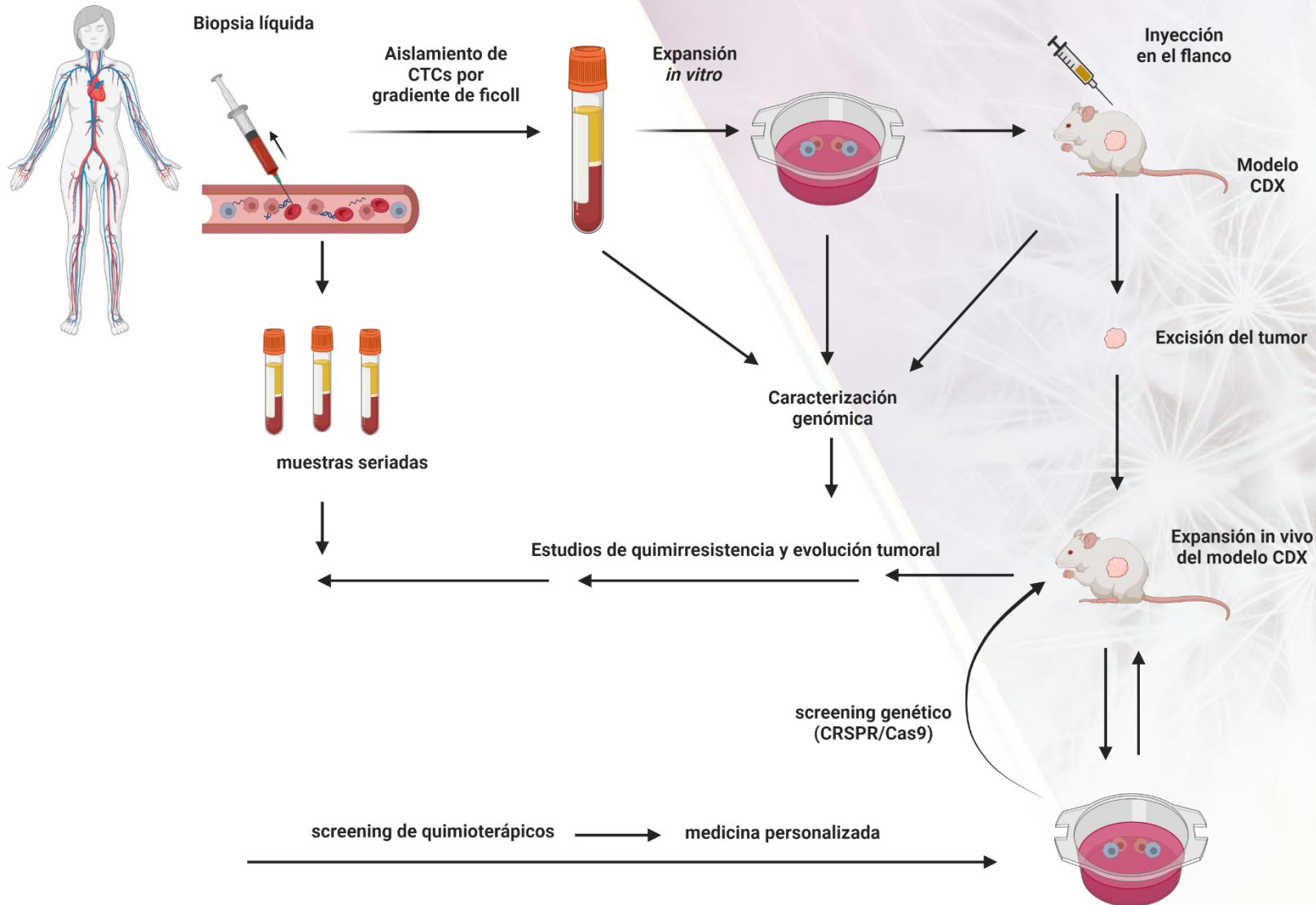
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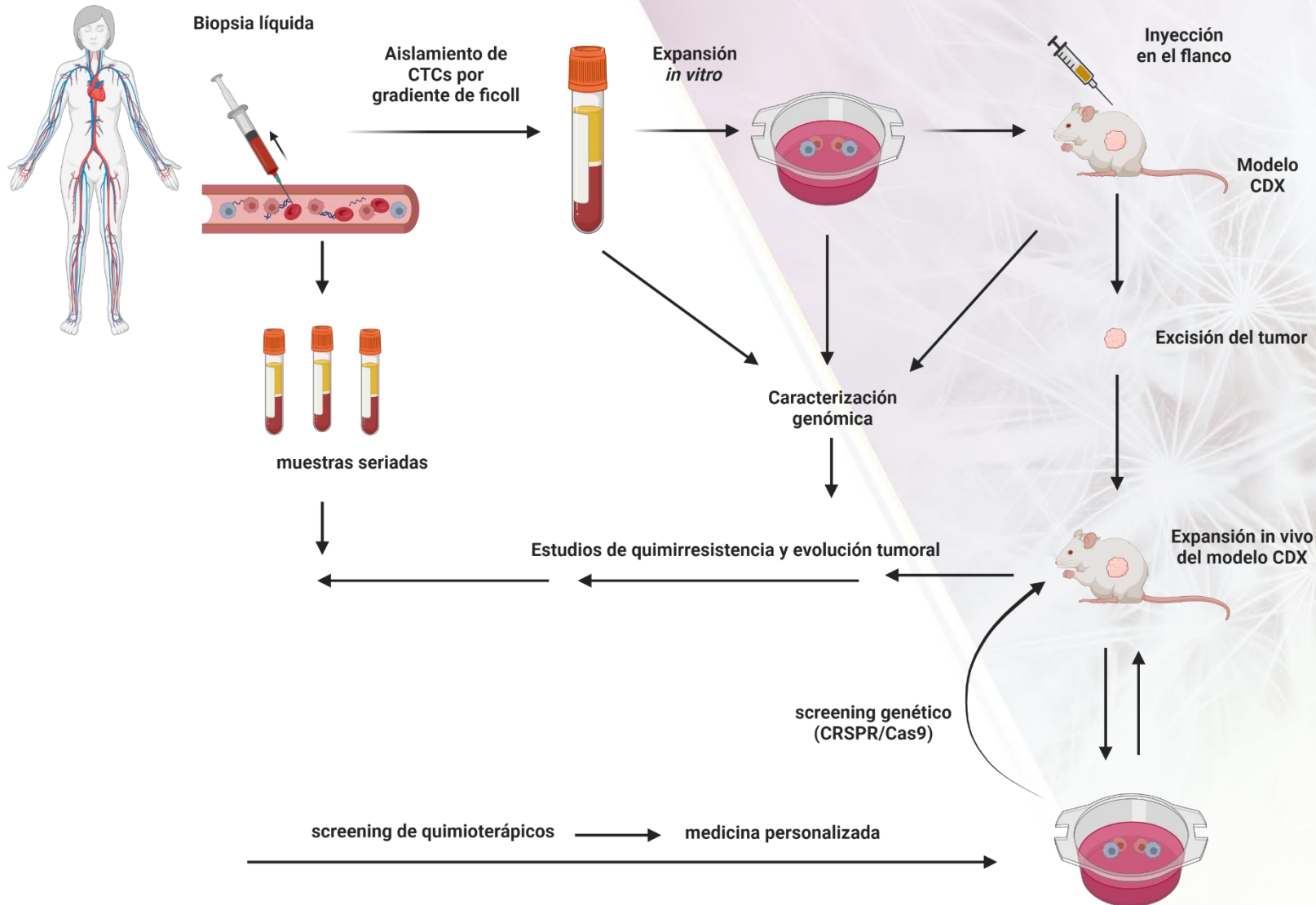
Los modelos basados en el co-cultivo de CTCs y CDX tienen un elevado potencial traslacional



