

Validación preclínica de la actividad antitumoral de nuevos compuestos

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Unidad NanoDrug

WORKSHOP INVESTIGACIÓN FACULTAD DE FARMACIA 2024

“La Investigación nuestro mejor medicamento”

Salón de Grados, 25 Noviembre 2024

SOPORTE TÉCNICO



Almudena Ruíz García



Antonio Martínez



Alberto Ocaña



Andrés Garzón



Carlos Alonso



SÍNTESIS DE POLÍMEROS



Felipe de la Cruz

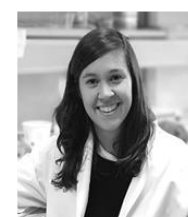


Carmen Moya



Eleonora Iannuzzi

NANOTECNOLOGÍA



Mar Noblejas



Cristina Blasco



María Arenas



Irene Sevilla

BIOSENSORES



Diego Herrera



Consuelo Ripoll



Sofía Blas Gómez



María Rosell



Cristina Martín



Iván Bravo

DISEÑO Y SÍNTESIS



Elena Domínguez

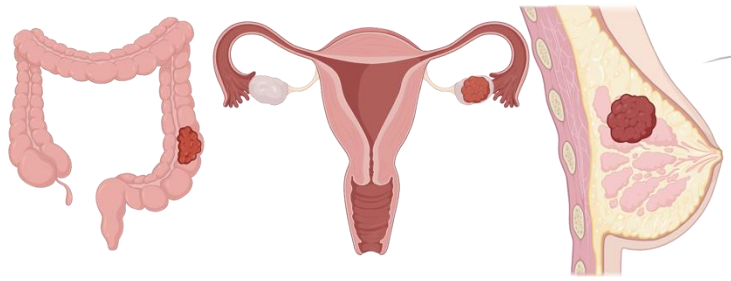


Almudena del Campo

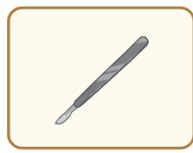


Beatriz Cuartero

Tumores sólidos



Terapias estándar



Cirugía

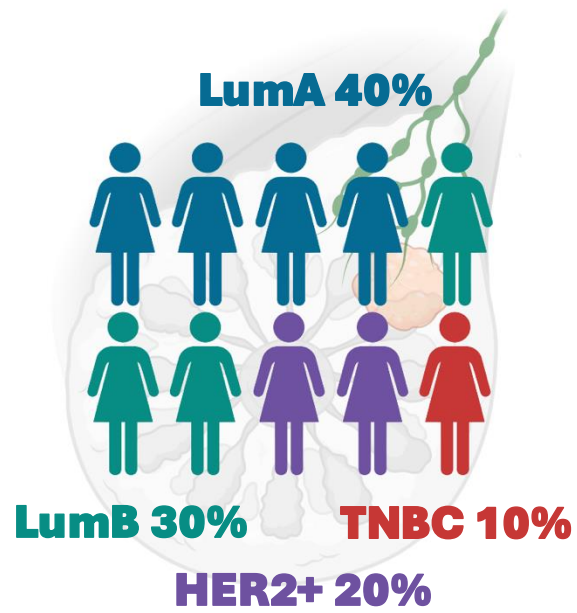


Radioterapia



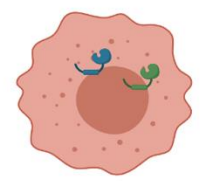
Quimio

Subtipos moleculares de cáncer de mama



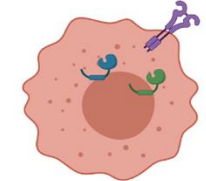
Luminal A

ER+/PR+/HER2-



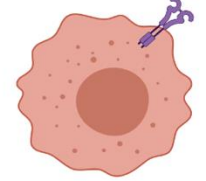
Luminal B

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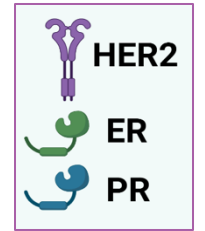
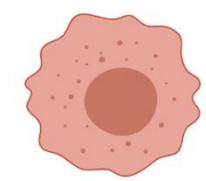
HER2+

ER-/PR-/HER2+

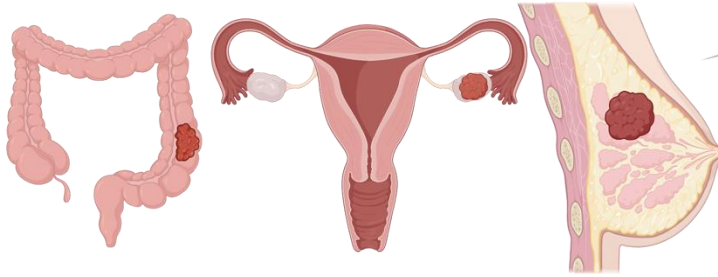


CMTN

ER-/PR-/HER2-



Tumores sólidos



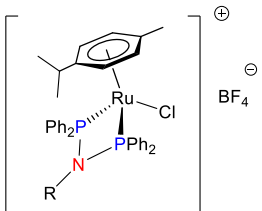
Terapias estándar



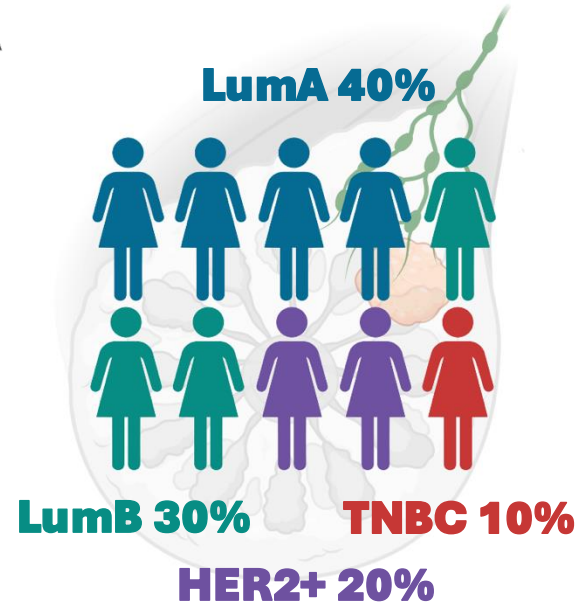
Cirugía Radioterapia Quimio

Nuevas estrategias

Mejora de los agentes quimioterápicos

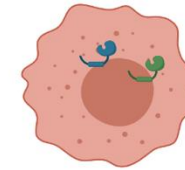


Subtipos moleculares de cáncer de mama



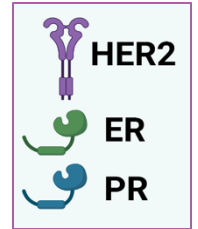
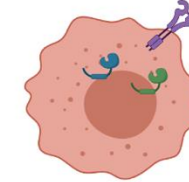
Luminal A

