NANOVEHICULOS PARA BNCT

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Radiobiología-Nanomedicina

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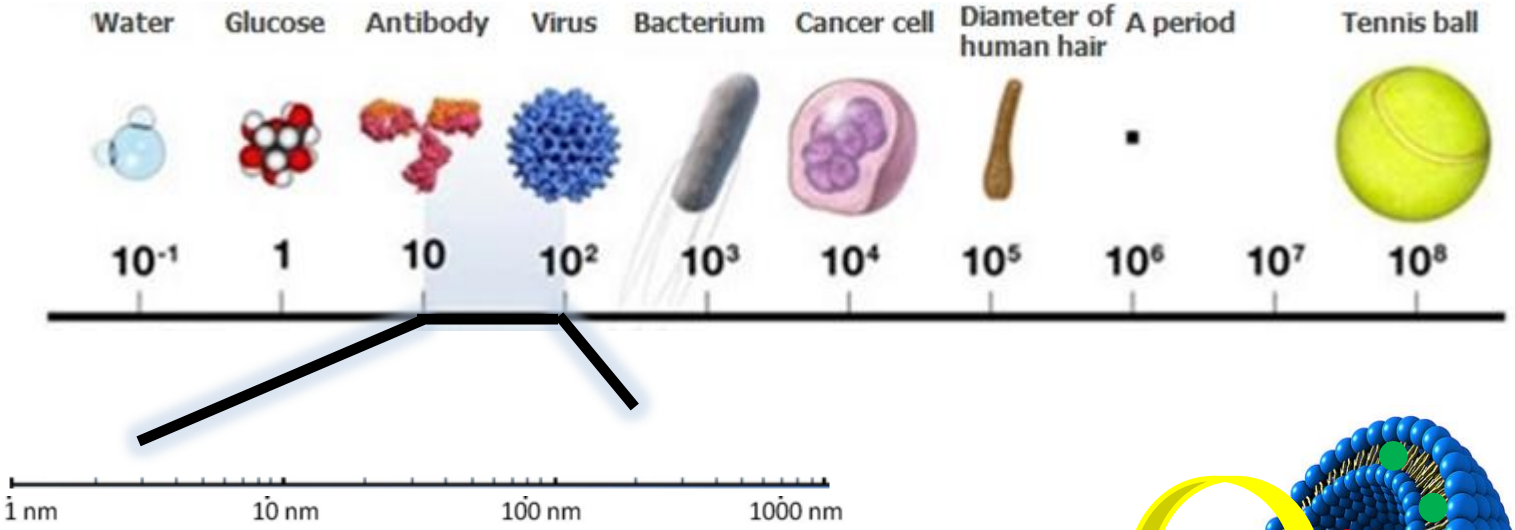
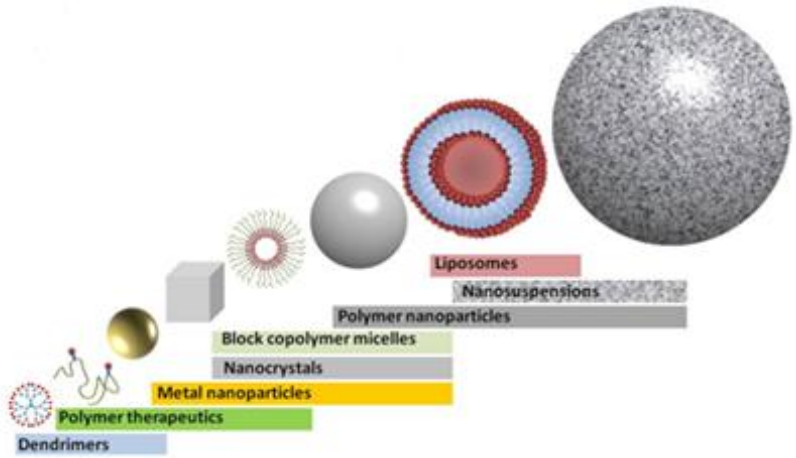
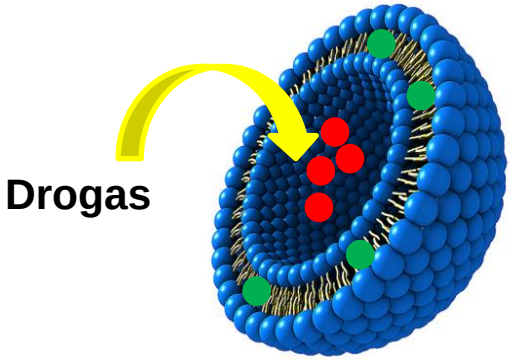
Nanomedicinas

Nanotecnología es el uso y aplicación de materiales en el rango nanométrico
Nanotecnología + medicina = Nanomedicina