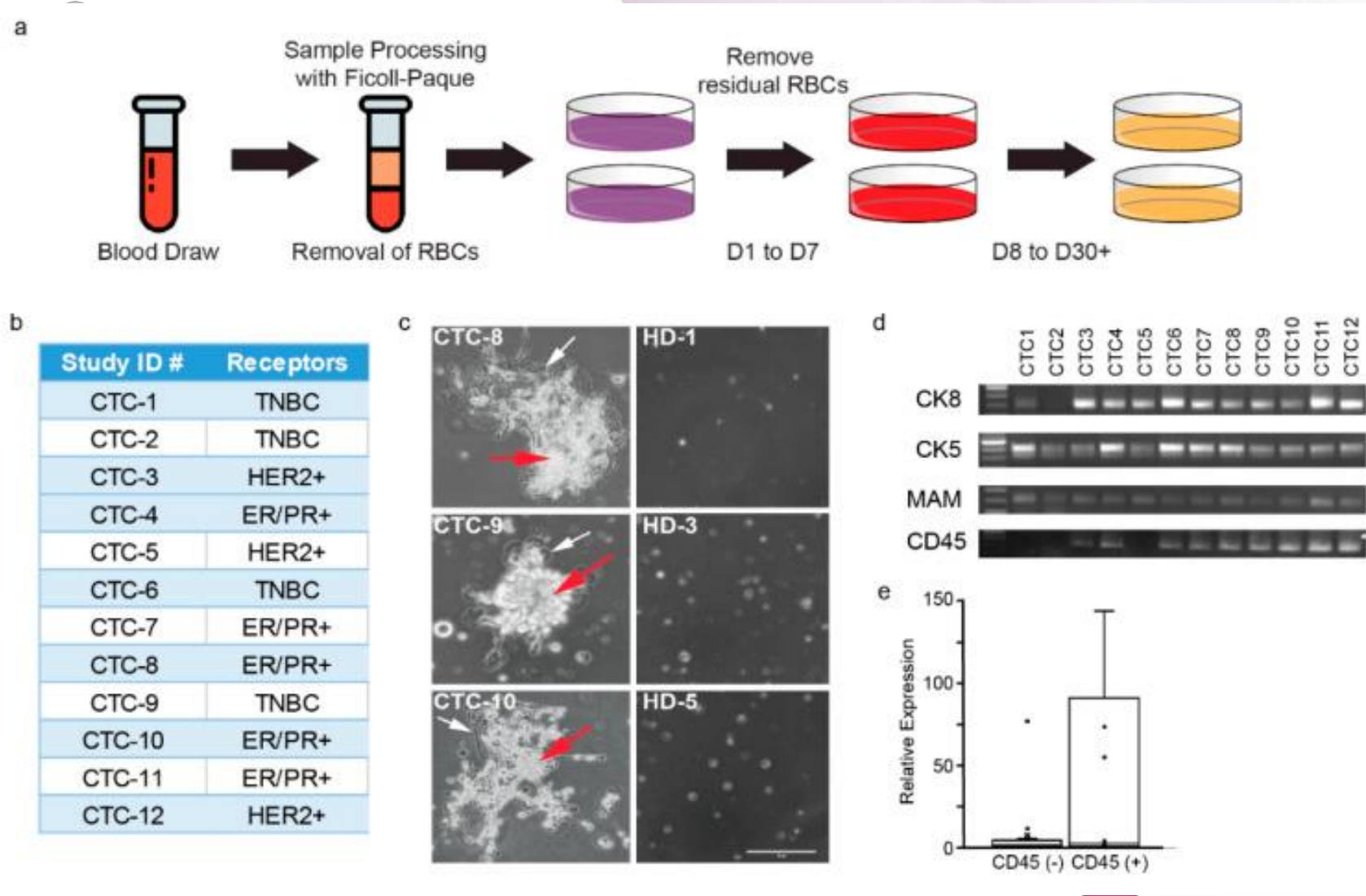
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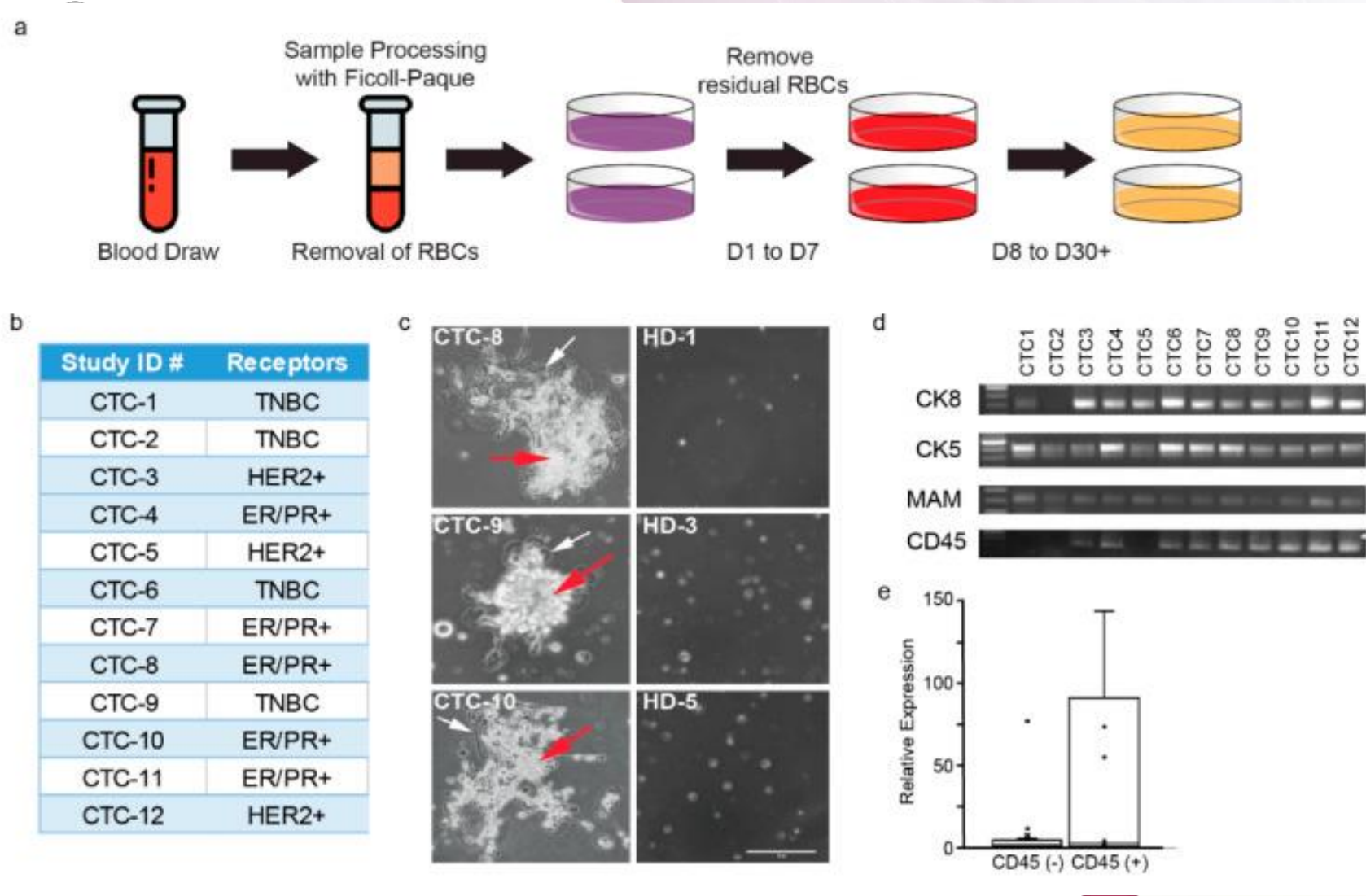