ER+/PR+/HER2-



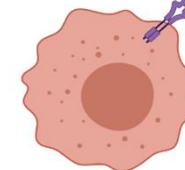
Luminal B

ER+/PR+/HER2+



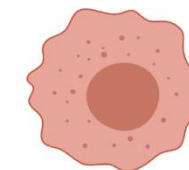
HER2+

ER-/PR-/HER2+

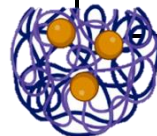


CMTN

ER-/PR-/HER2-



Uso de terapias dirigidas y nanotecnología

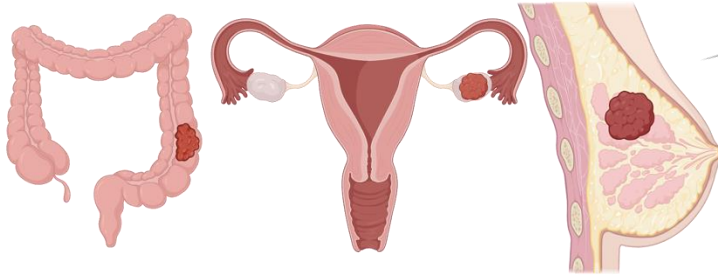


Combinación de fármacos

SYNERGY
1+1=3



Tumores sólidos



Terapias estándar



Cirugía

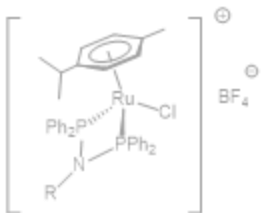


Radioterapia



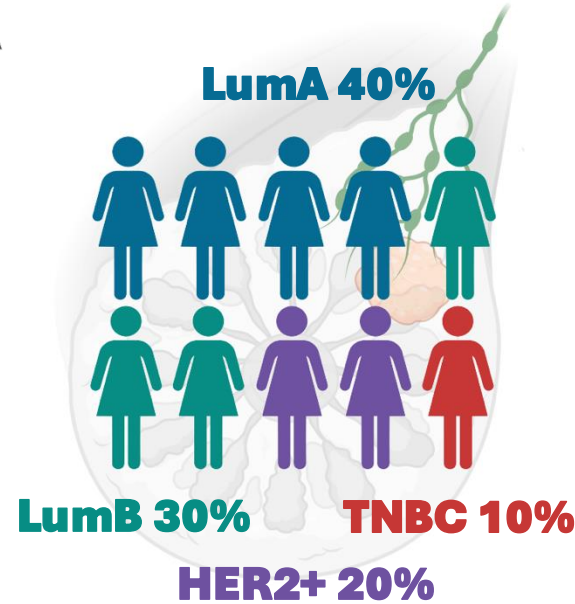
Quimio

Nuevas estrategias



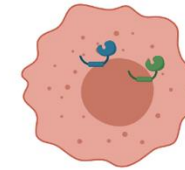
Mejora de los agentes quimioterápicos

Subtipos moleculares de cáncer de mama



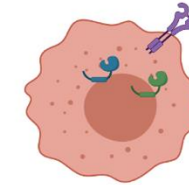
Luminal A

ER+/PR+/HER2-