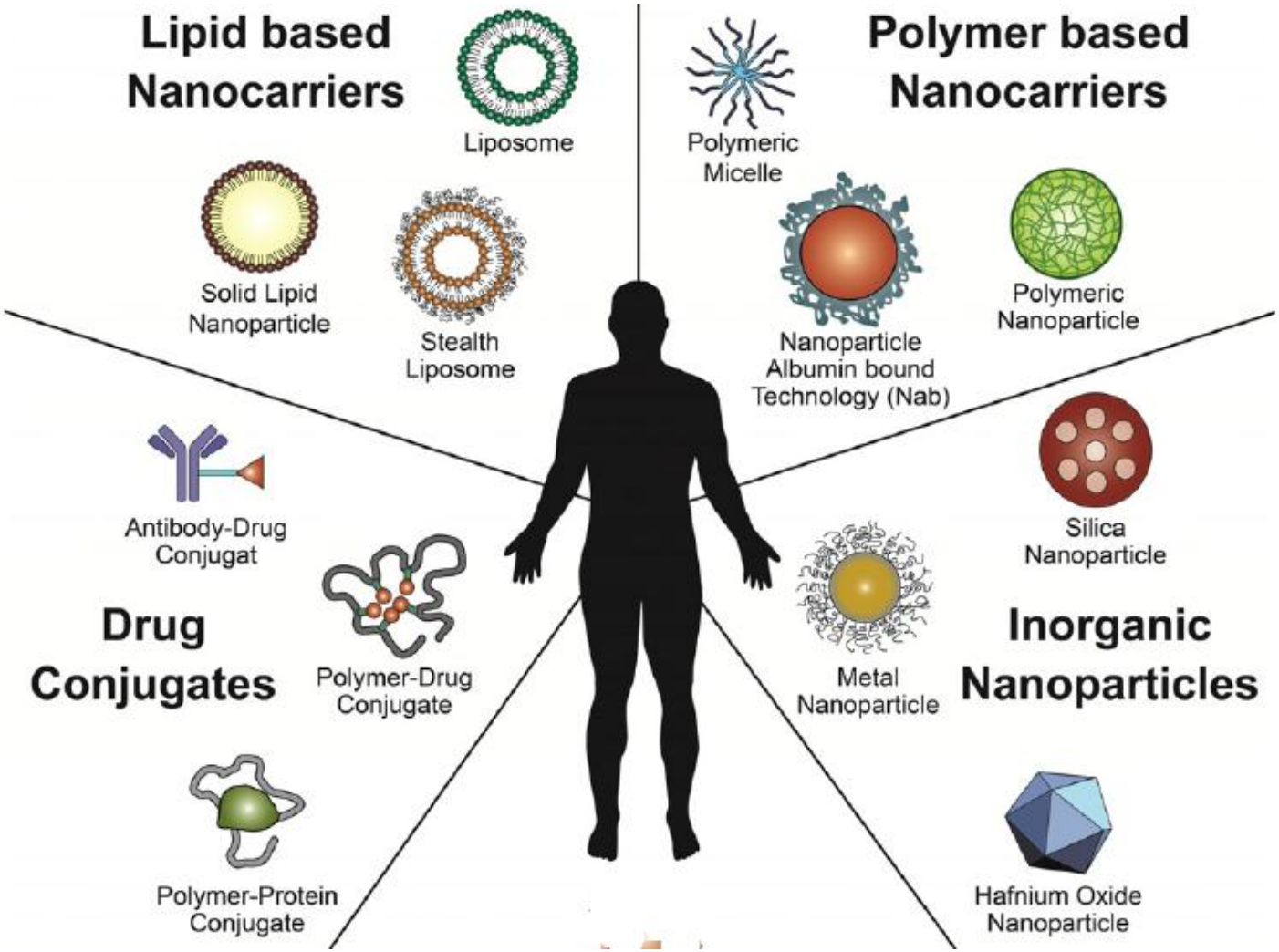






Mejoran la efectividad de las drogas y disminuyen sus efectos tóxicos

Plataformas más utilizadas para la generación de nanomedicinas

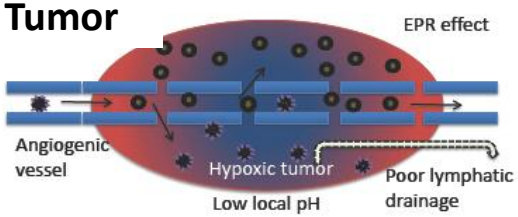


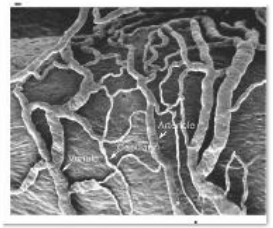
Nanomedicinas: efecto del tamaño y modificación superficie

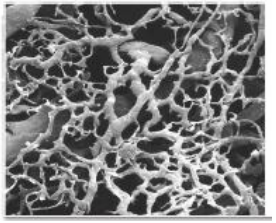
Efecto del tamaño

Tejido normal

Tumor

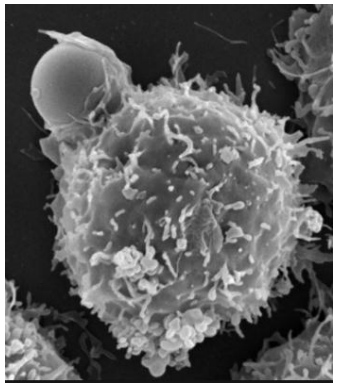


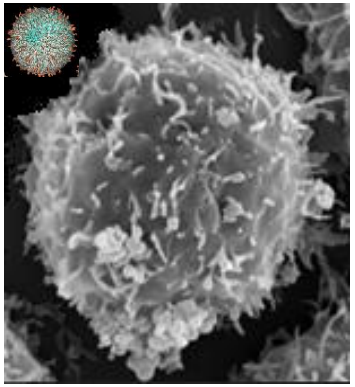




Modificación de la superficie:

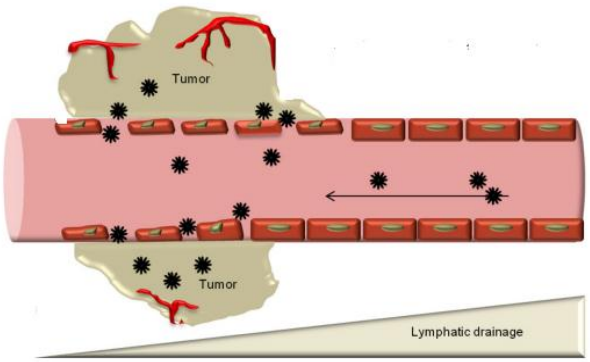
Invisibles al sistema inmune

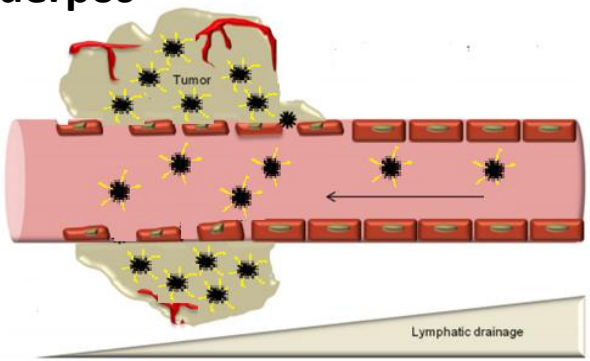




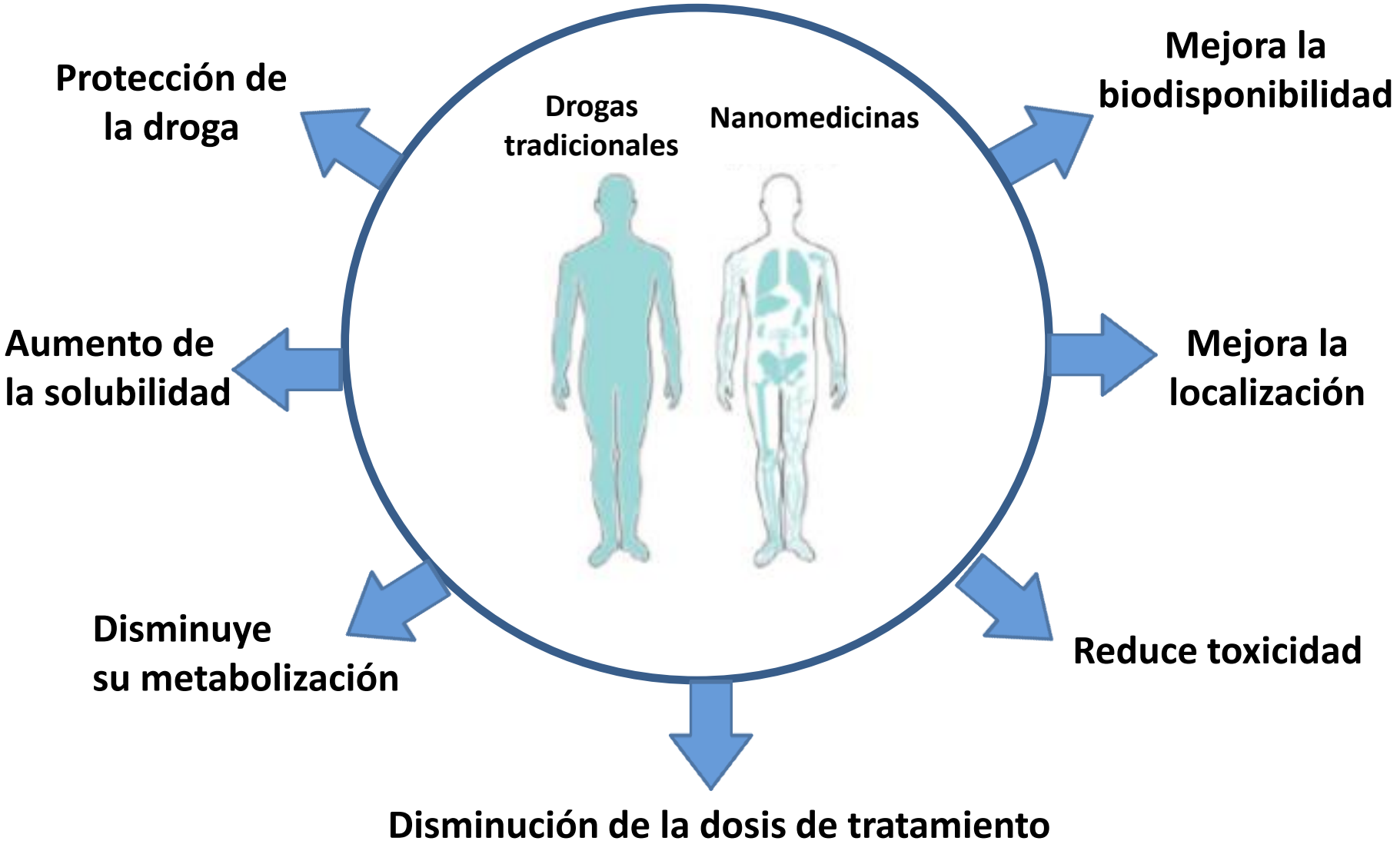
Modificación de la superficie:

Direccionamiento con anticuerpos





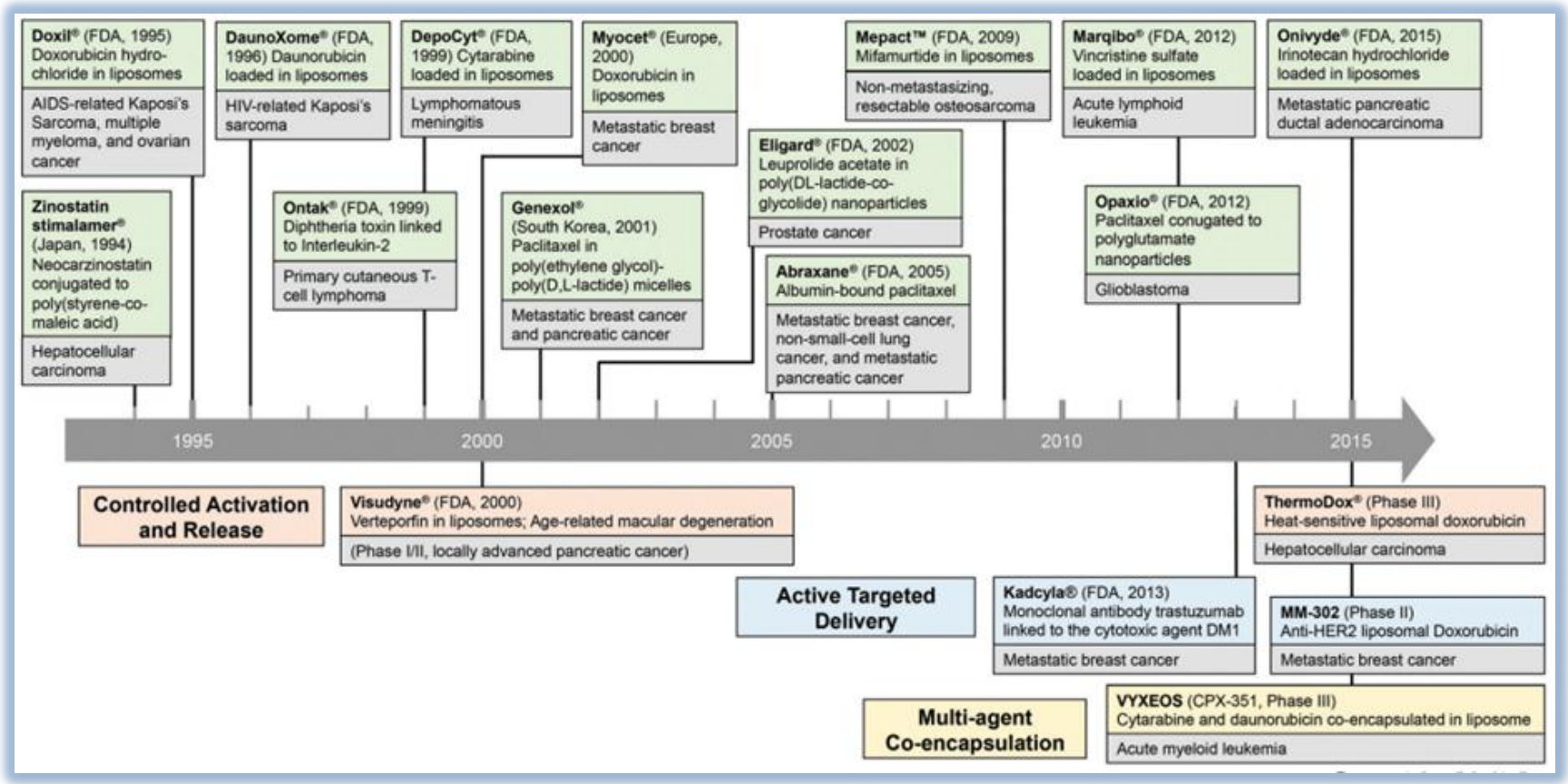
¿Por qué nanomedicinas?



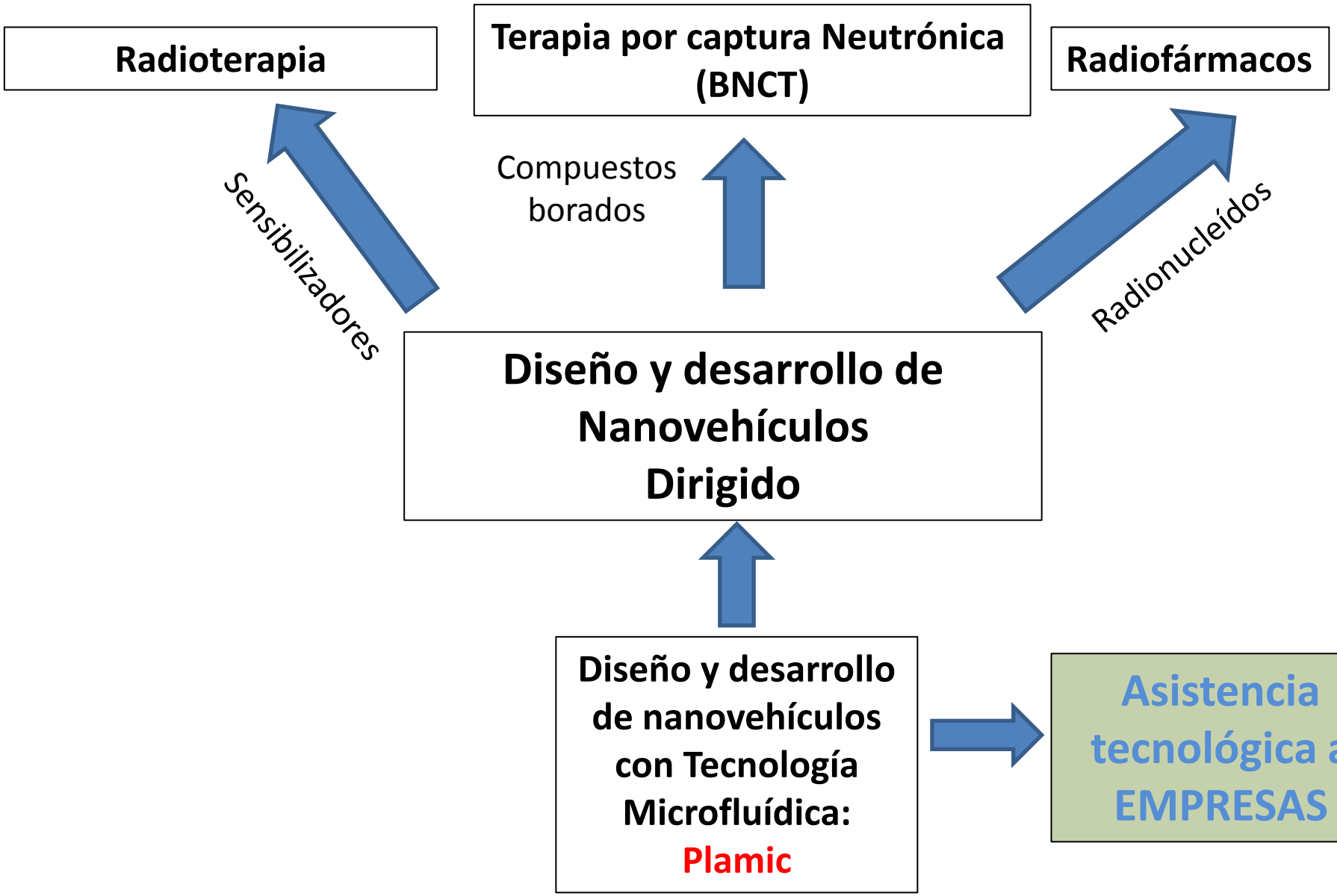
Nanomedicinas:aprobadas y en investigación clínica