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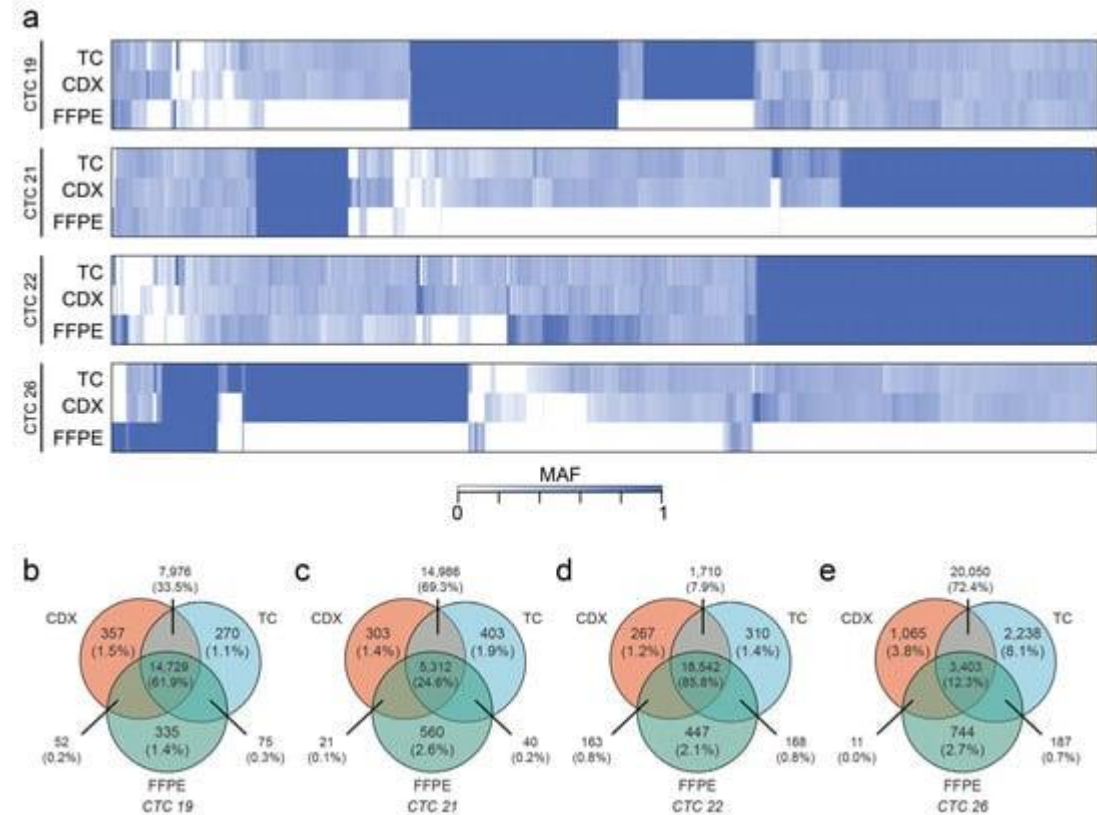
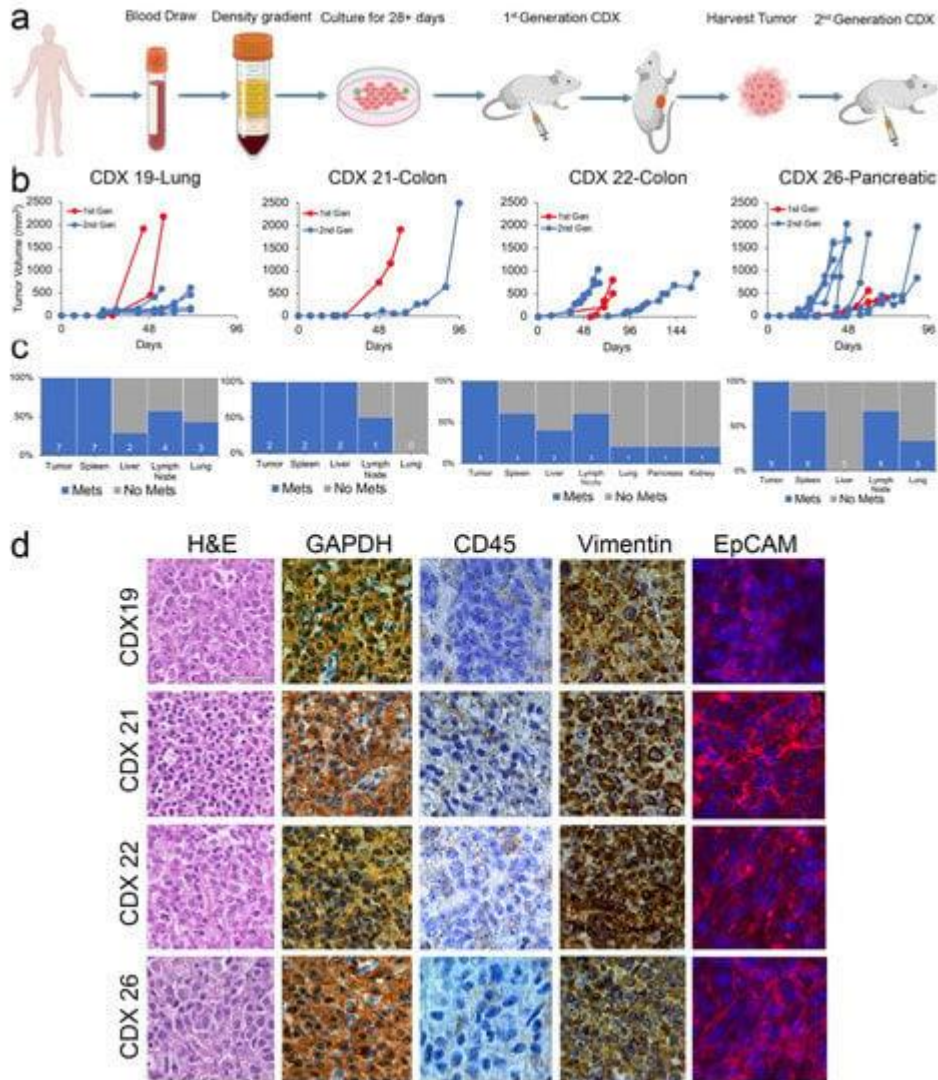