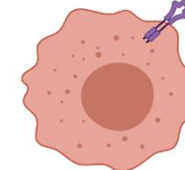
Luminal B

ER+/PR+/HER2+



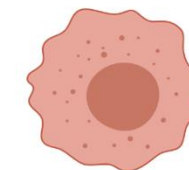
HER2+

ER-/PR-/HER2+

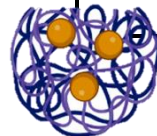


CMTN

ER-/PR-/HER2-



Uso de terapias dirigidas y nanotecnología

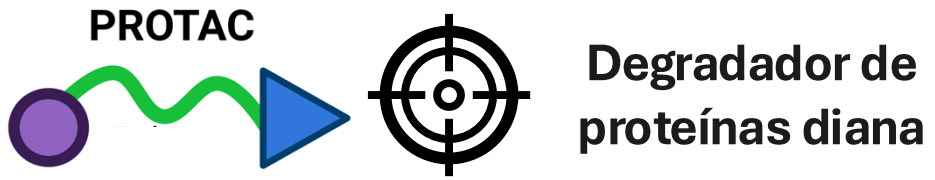


Combinación de fármacos

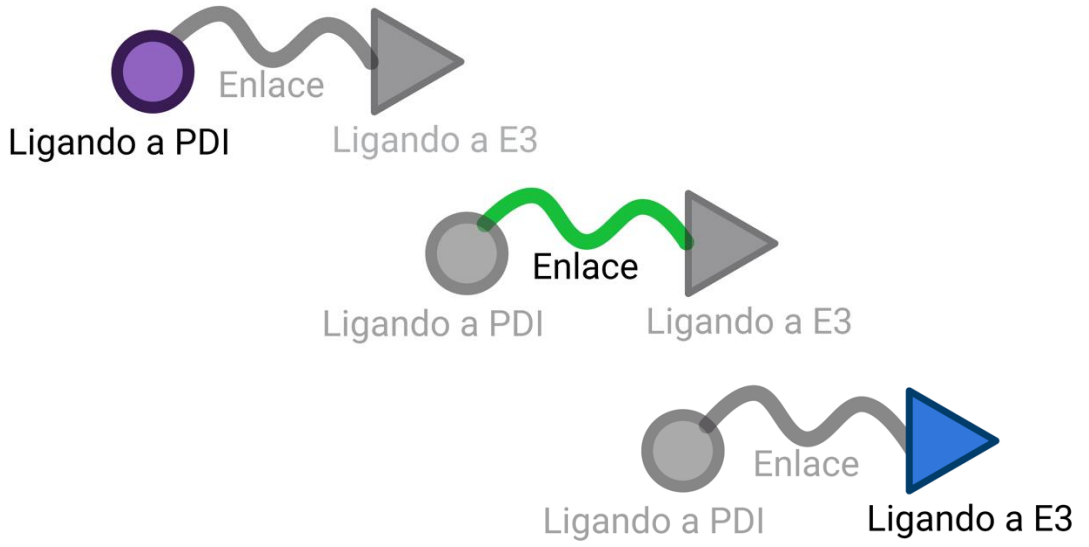
SYNERGY
1+1=3



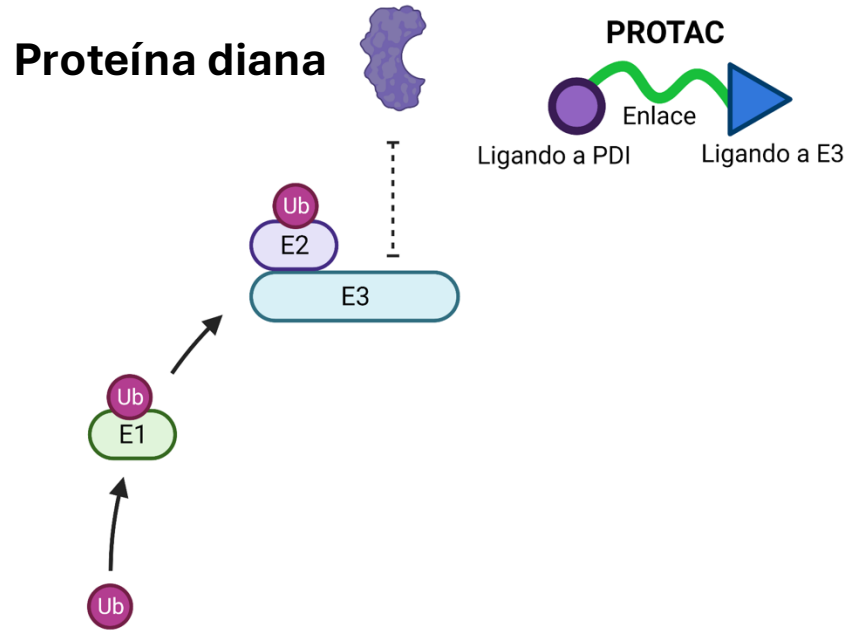
Mejora de las terapias dirigidas



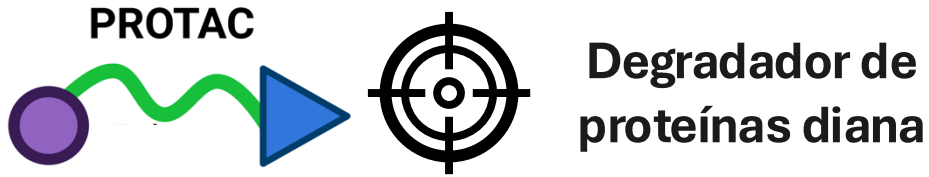
Proteolysis targeting chimeras



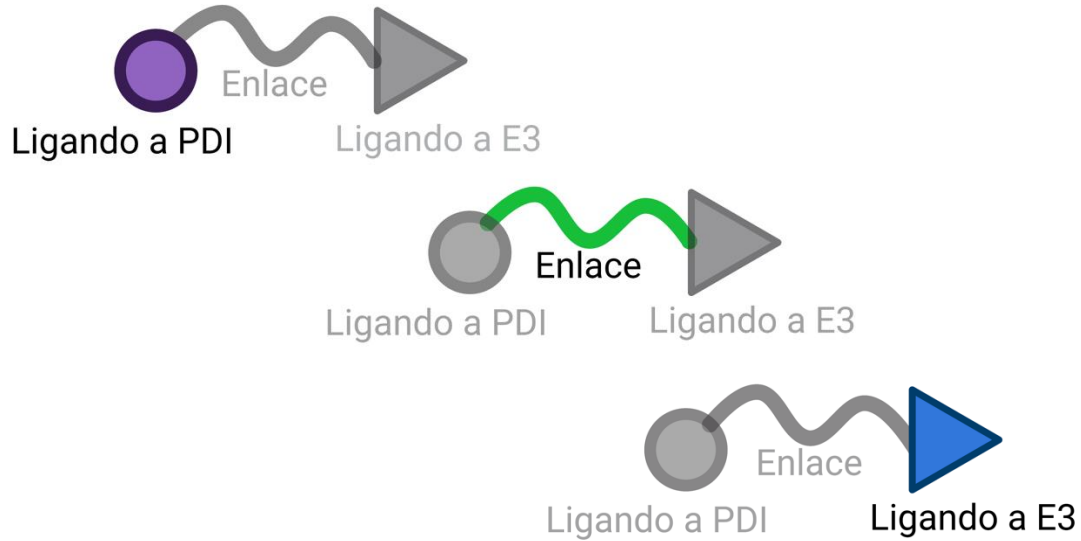
Mecanismo de acción



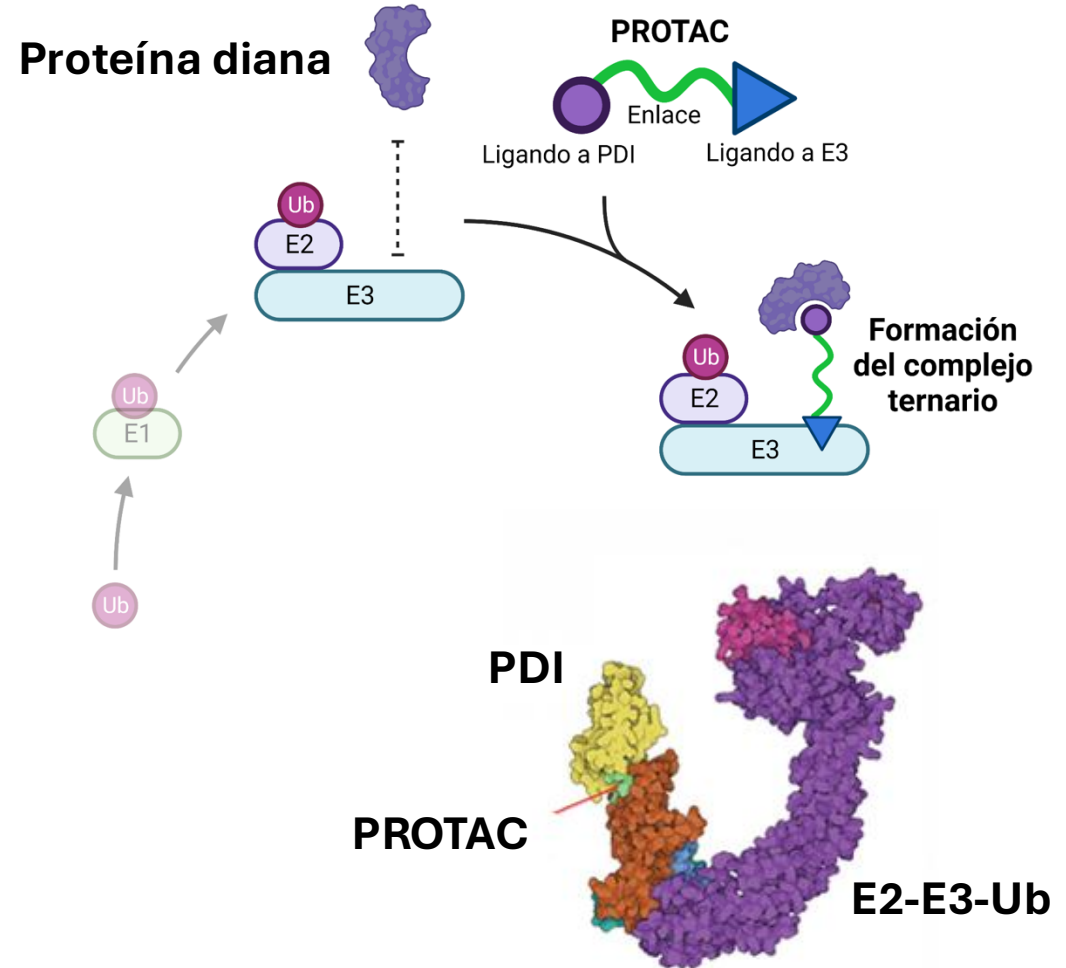
Mejora de las terapias dirigidas



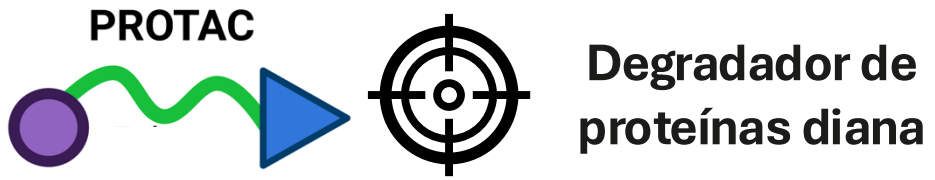
Proteolysis targeting chimeras