Summary of translational activities of nanomedicines.

Status	Liposomes	Micelles	Nanoparticles	Prodrugs	Active targeting
Marketed	8	1	1	2	0
Phase 3	3	2	1	0	0
Phase 2	6	2	1	1	1
Phase 1	5	2	1	1	3

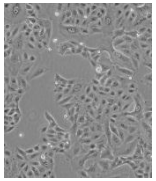


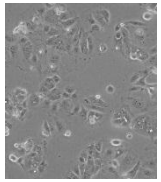
Proyectos Laboratorio Nanomedicina



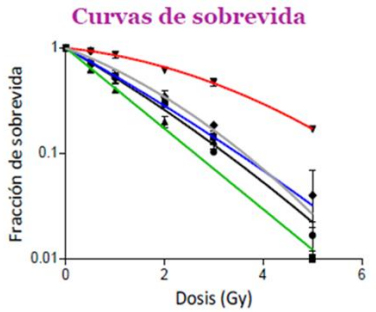
Estudio y caracterización de Modelos Biológicos

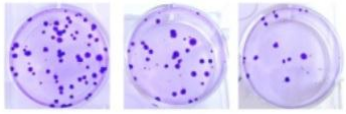
Generación de Líneas Tumorales Humanas resistentes a la radiación y a la quimioterapia



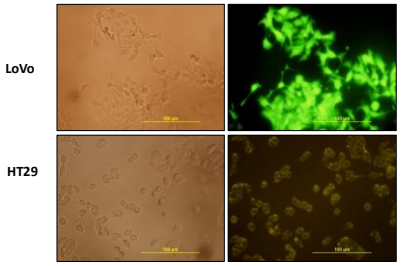


Cultivo de células tumorales en 3 dimensiones

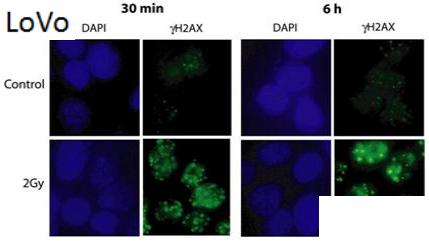




Determinación ROS



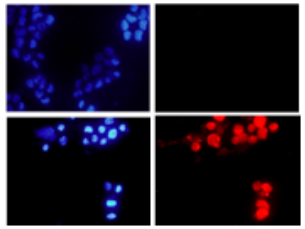
Ensayo de daño al ADN

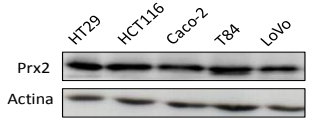


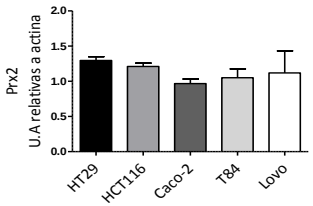
Ensayos en modelos *in vivo*

Tumorigénesis

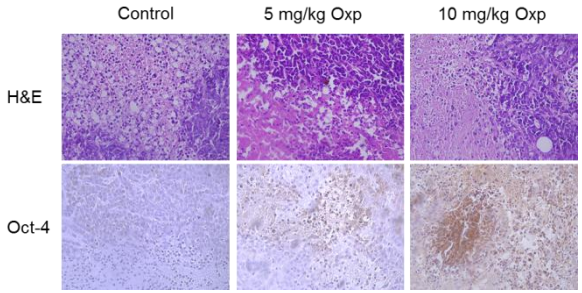
Inmunocitoquimica







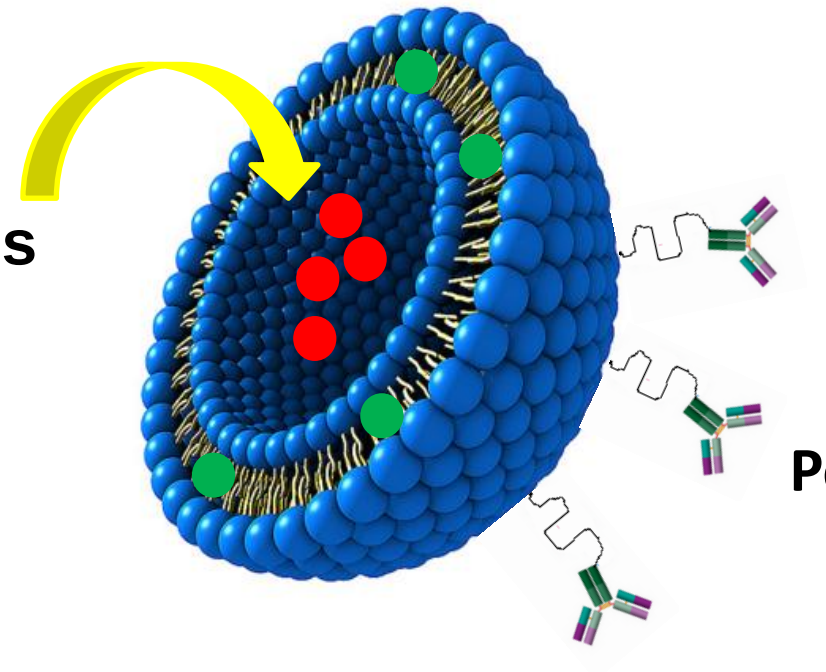
Inmunohistoquímica



Nanovehículos para BNCT

Liposomas

Compuestos Borados



Trastuzumab

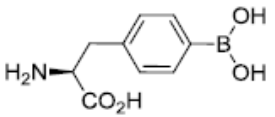
Cetuximab

Péptidos sensibles a pH

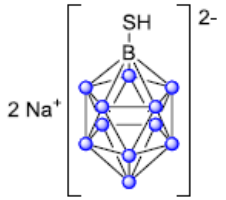
Nanoanticuerpos

Compuestos Borados para BNCT

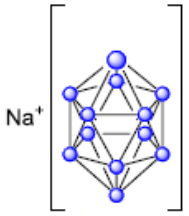
Borofenilalanina (BPA: $C_9H_{12}{}^{10}BNO_4$)



Borocaptato de sodio (BSH: $Na_2{}^{10}B_{12}H_{11}SH$)



