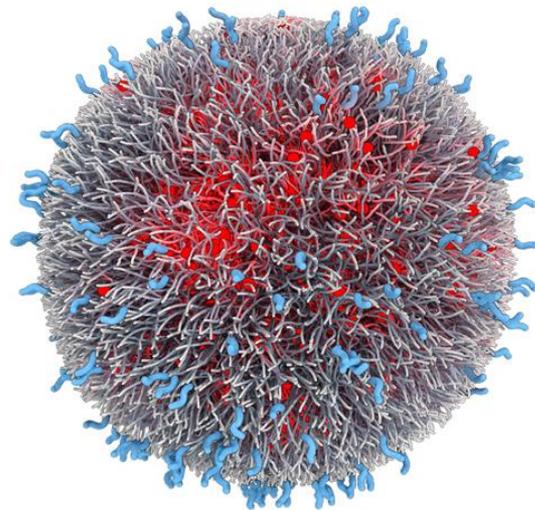


Nanomedicine of infectious diseases



Marco Siccardi



UNIVERSITY OF
LIVERPOOL

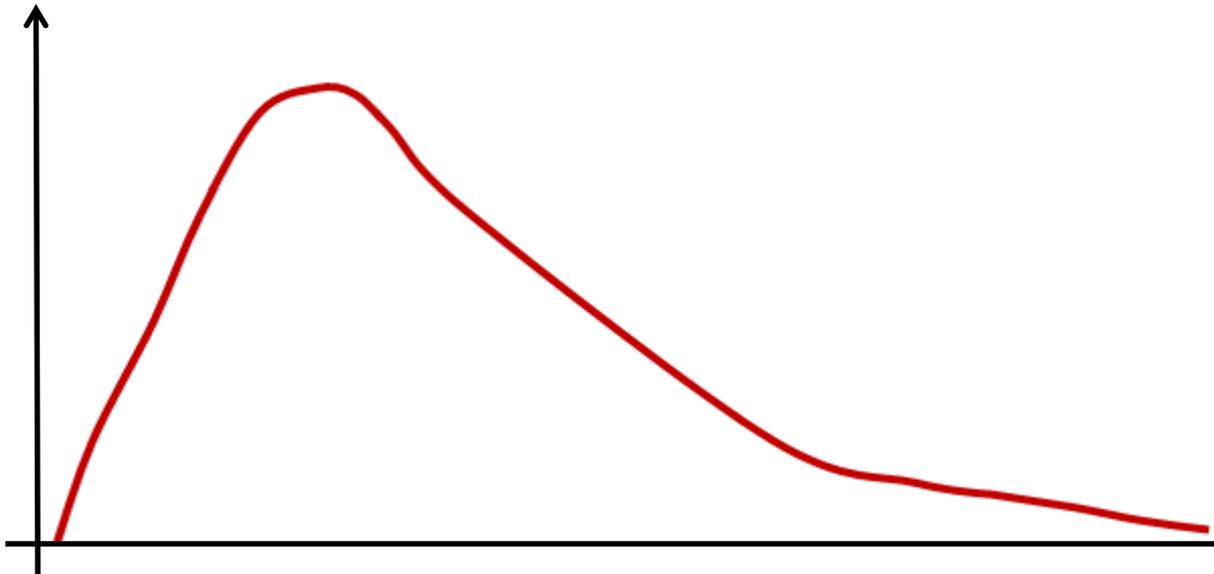


BRITISH SOCIETY FOR
NANOMEDICINE

ABSORPTION

**VOLUME OF
DISTRIBUTION**

CLEARANCE



ABSORPTION

**VOLUME OF
DISTRIBUTION**