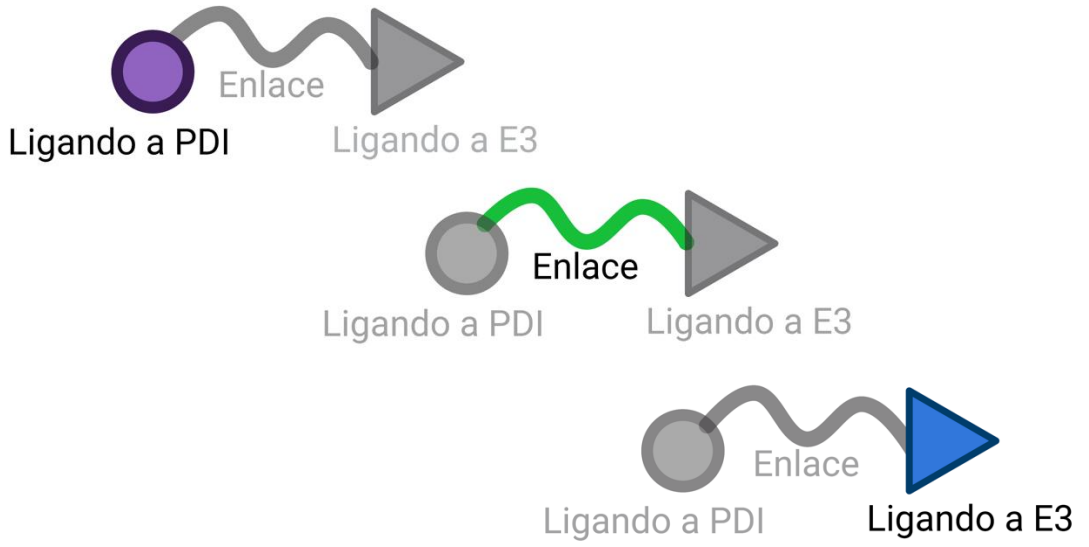
Mecanismo de acción



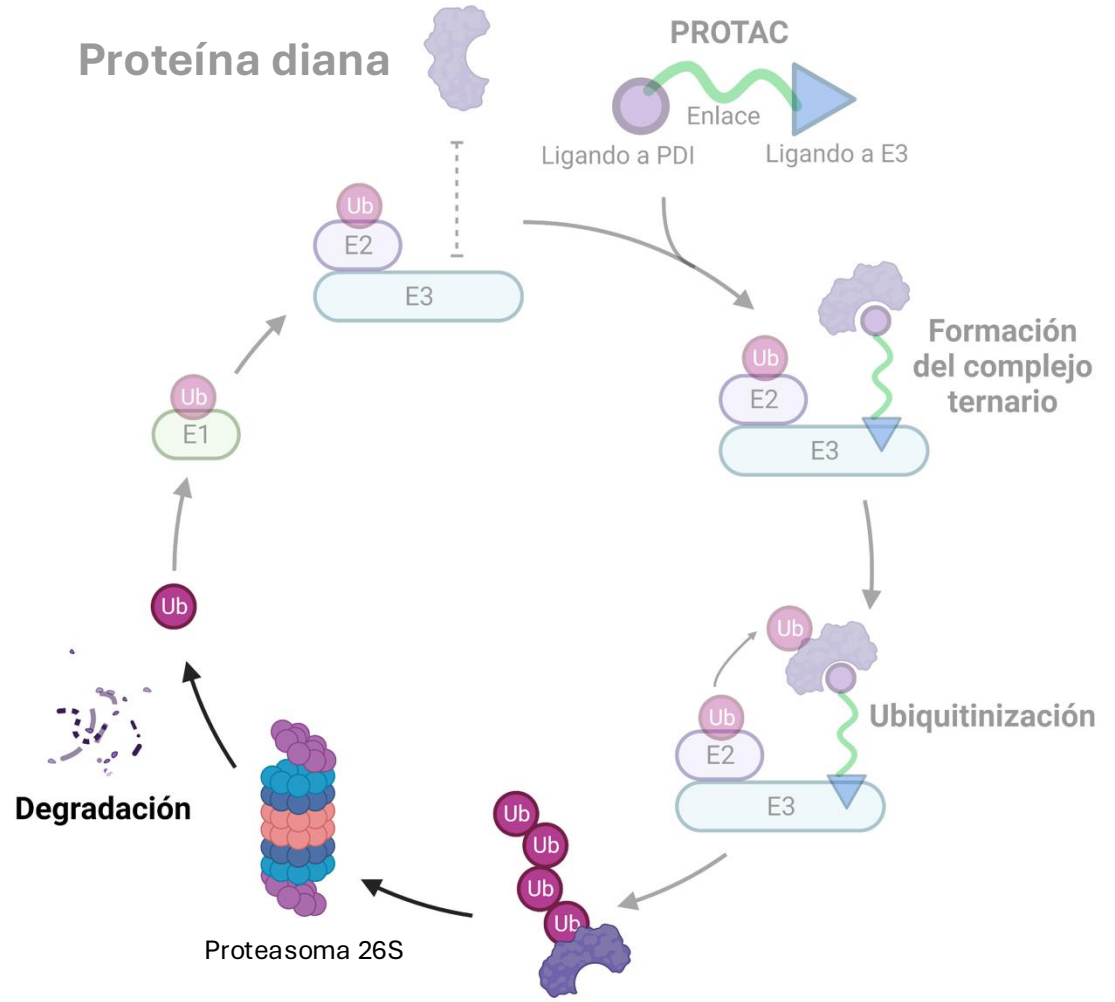
Mejora de las terapias dirigidas



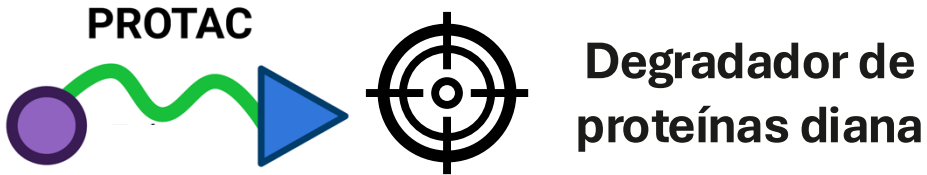
Proteolysis targeting chimeras



Mecanismo de acción



Mejora de las terapias dirigidas



Proteolysis targeting chimeras

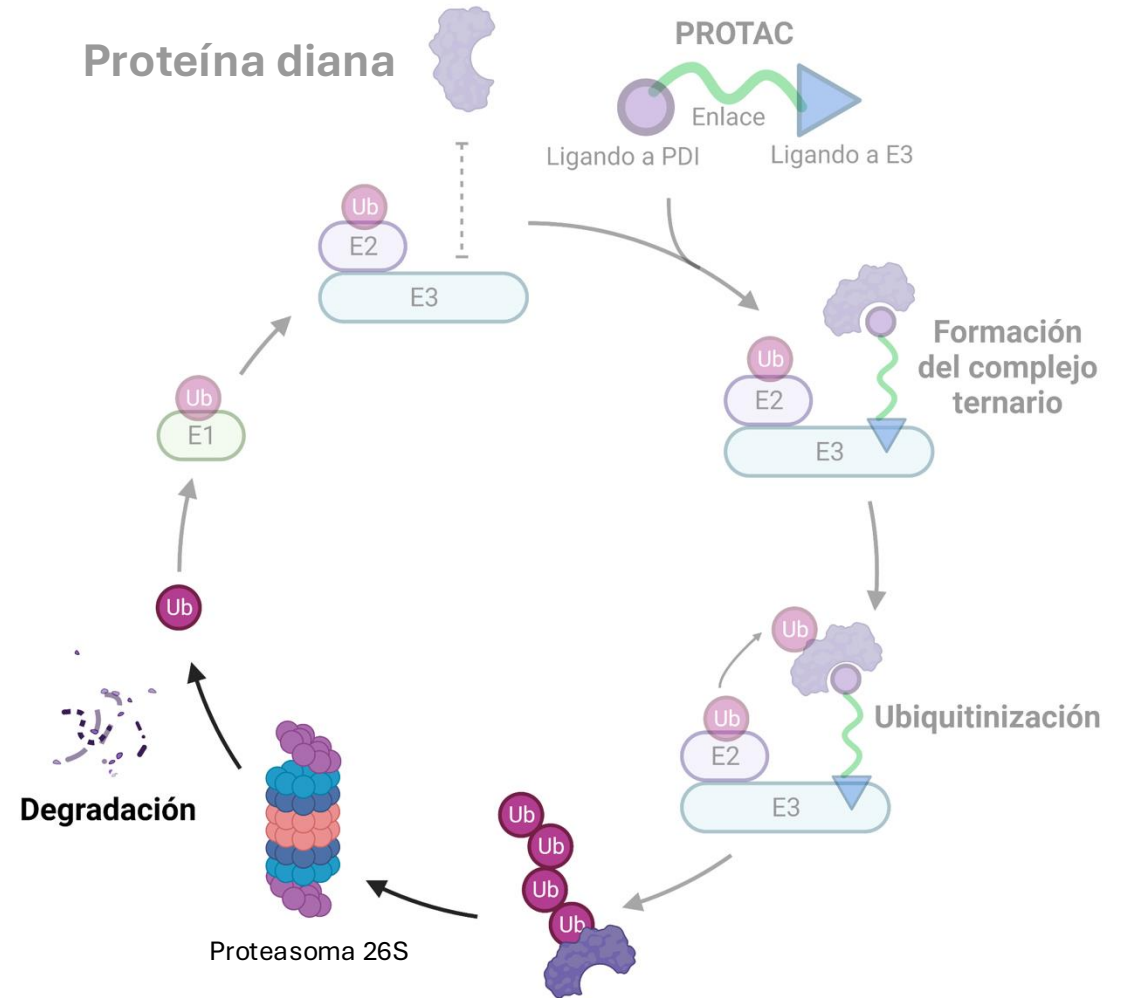


- Degradar todo tipo de proteínas
- Periodo de acción más largo
- Ayuda a superar resistencias
- Dosis más bajas

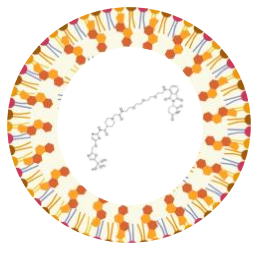


- Efectos tóxicos por no ser específico
- Moléculas muy grandes poco permeables

Mecanismo de acción



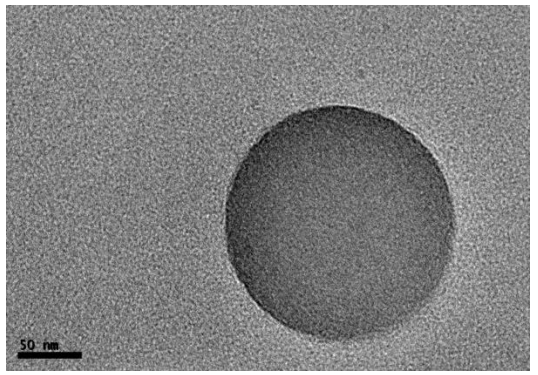
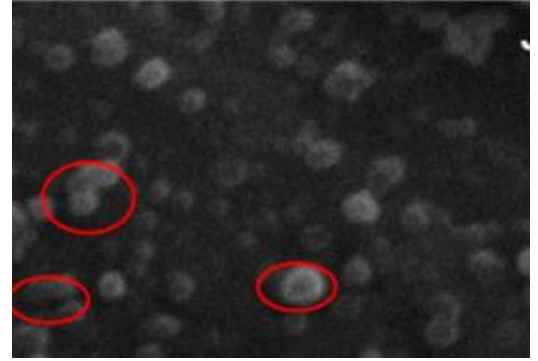
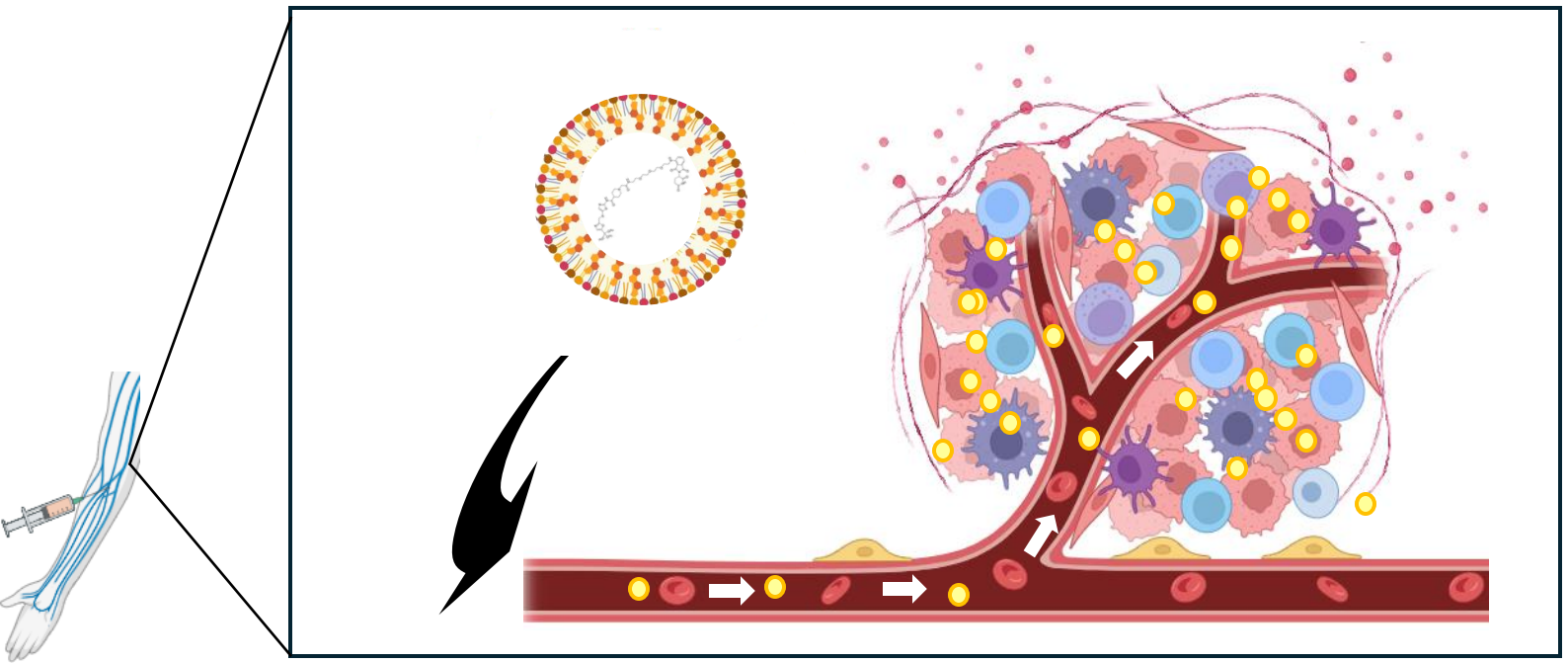
~100 nm