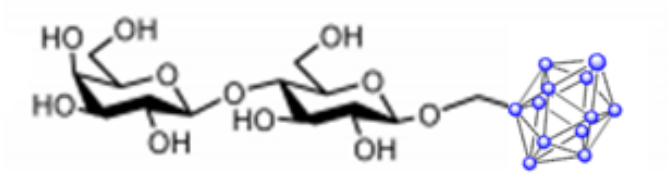
GB-10 ($Na_2B_{10}H_{10}$)



o-closocarboranyl β-lactoside (LCOB: lactosa-$C_2{}^{10}B_{10}H_{12}$)

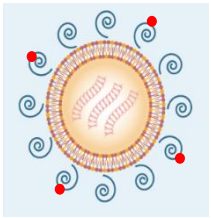
Colaboración CNEA, Argentina-Universidad de Piemonte Orientale, Italia

Dr. Luigi Panza



Desarrollo de un Inmunonanovector

1



+/- POPC

+ DDAB-DSPE-PEG

DSPE-PEG-mal

Solvente orgánico

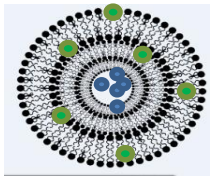
↓

Secado y formación de film

2

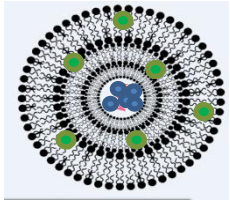
Compuesto borado

Lípidos resuspendidos en buffer y sonicados



Liposomas multilamelares MLV > 500nm

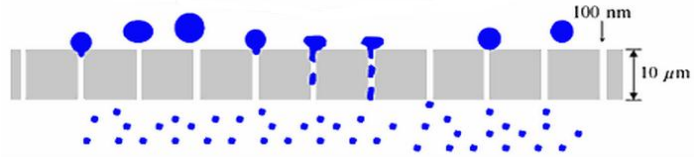
3



MLV > 500nm

Extrusión

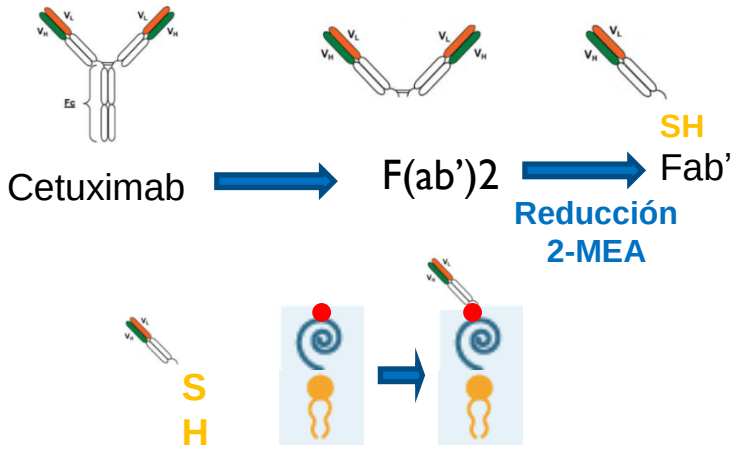
SUV 40-100 nm

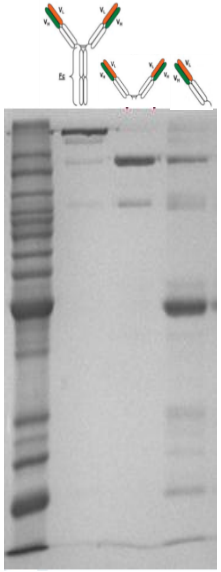


400 nm
200 nm
100 nm

Desarrollo de un Inmunonanovector

4





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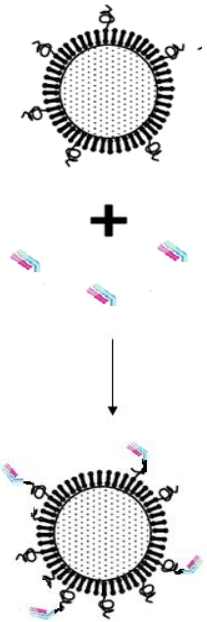

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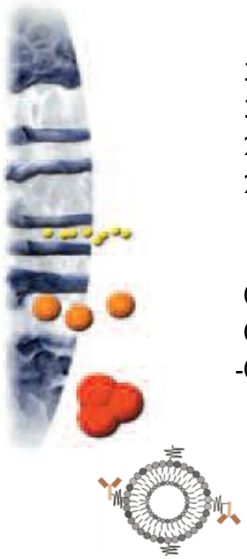
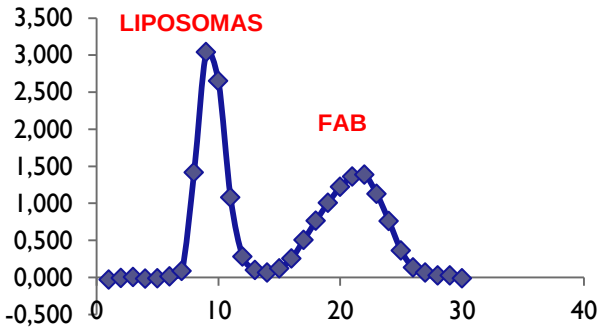
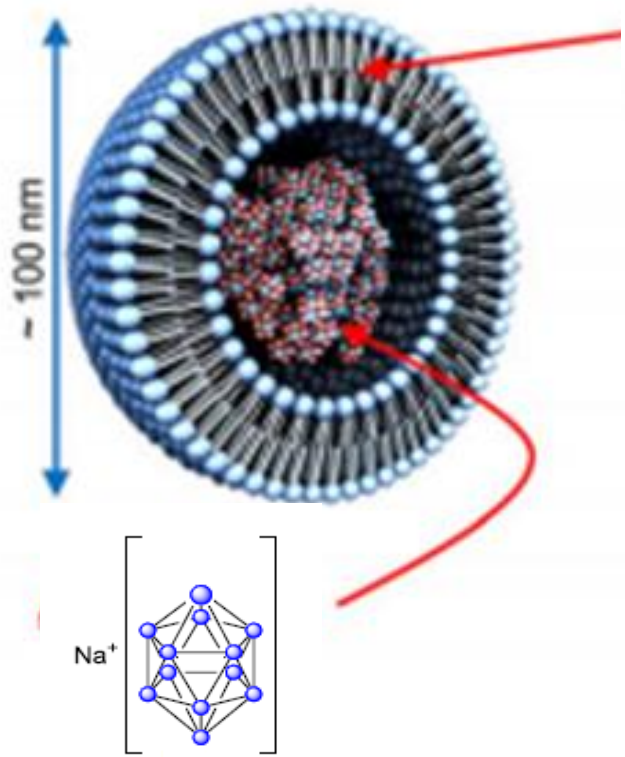
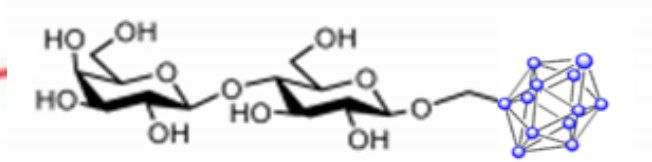