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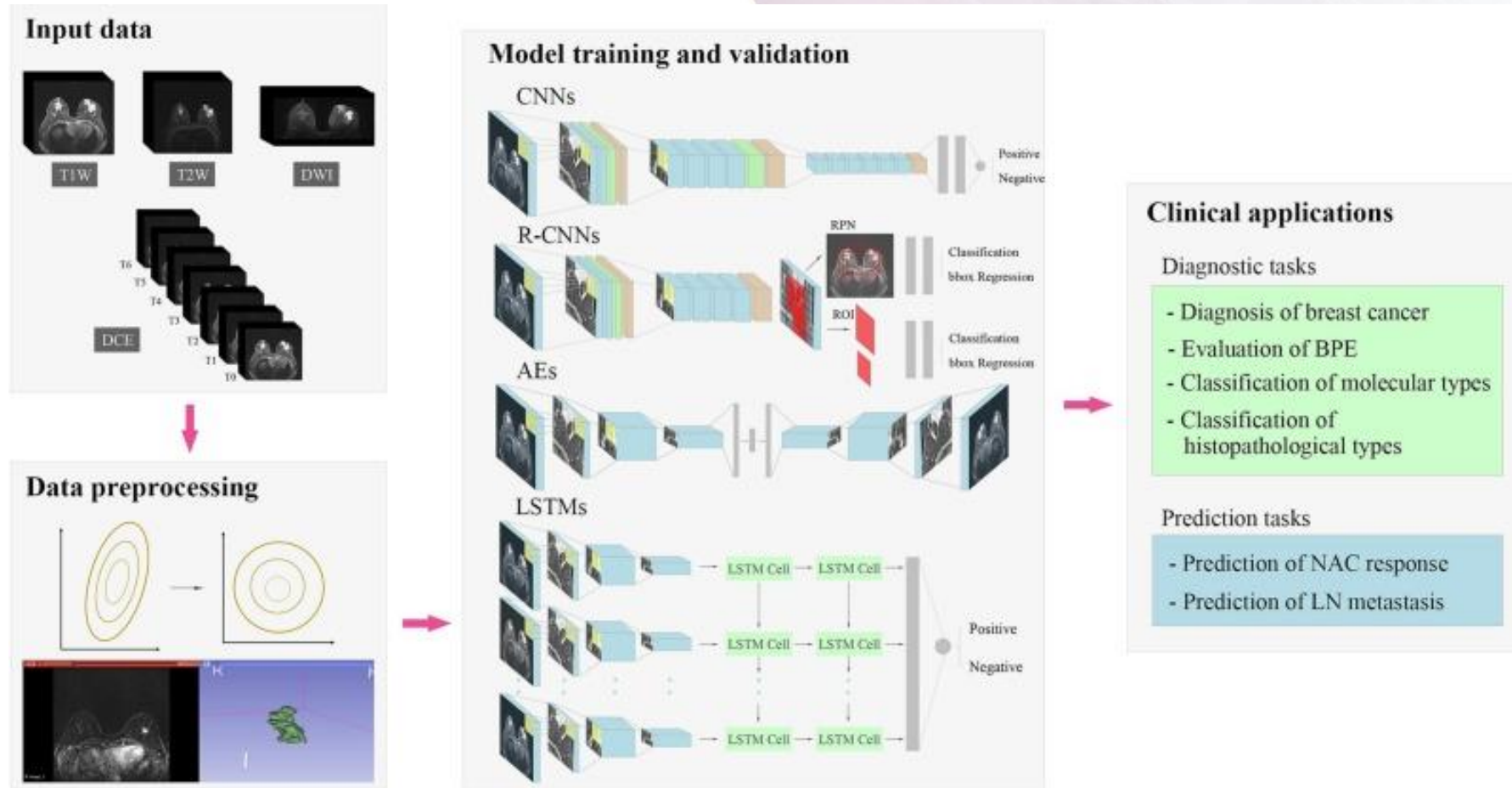
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