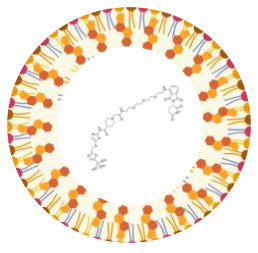
INCREMENTAR LA BIODISPONIBILIDAD

1. PROTECCIÓN

2. DIRECCIÓN

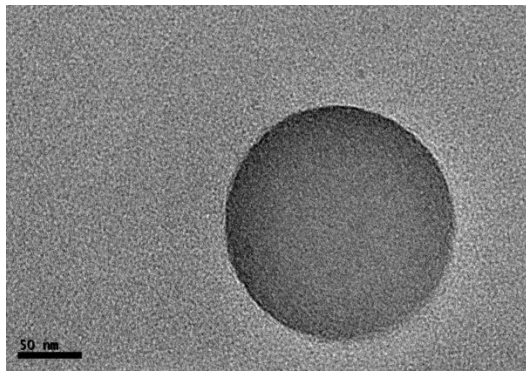
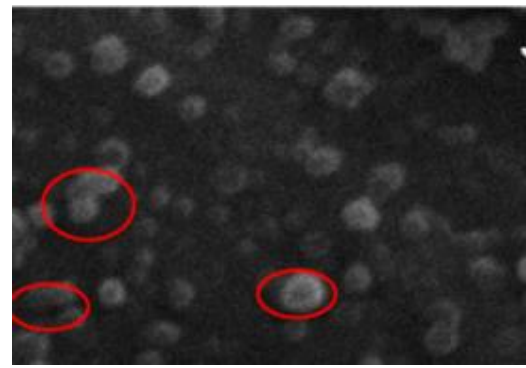
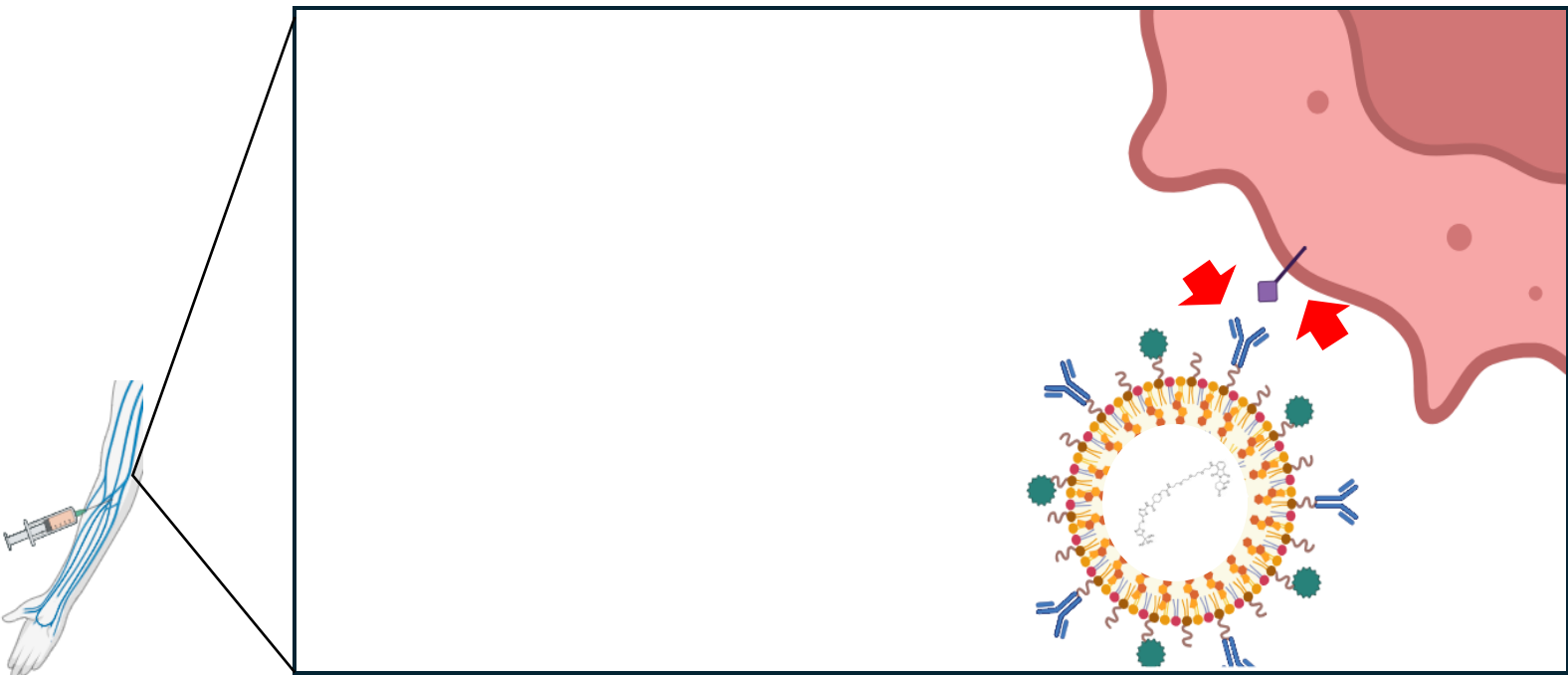