CLEARANCE

Pharmacological issues

ORAL BIOAVAILABILITY

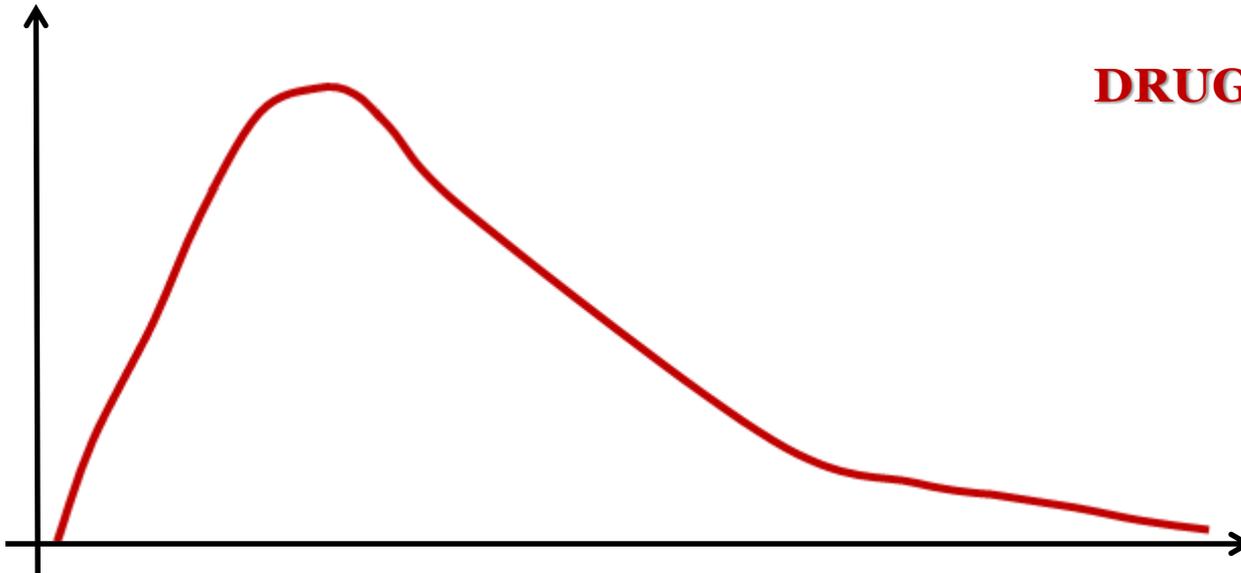
SUSTAINED RELEASE

**NON-SPECIFIC
DISTRIBUTION**

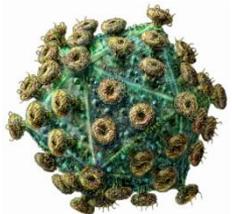
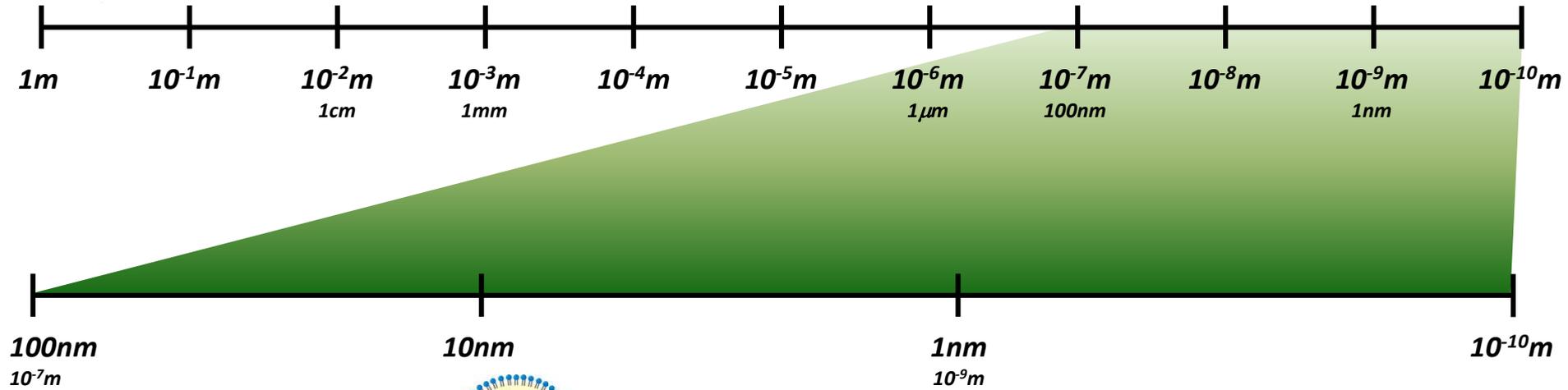
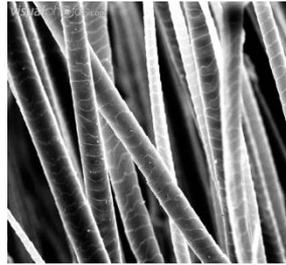
**POOR PENETRATION IN
TISSUES**