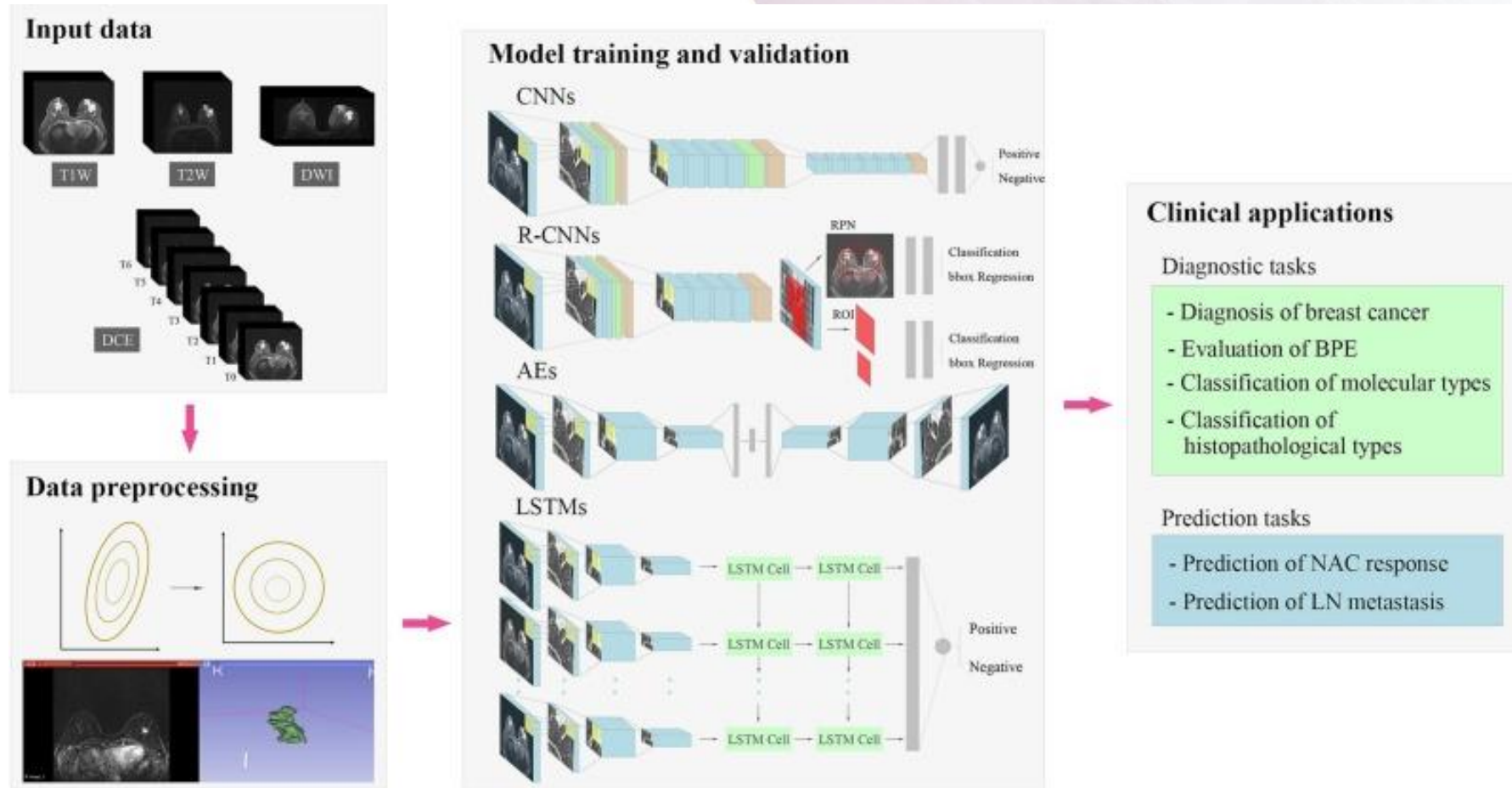
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