~100 nm

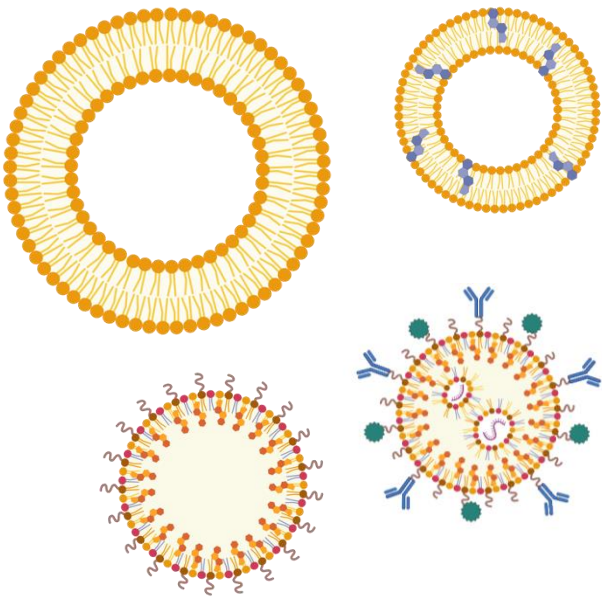


INCREMENTAR LA BIODISPONIBILIDAD

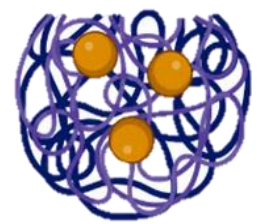
- 1. PROTECCIÓN
- 2. DIRECCIÓN



NANOMEDICINAS



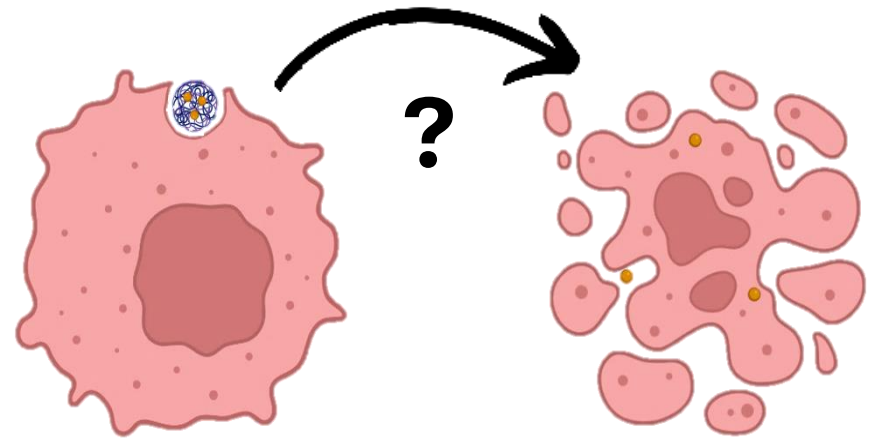
NPS BASE LIPÍDICA



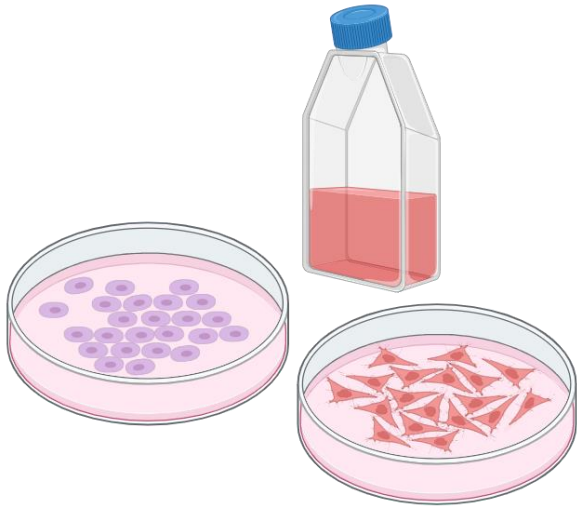
NPS BASE POLIMÉRICA



HIDROGELES

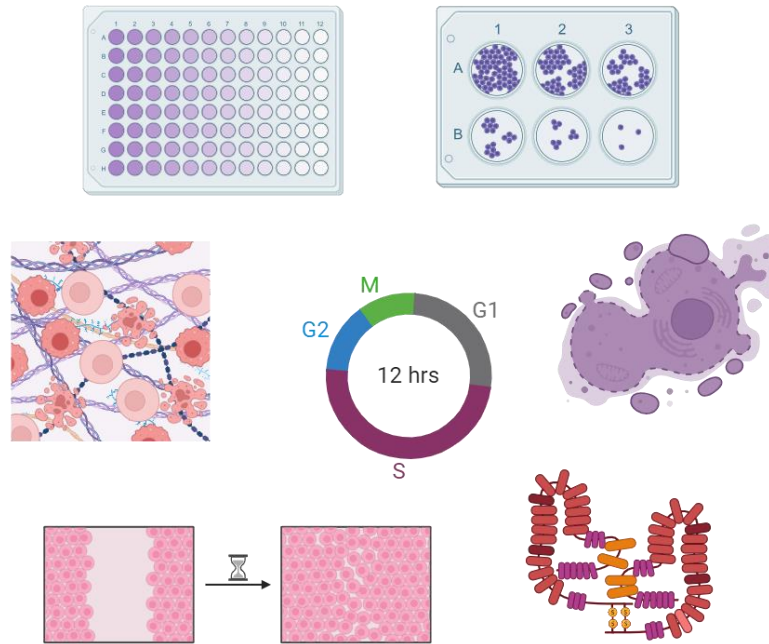


MODELOS CELULARES



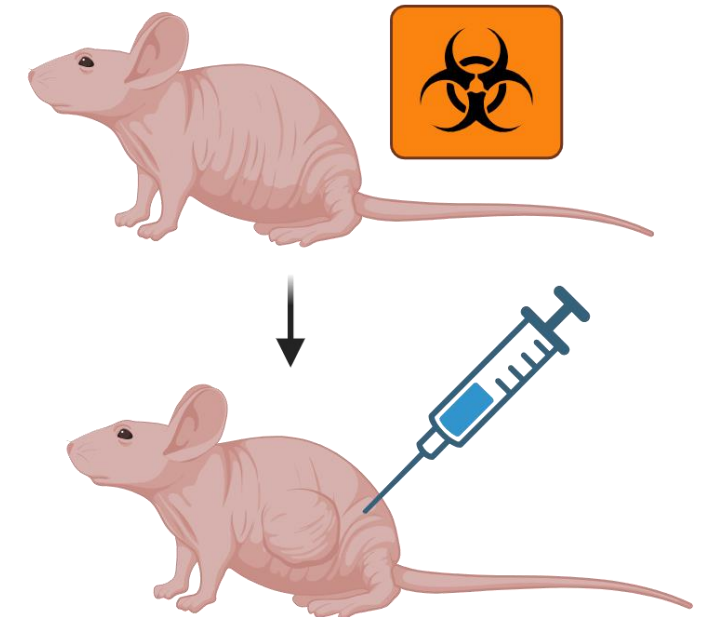
- Modelos células tumorales
- Modelos células sanas

ENSAYOS *IN VITRO*

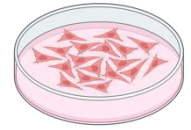


- Análisis de actividad antitumoral
- Análisis del mecanismo de acción

ENSAYOS *IN VIVO*

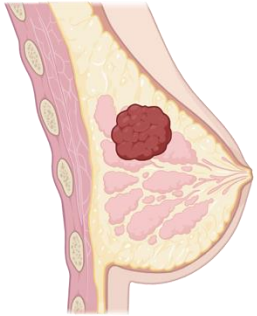


- Estudio piloto de toxicidad inicial
- Ensayos del efecto antitumoral

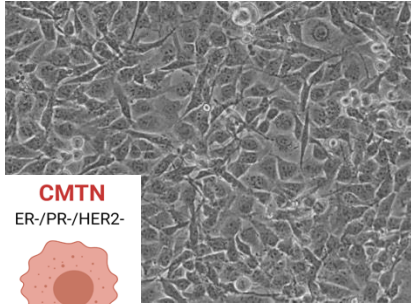


CÉLULAS TUMORALES

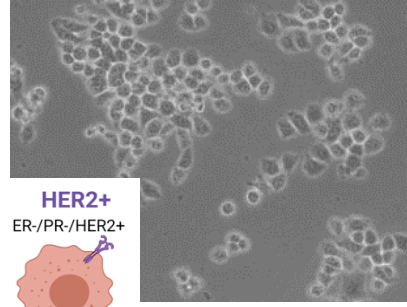
Cáncer de mama



MDA-MB-231



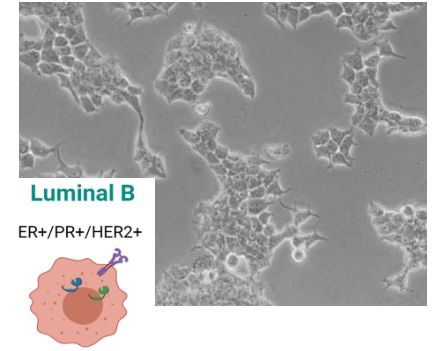
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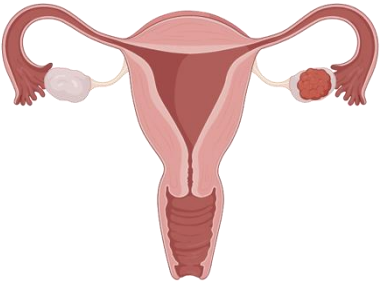
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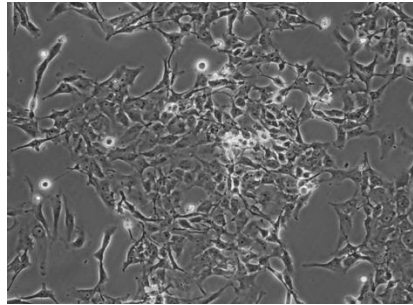
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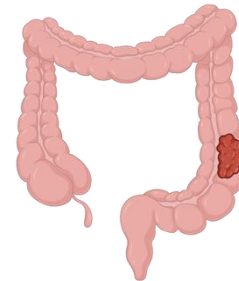
Cáncer de ovario



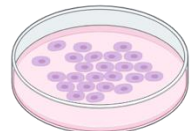
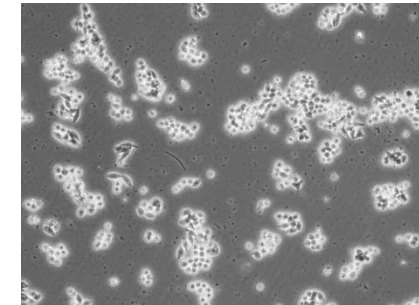
OVCAR8