RAPID ELIMINATION

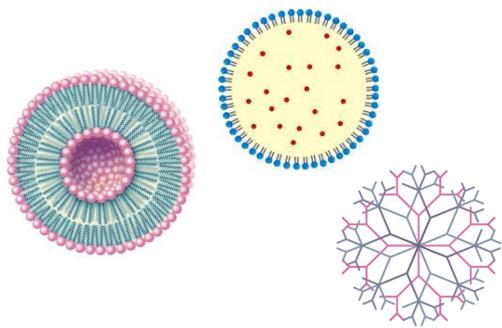
DRUG-DRUG INTERACTIONS



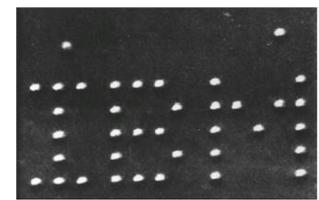
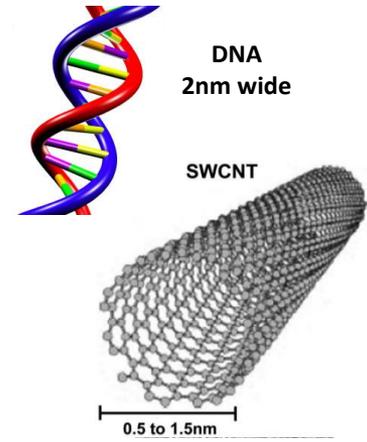
Size in perspective



HIV
100nm

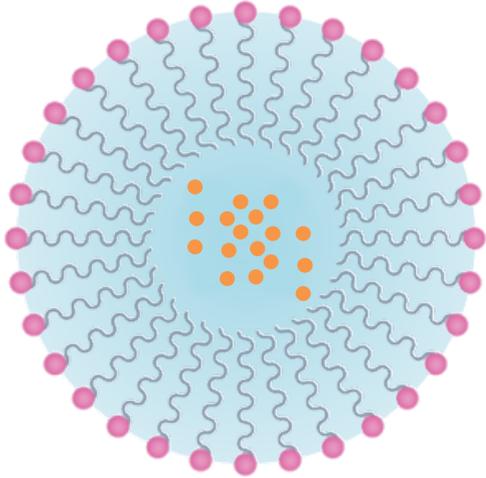


NANOPARTICLES

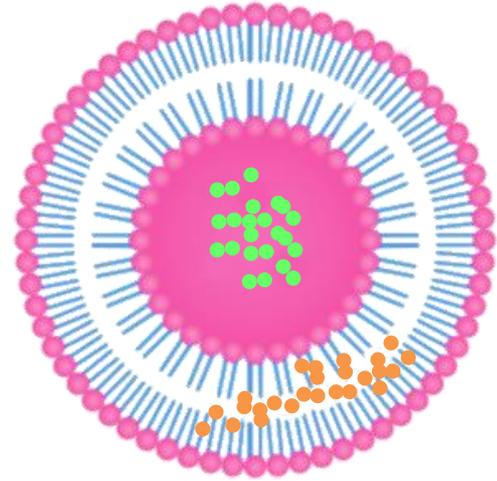


Xenon atoms
130pm

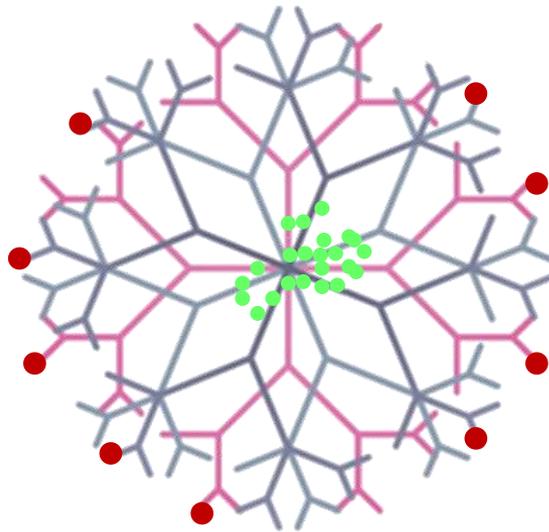
Solid lipid nanoparticles



Liposomes



Dendrimers

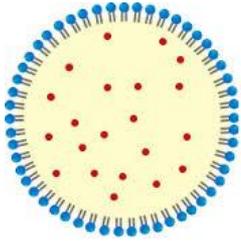


TARGETING

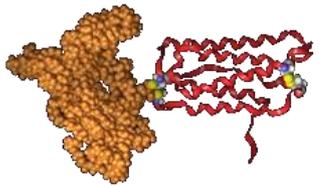
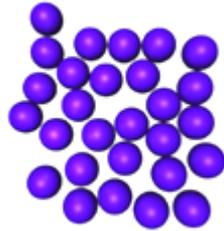
PASSIVE