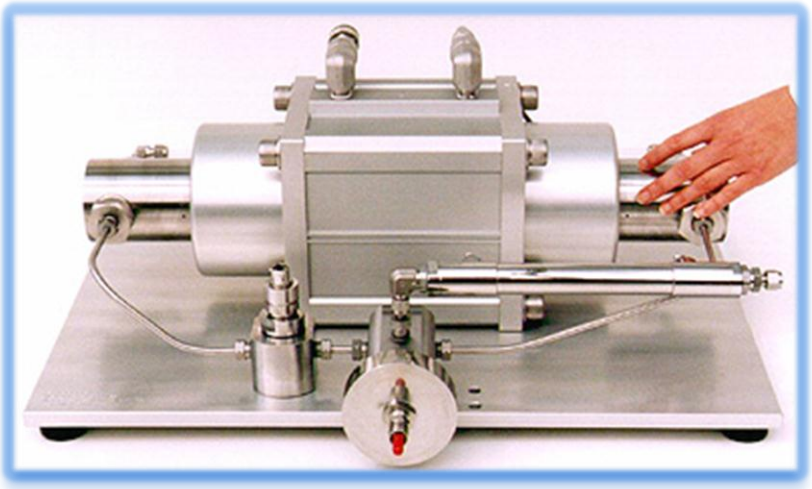
Inmunoliposomas para BNCT:
colaboración CNEA-Universidad Piamonte Oriental





	Boro en volumen final (nmoles)	Posforo en volumen final (nmoles)	B/P	Tamaño (nm)	PDI
Liposomas GB-10	5,57E+04	1,01E+04	5,5	142,5	0,212
Liposomas LCOB	1,83E+04	7,8E+03	2,4	144,4	0,24
Liposomas GB-10+LCOB	3,6E+04	4,7E+03	7,7	92,4	0,218

Tecnología tradicionales para la síntesis de Nanomedicinas



⬇ **Rendimiento**

⬇ **Reproducibilidad**

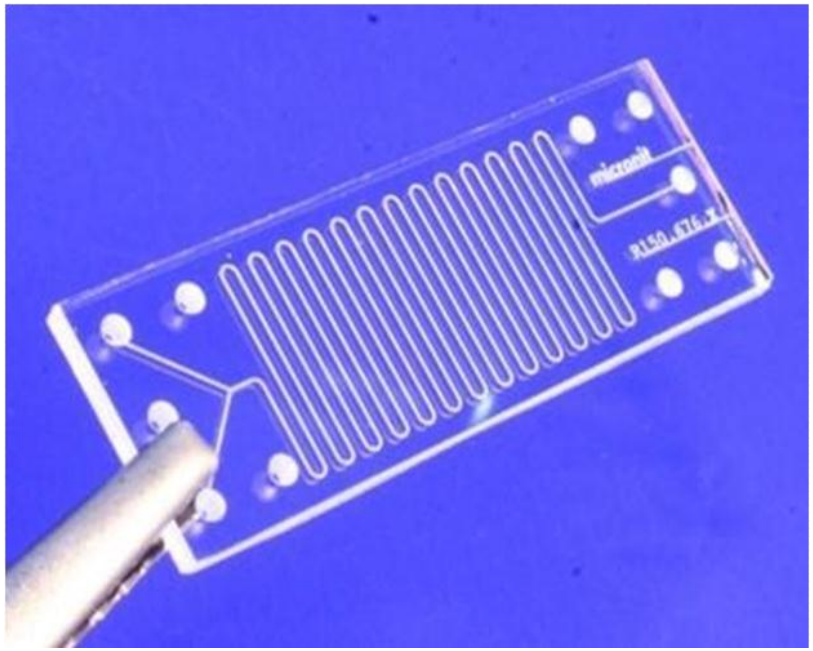
⬇ **Escalado**

⬆ **Costos**

¿Qué es la microfluídica?

"Es el manejo de los fluidos a escala microscópica"

- **Difusión**
- **Flujo laminar**
- **Elevada relación superficie/volumen**
- **Predecible matemáticamente**