Cáncer colorrectal

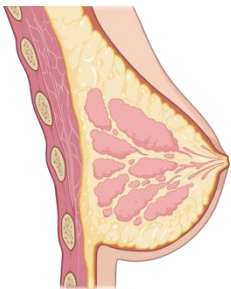


SW620

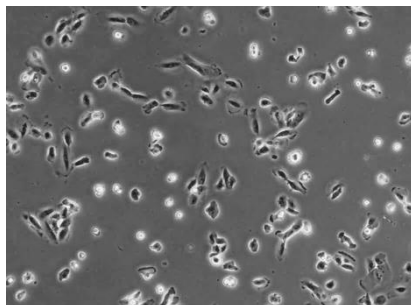


CÉLULAS SANAS

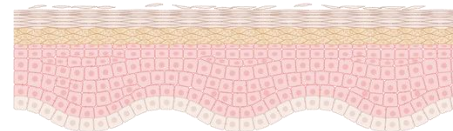
Epitelio mamario



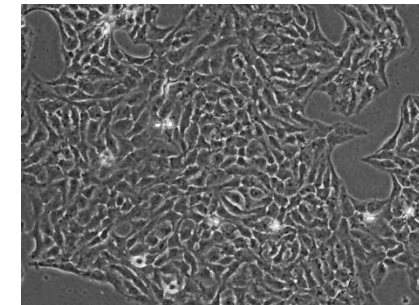
MCF10A



Epitelio de la piel

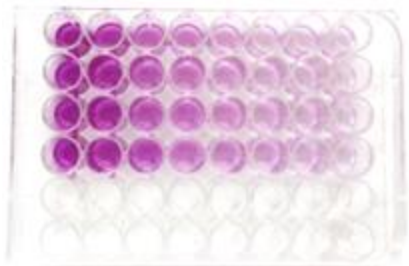


HaCaT

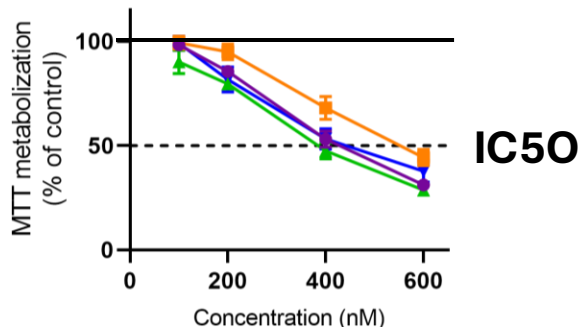


Ensayos de viabilidad celular

Titulación de nuevos fármacos: Curvas dosis-respuesta



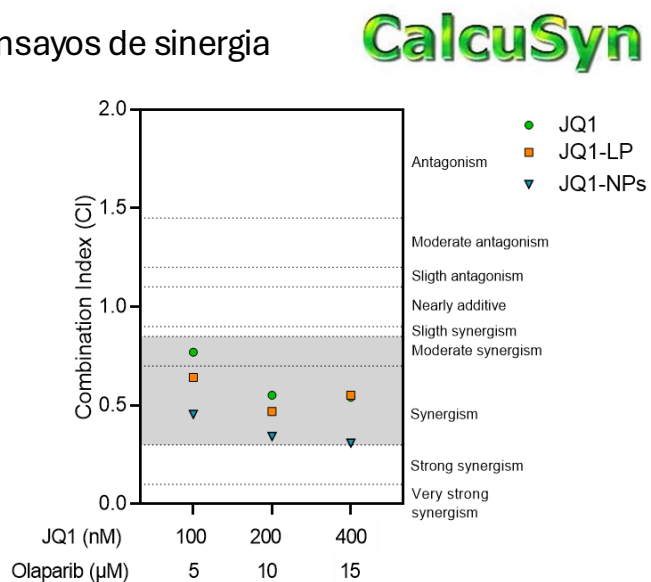
MTT
CellTiter Blue



Combinación de fármacos: ensayos de sinergia

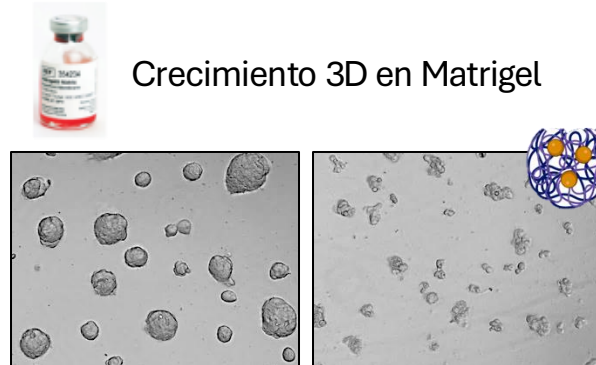


Obtención de **índices de combinación (CI)** entre dosis de fármacos

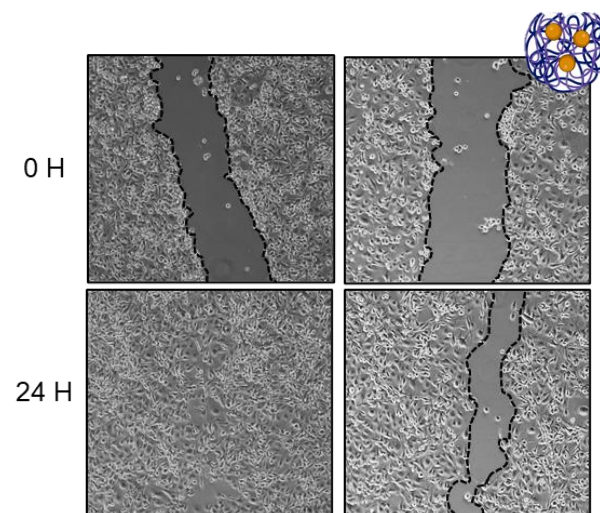


Ensayos de invasión en 3D

Crecimiento 3D en Matrigel

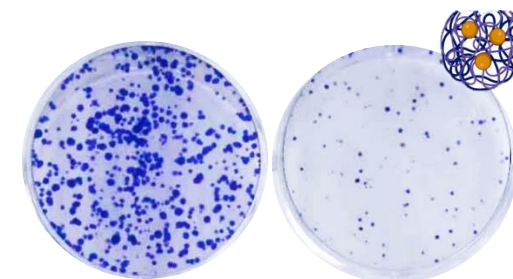


Migración por cierre de herida



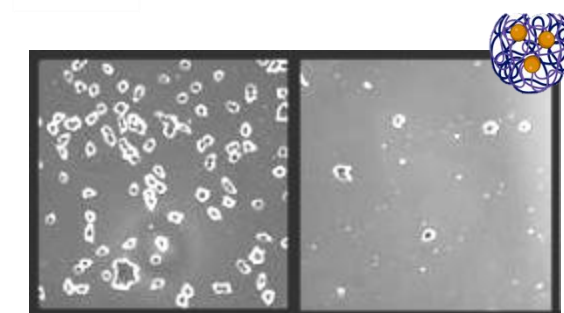
Reanudación: clonógenicos

Capacidad de generar clones tras tratamiento

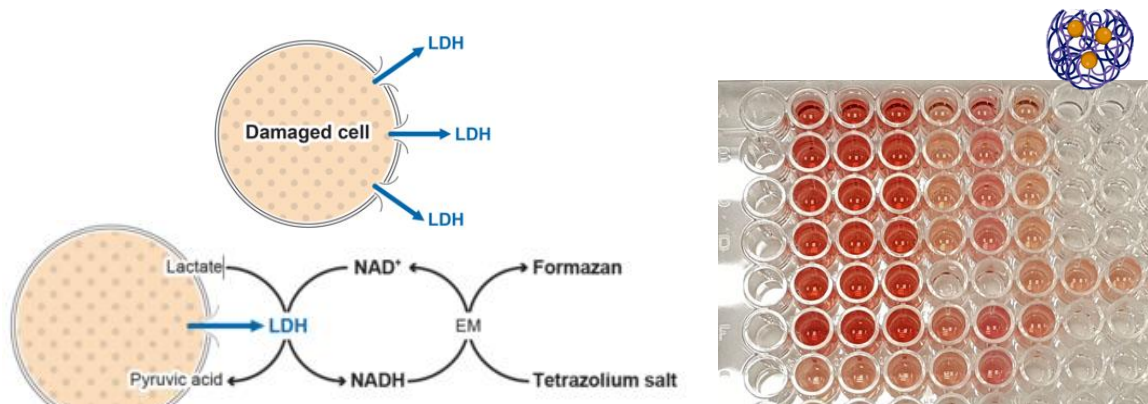


Ensayos de adhesión

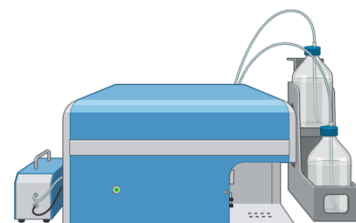
Capacidad de adhesión a la glucoproteína fibronectina