ACTIVE

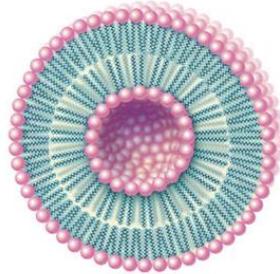
NANOEMULSION



NANOSUSPENSION



BIO-POLYMERS



LIPOSOME



NANO MATERIAL

SMALL LIGANDS

ANTIBODIES



NUCLEIC ACIDS



PEPTIDES



PROTEINS



SOLUBILITY

BIOAVAILABILITY

TISSUE PENETRATION

TOPICAL

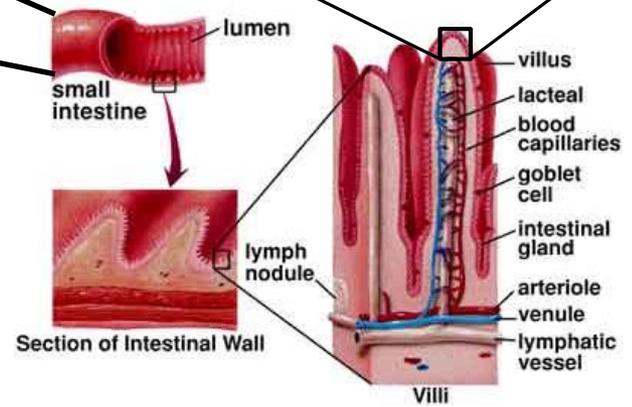
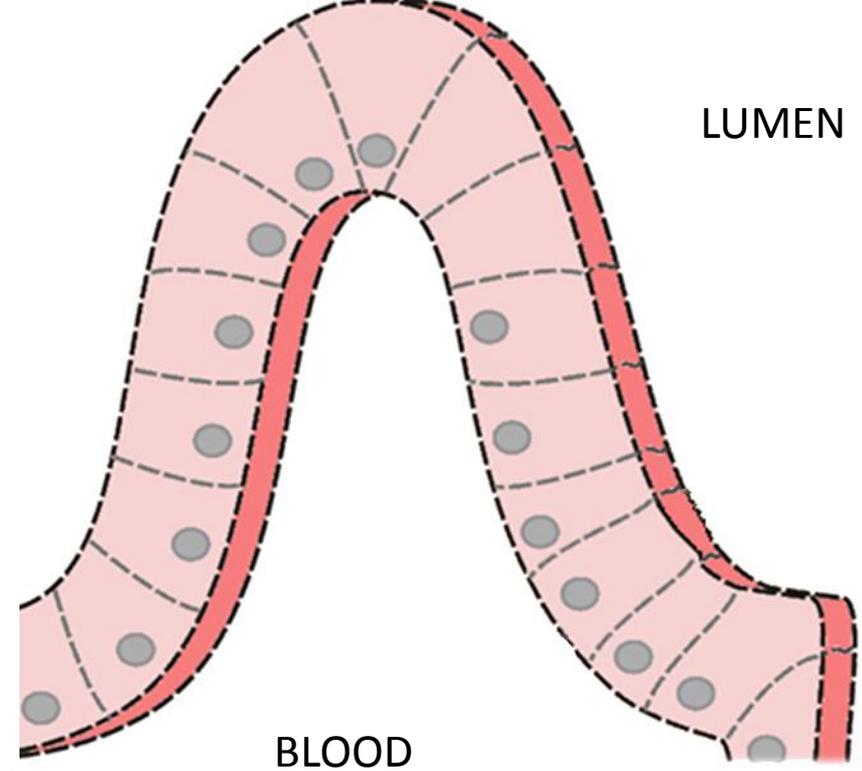
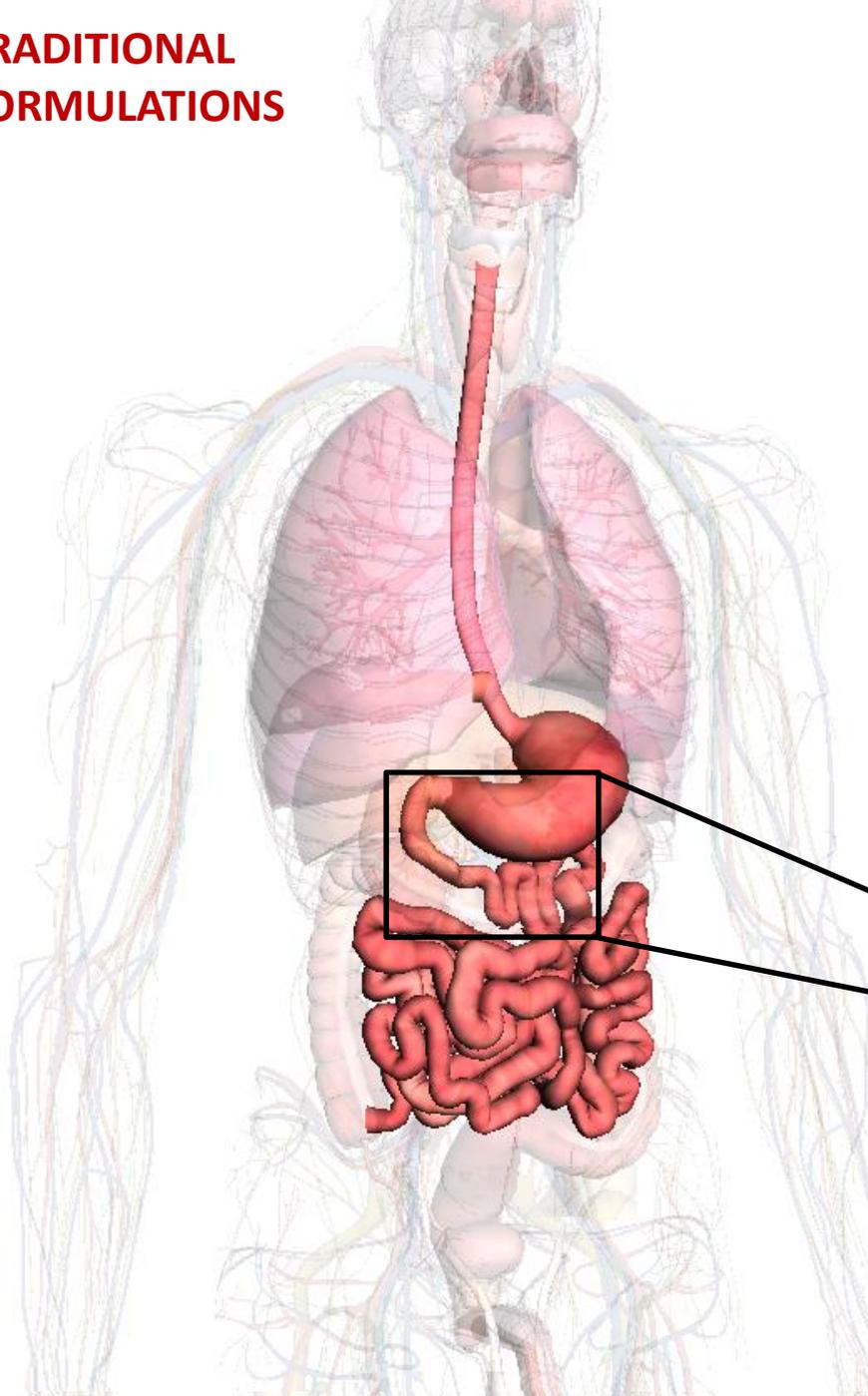
ADMINISTRATION