Reducción del tamaño de los dispositivos

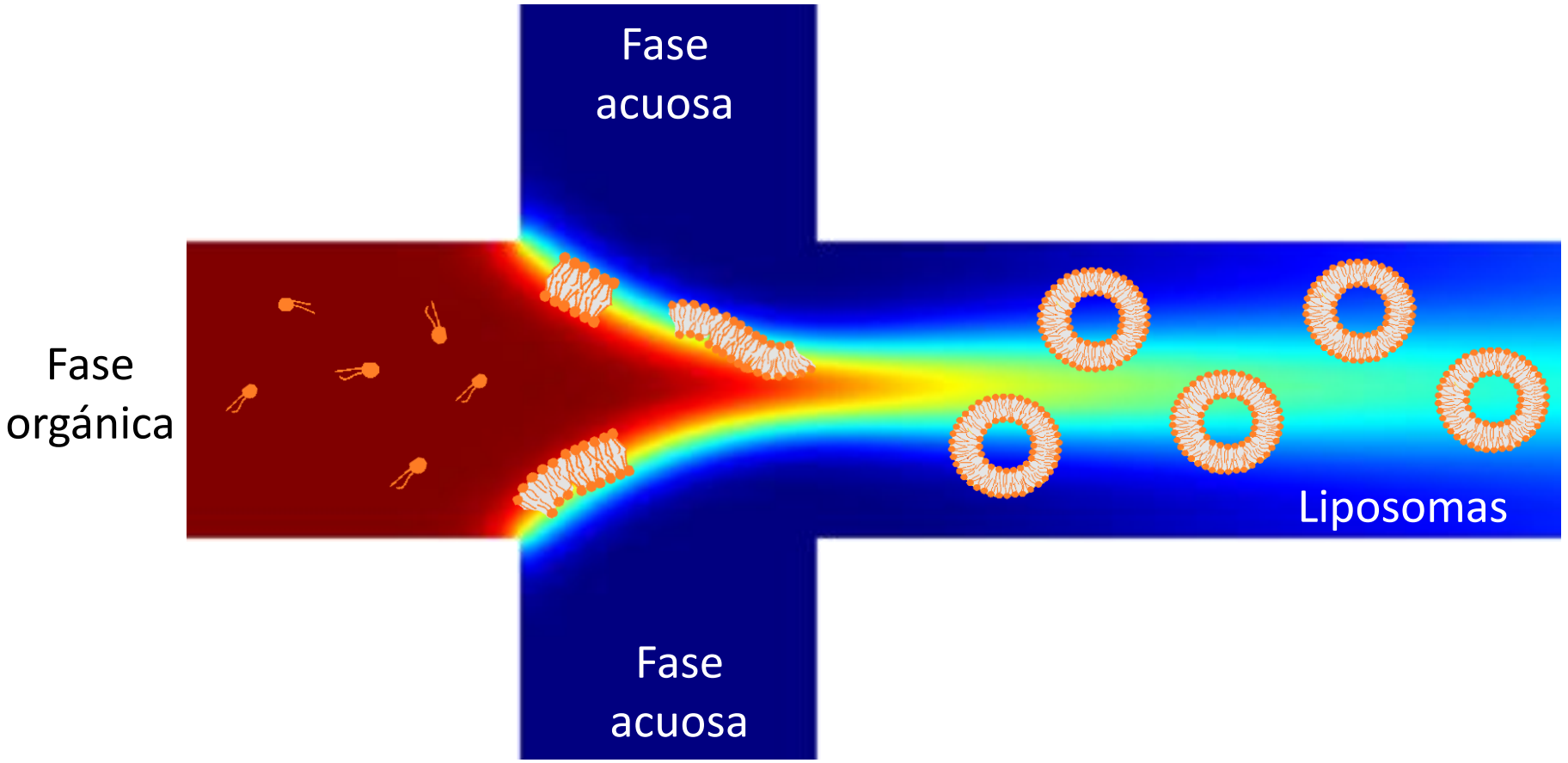
↓

Reducción de los volúmenes de reactivos y muestras

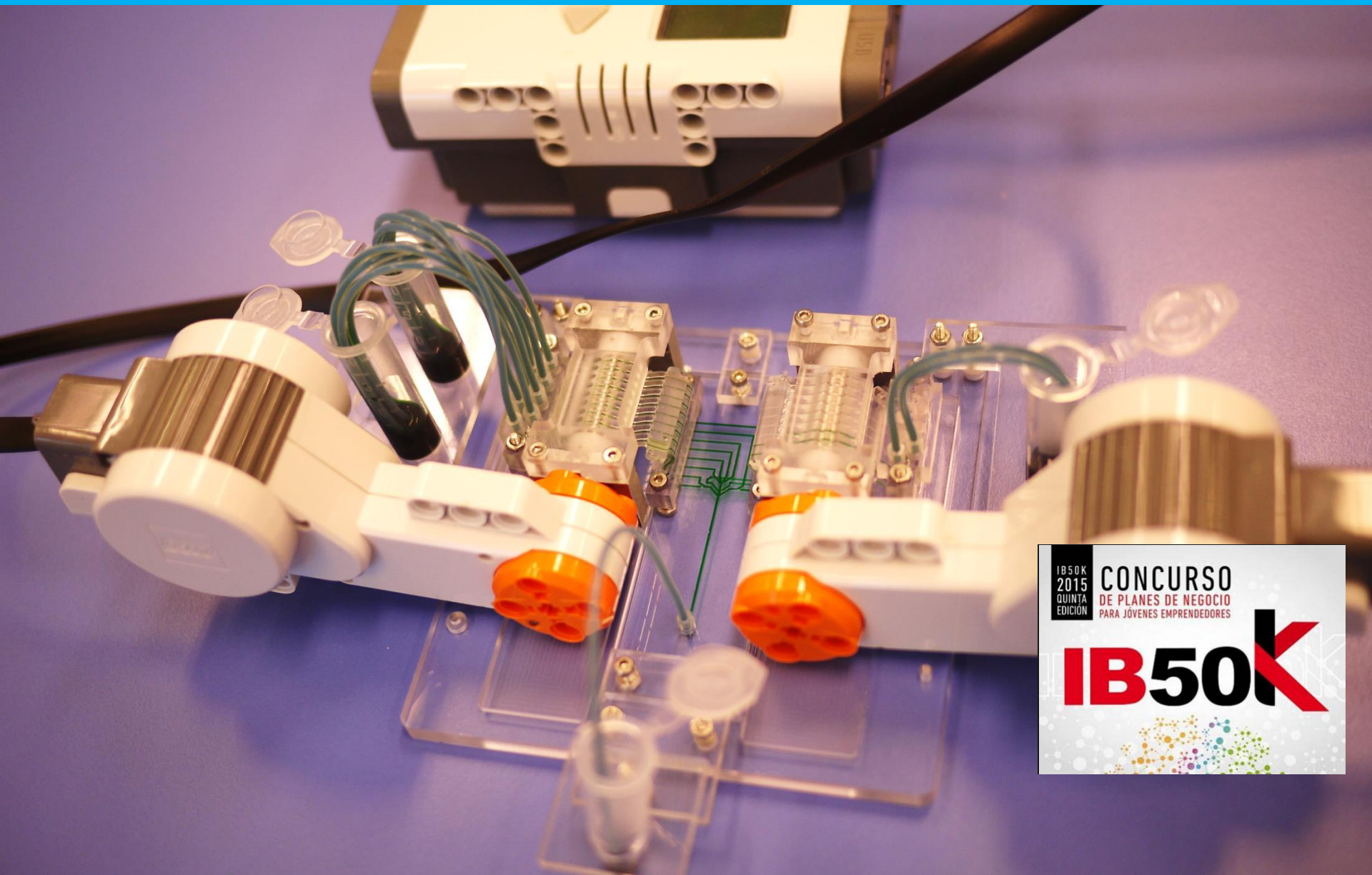
↓

Reducción de costos

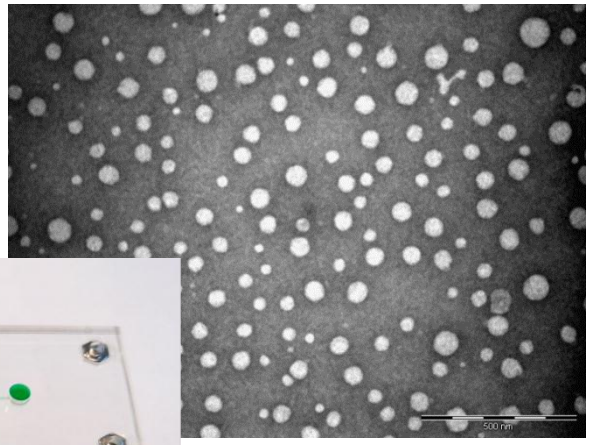
Síntesis de liposomas por microfluídica

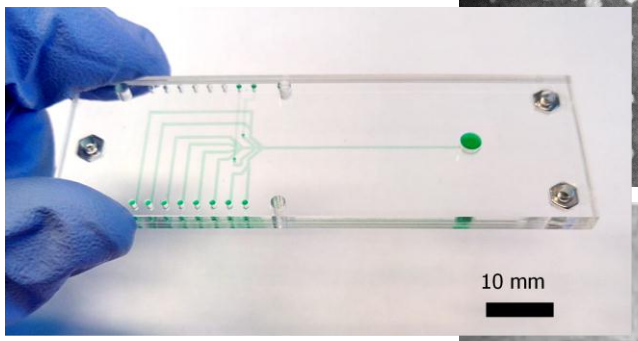


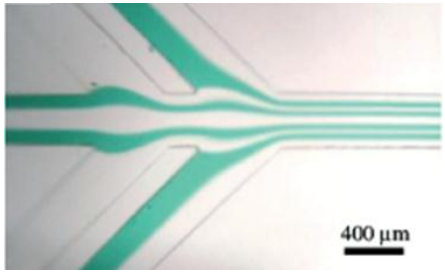
Tecnología microfluídica para la síntesis de nanomedicinas