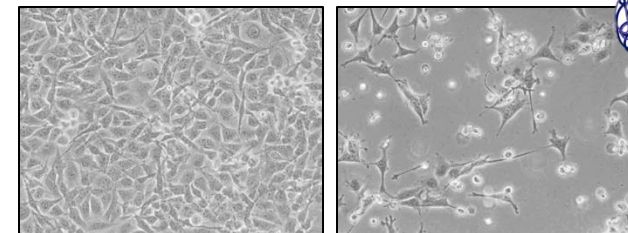
Ensayos de citotoxicidad: LDH



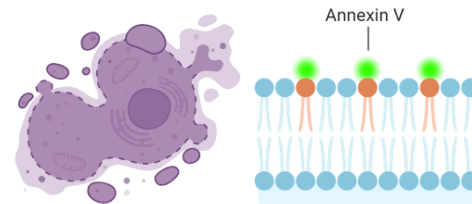
Análisis de la muerte y parada del ciclo celular



Citometría de flujo



APOPTOSIS

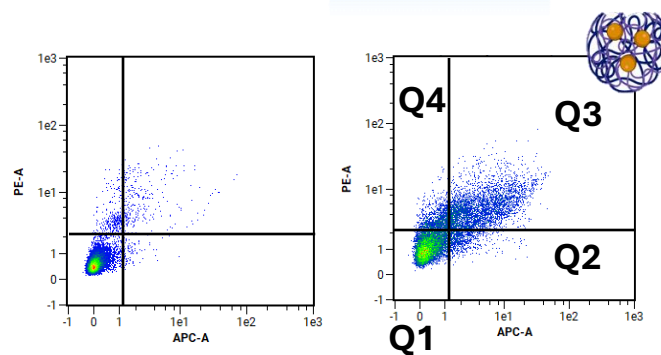
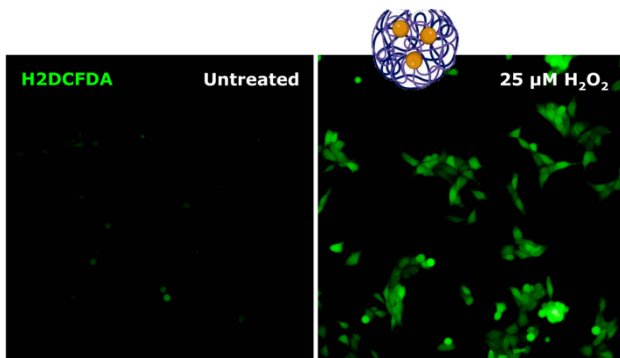
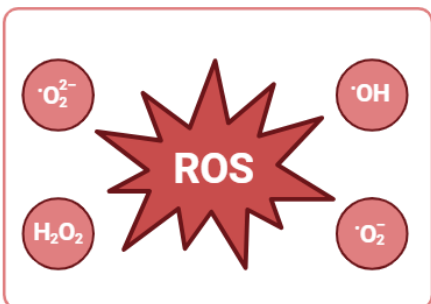
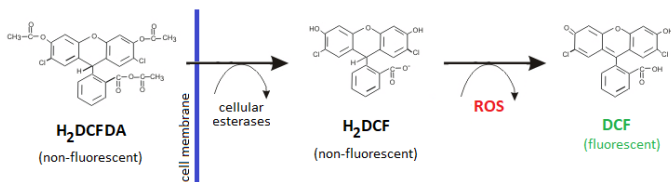


CICLO CELULAR

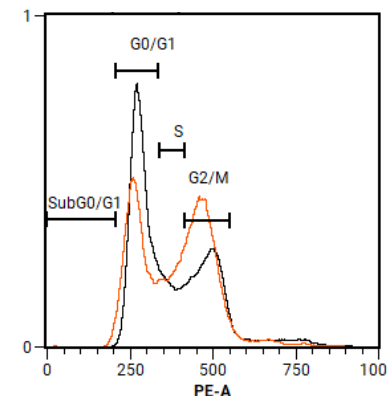


Evaluación de ROS

Determinación de especies reactivas de oxígeno



Q1 (vivas) Q2 (apop temprana)
Q3 (apop tardía) Q4 (necrosis)

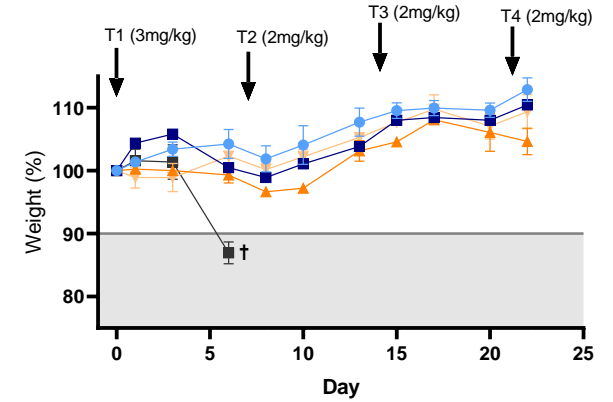


— Control
— Tratamiento

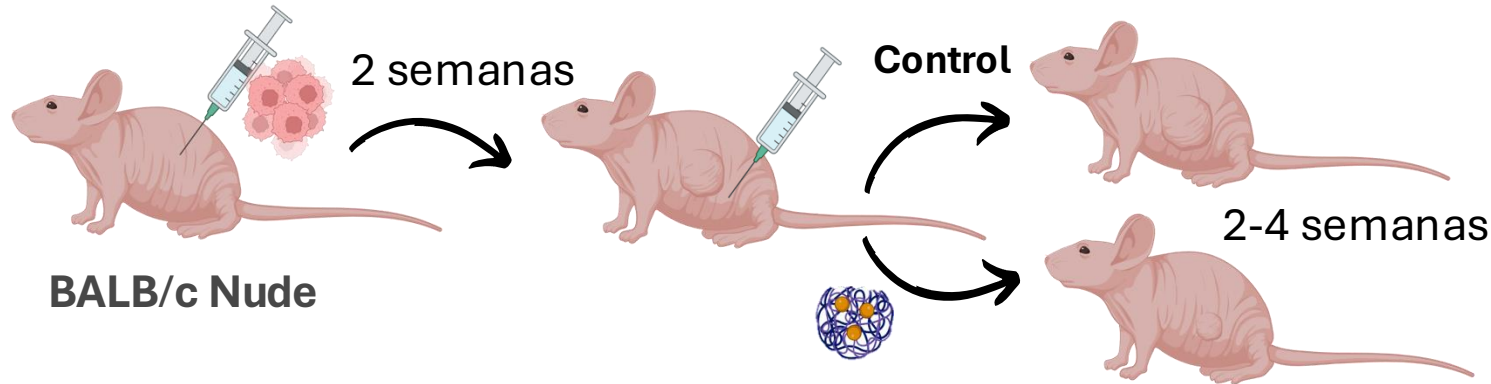


Estudio piloto de toxicidad

- Número reducido de **animales sanos** (2-3 por grupo)
- Dosis secuencialmente más bajas si es necesario
- Puede cambiar la pauta de administración
- Se evalúa el **peso y el bienestar** de los animales



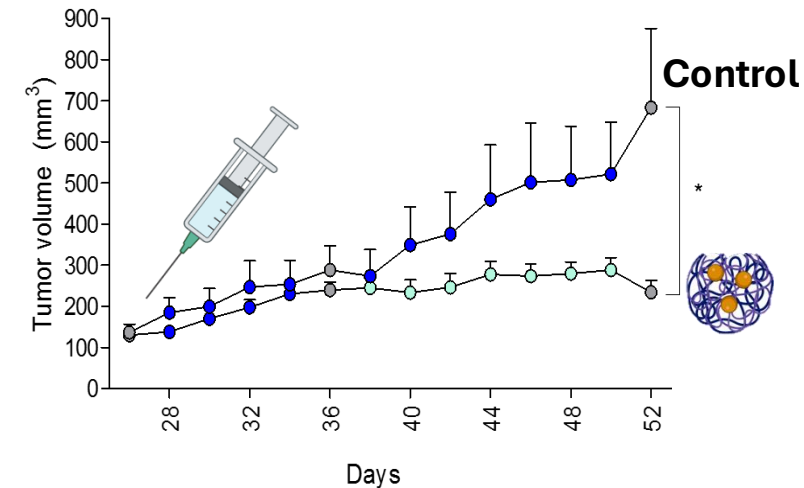
Evaluación de la reducción de tumor



- Inyección subcutánea de células tumorales → **tumores medibles**
- *n* por grupo 6-7 ratones
- Administración intraperitoneal/intravenosa
- Se valorar la **reducción del tamaño del tumor a lo largo del tiempo**



Efecto antitumoral



**Muchas gracias
por vuestra
atención**



Validación preclínica de la actividad antitumoral de nuevos compuestos

María del Mar Noblejas López

Unidad NanoDrug

WORKSHOP INVESTIGACIÓN FACULTAD DE FARMACIA 2024

“La Investigación nuestro mejor medicamento”

Salón de Grados, 25 Noviembre 2024