BIOAVAILABILITY

PATHOGEN TARGETING

TISSUE TARGETING

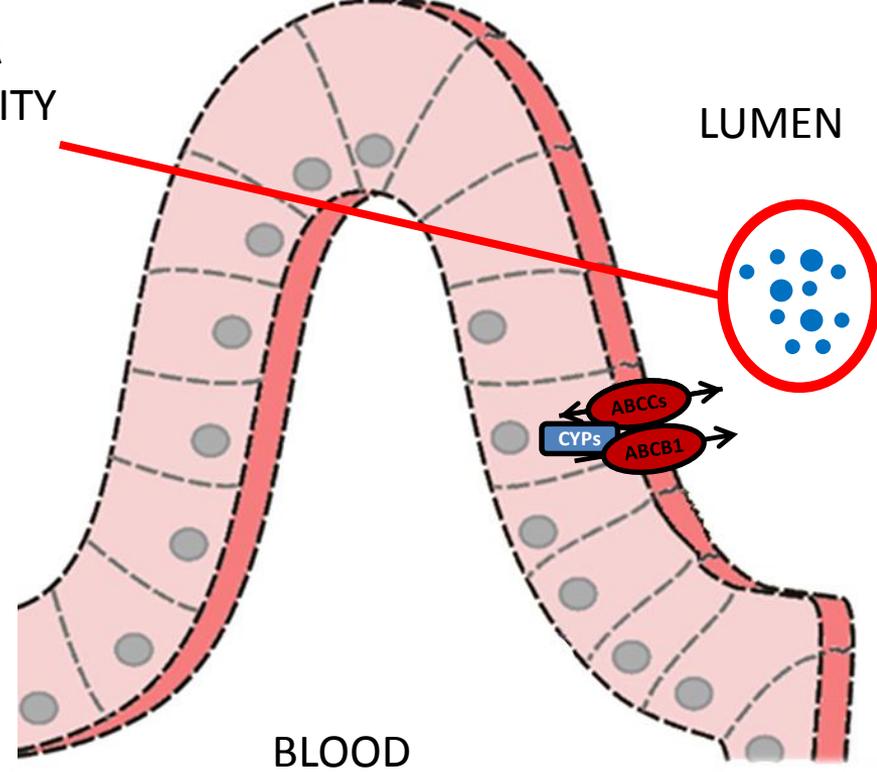
TRADITIONAL FORMULATIONS



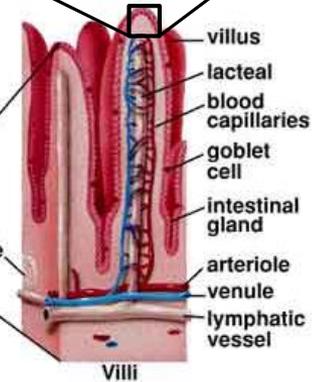
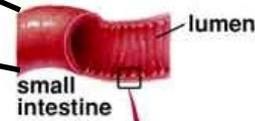
TRADITIONAL FORMULATIONS