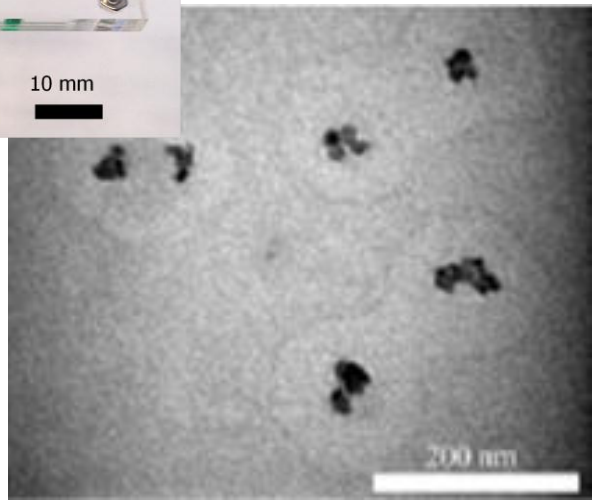


Tecnología microfluídica para la síntesis de nanomedicinas

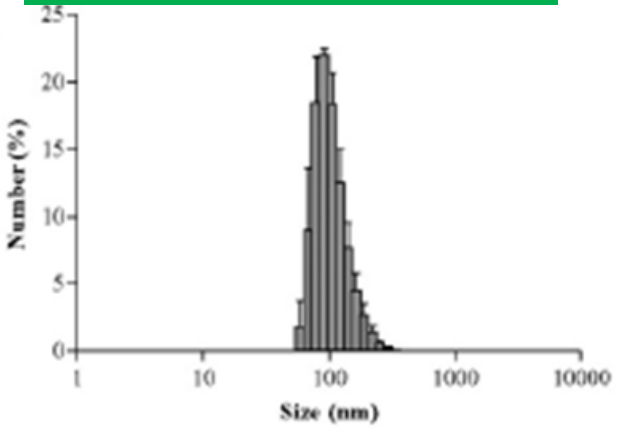






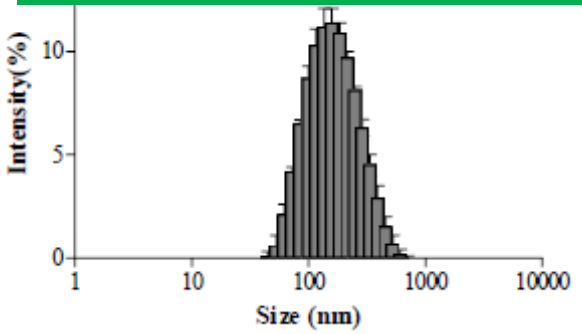


Liposomas



DLS: 90 ± 28 nm (PI 0.165)

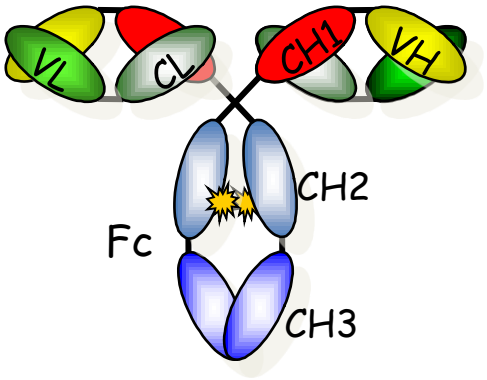
Magnetoliposomas

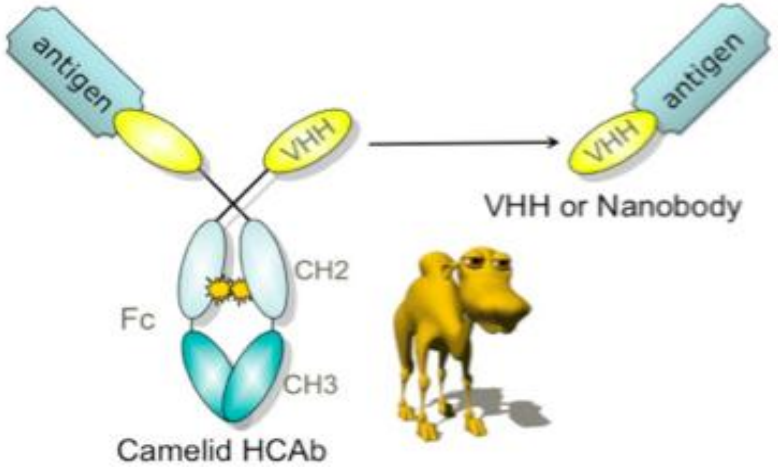


Liposomas para BNCT obtenidos por microfluíca (LCOB)

	Método Tradicional (hidratación film)	Microfluídica (chip)
% de Recuperación de Lípidos (final proceso/inicial)	10%	35%
Encapsulamiento (B/P)	2,4	3,5
Tamaño (nm)	144,4	89,9
Indice de polidispersión	0,24	0,18
Tiempo del proceso de síntesis	2-3 días	30 min

Anticuerpos monoclonales y Nanoanticuerpos

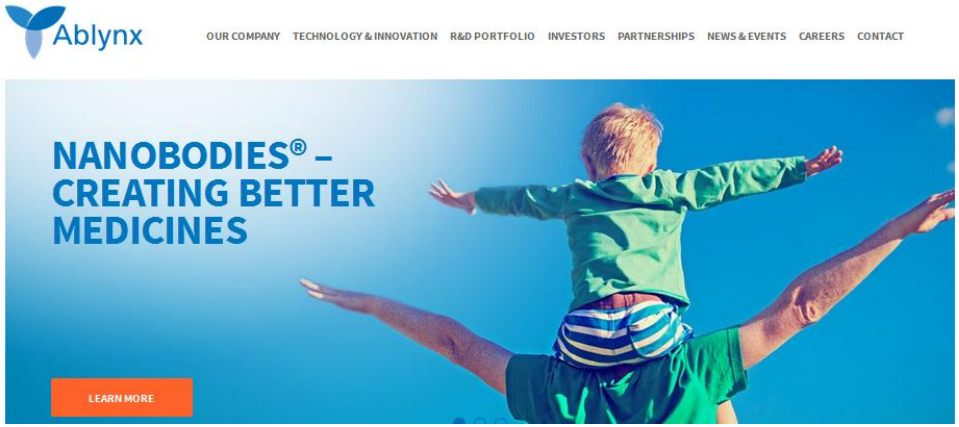




VHHs :
Diferencias respecto a los anticuerpos convencionales

***Pequeños**
***Económicos**
***Fácil manipulación genética**

Ablynx: Nanoanticuerpos



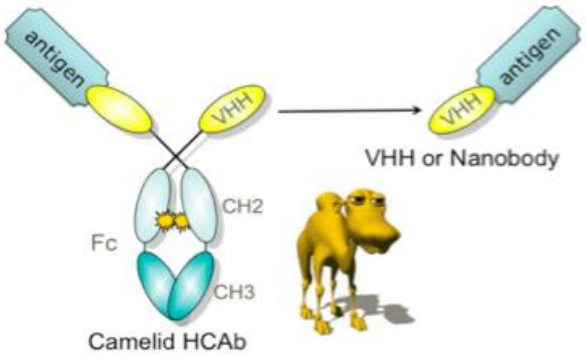
	Therapeutic area	Product name	Target	Discovery	Pre-clinical	Phase I	Phase II	Phase III	Filing
FULLY OWNED	Haematology	caplacizumab	vWF						
	Respiratory	ALX-0171	RSV						
	Oncology/ Immuno-oncology	Various							
	Inflammation/ Immunology	Various							
	Ocular	Various							
	Other	Various							
PARTNERED	Inflammation/ Immunology	ALX-0061	IL-6R						
		ALX-0761	IL-17F/IL-17A						
		ozoralizumab	TNFα				Japan		
							Greater China		
		Various							
	Oncology/ Immuno-oncology	Various	VEGF/Ang2						
	Bone disorders	ALX-0141	RANKL				Greater China		
	Neurology								
	Various		CXCR2						
	Other	Various							

abbvie
Merck
TAISHO
EDDINGpharm
Merck
Boehringer Ingelheim
Boehringer Ingelheim
MERCK
Merck
EDDINGpharm
MERCK
genzyme
A SANOFI COMPANY
NOVARTIS
Boehringer Ingelheim
novo nordisk

Desarrollo de radiofarmacos basados en nanoanticuerpos.

Proyecto NADIMEN (Nanovehículos Dirigidos Medicina Nuclear)

INSTITUTO LELOIR
FUNDACIÓN



Proyectos Nano-Nuclear 2015 INN

Diagnóstico **Terapia**

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Muchas Gracias!
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