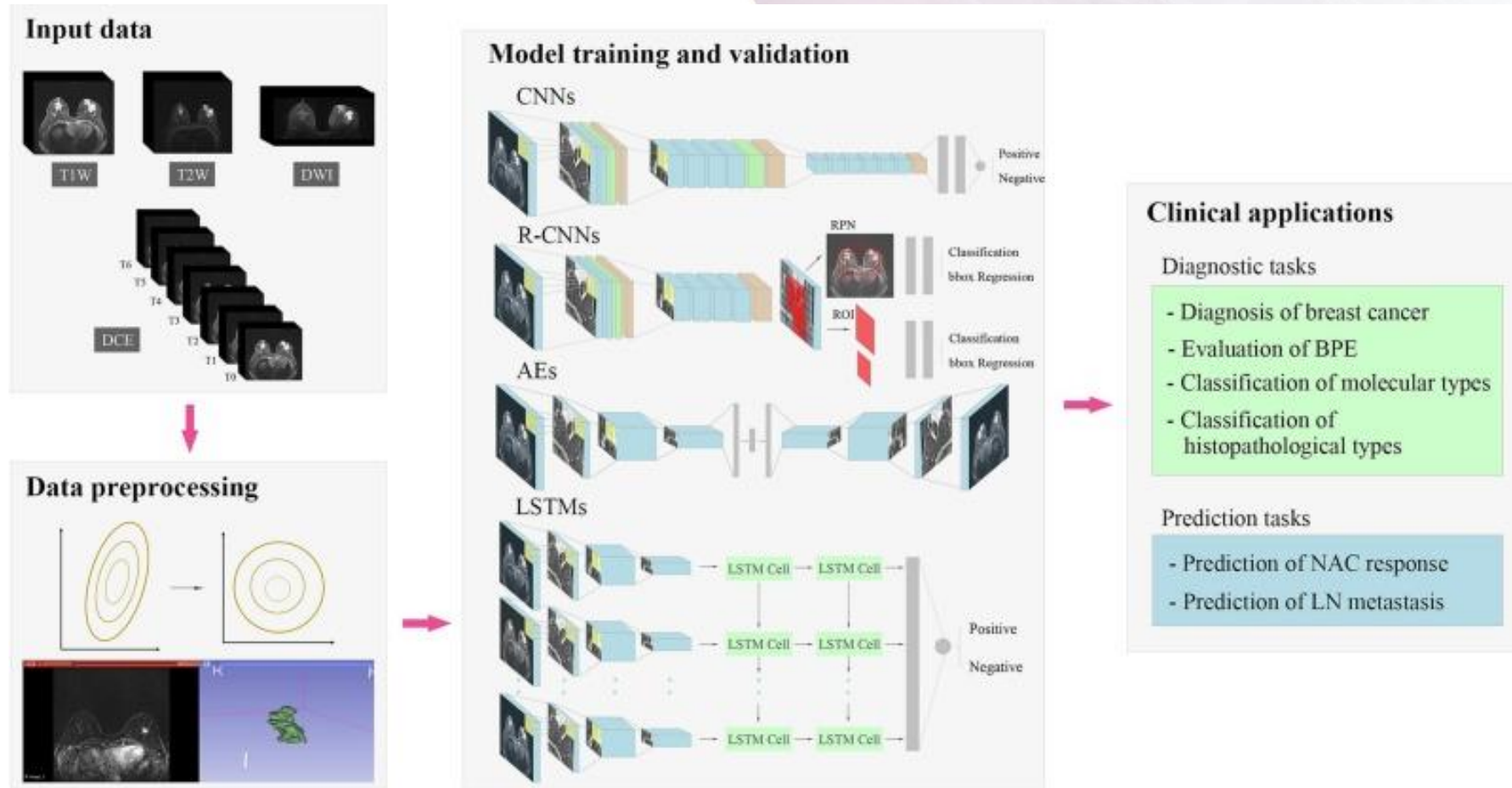
Los modelos computacionales e inteligencia artificial son potentes herramientas de aplicación clínica y...