POOR SOLUBILITY

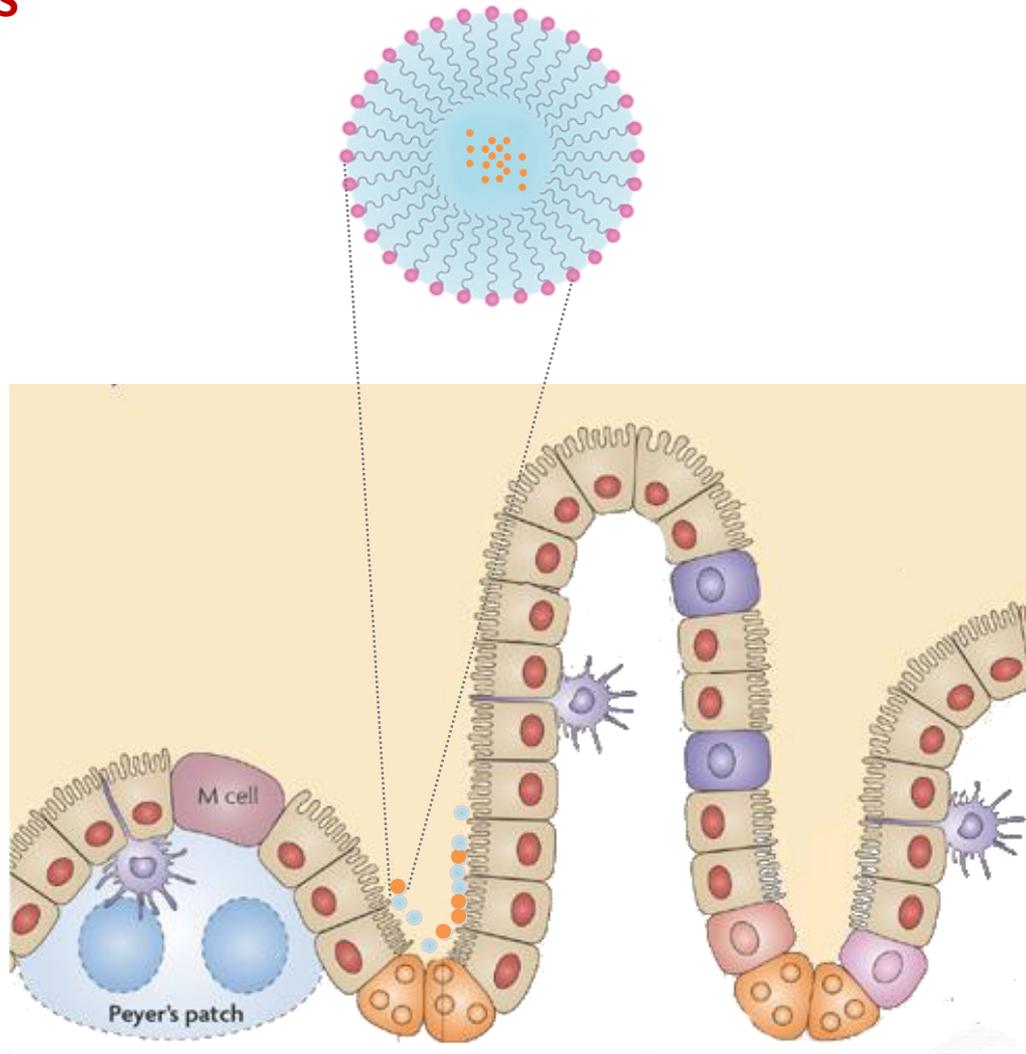
LUMEN



BLOOD



NANO FORMULATIONS



Antiretroviral Solid Drug Nanoparticles with Enhanced Oral Bioavailability: Production, Characterization, and In Vitro–In Vivo Correlation

Tom O. McDonald, Marco Giardiello, Philip Martin, Marco Siccardi, Neill J. Liptrott, Darren Smith, Phill Roberts, Paul Curley, Alessandro Schipani, Saye H. Khoo, James Long, Alison J. Foster, Steven P. Rannard,* and Andrew Owen*

Surface-stabilized lopinavir nanoparticles enhance oral bioavailability without coadministration of ritonavir

Nanomedicine (2013) 8(10), 1639–1655

Sanyog Jain^{*1},
Jagadish M Sharma¹,
Amit K Jain¹
& Rahul R Mahajan¹

Nanomedicine

Nanomedicine (Lond.) (2014) 9(12), 1821–1833

Lesego Tshweu¹,
Lebogang Katata^{1,2},
Lonji Kalombo¹,
Diego A Chiappetta^{3,4},
Christian Höcht⁵,
Alejandro Sosnik^{3,4,6}
& Hulda Swai^{*1}

Enhanced oral bioavailability of the antiretroviral efavirenz encapsulated in poly(epsilon-caprolactone) nanoparticles by a spray-drying method



Colloids and Surfaces B: Biointerfaces 123 (2014) 515–523

Spray-dried didanosine-loaded polymeric particles for enhanced oral bioavailability

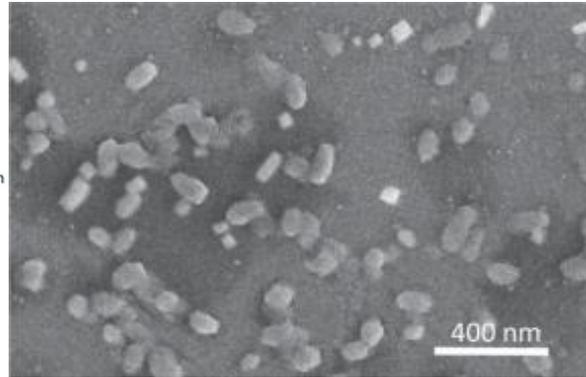
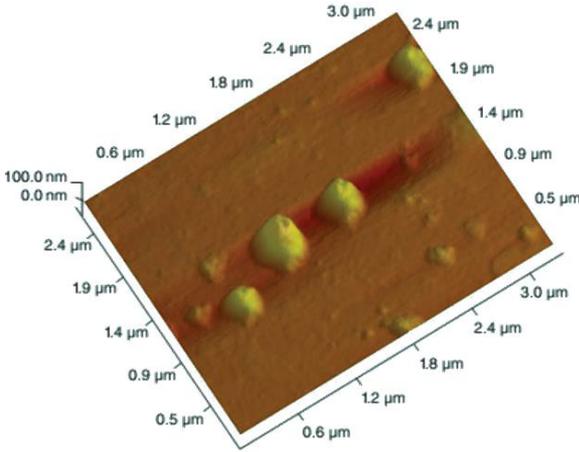
Katia P. Seremeta^{a,b}, María I. Reyes Tur^c, Sandra Martínez Pérez^d, Christian Höcht^e, Carlos Taira^{b,e}, Orestes D. López Hernández^f, Alejandro Sosnik^{g,*}