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...experimental



HORIZON
2020

Generation of the CanPath prototype - a platform for predictive cancer pathway modeling

Ficha informativa

Información del proyecto

CanPathPro

Identificador del acuerdo de subvención:
686282



DOI
[10.3030/686282](https://doi.org/10.3030/686282)

Proyecto cerrado


Fecha de inicio
1 Marzo 2016

Fecha de
finalización
30 Noviembre 2021

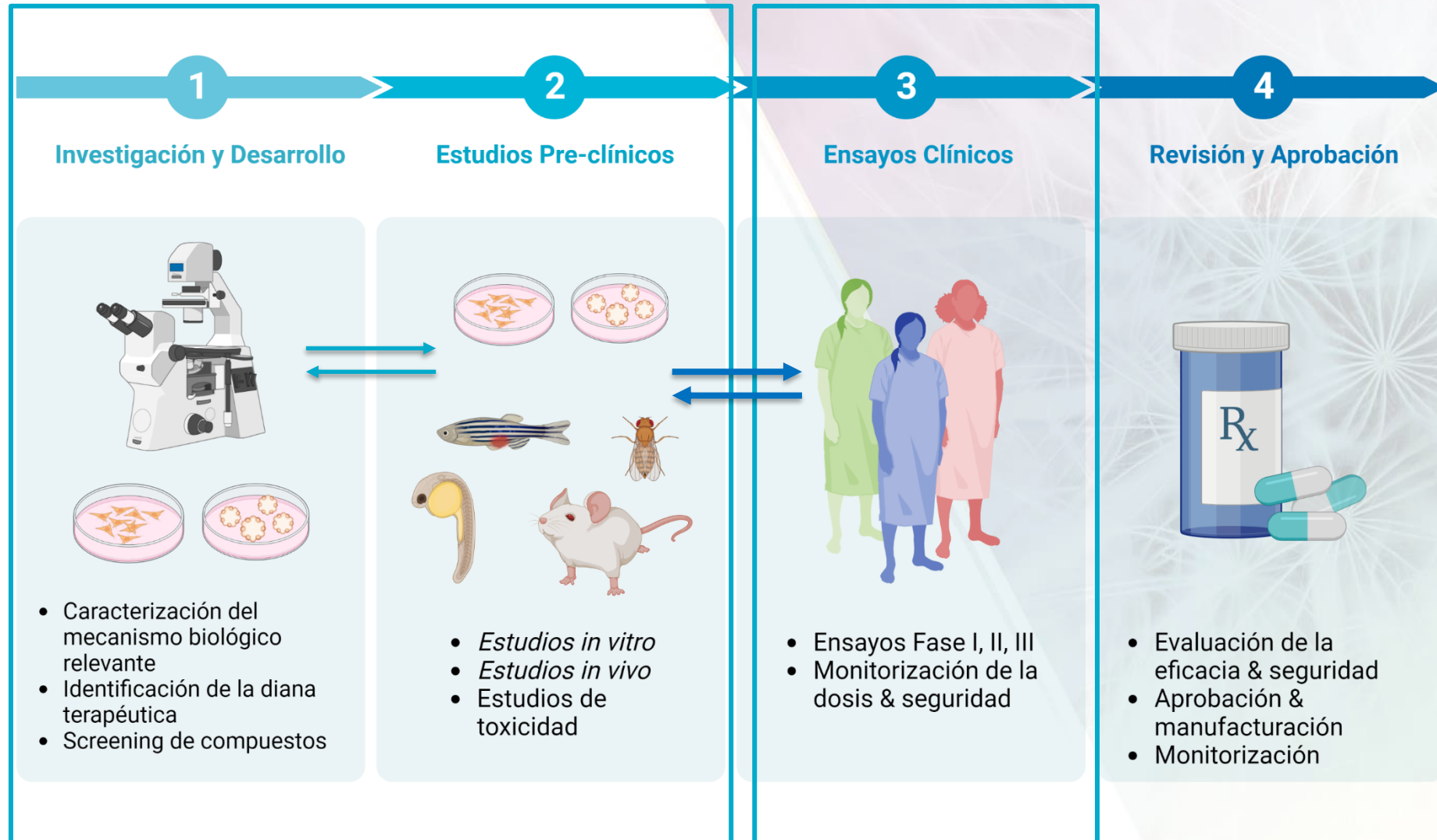
Financiado con arreglo a
INDUSTRIAL LEADERSHIP - Leadership in
enabling and industrial technologies -
Biotechnology

Coste total
€ 10 713 058,48

Aportación de la
UE
€ 9 862 545,98

Coordinado por
ALACRIS THERANOSTICS
GMBH
 Alemania

Modelos preclínicos de cáncer



RAGMA
23 16ª Revisión Anual
GEICAM de Avances
en Cáncer de Mama

Realidades y esperanzas

Muchas gracias

Dra. Laura Vera Ramírez
Área de Medicina Genómica (GENYO). Universidad de Granada

Organizado por:

GEICAM
investigación en
cáncer de mama