Biomaterials 37 (2015) 383–394

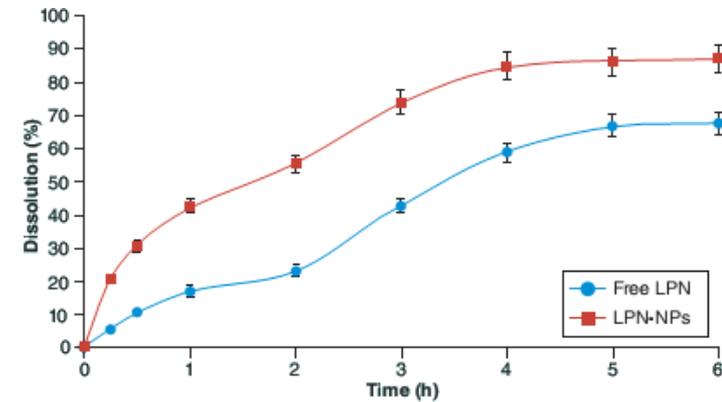
Novel protease inhibitor-loaded Nanoparticle-in-Microparticle Delivery System leads to a dramatic improvement of the oral pharmacokinetics in dogs

Julietta C. Imperiale^a, Pablo Nejamkin^b, Maria J. del Sole^b, Carlos E. Lanusse^{b,c}, Alejandro Sosnik^{d,*}

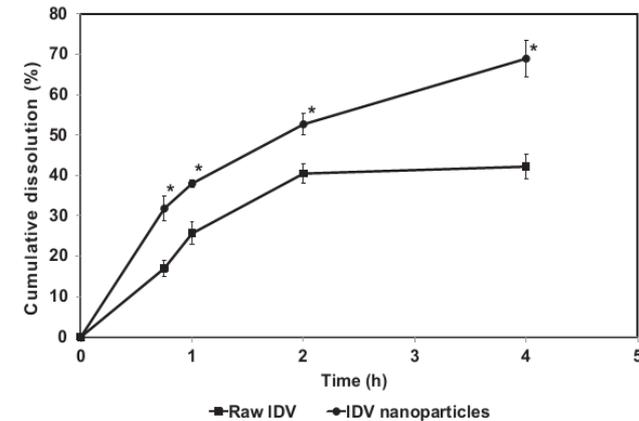
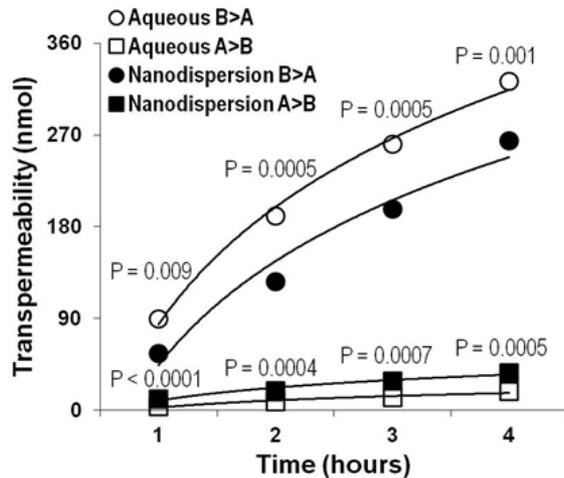
NANOPARTICLE SYNTHESIS



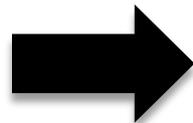
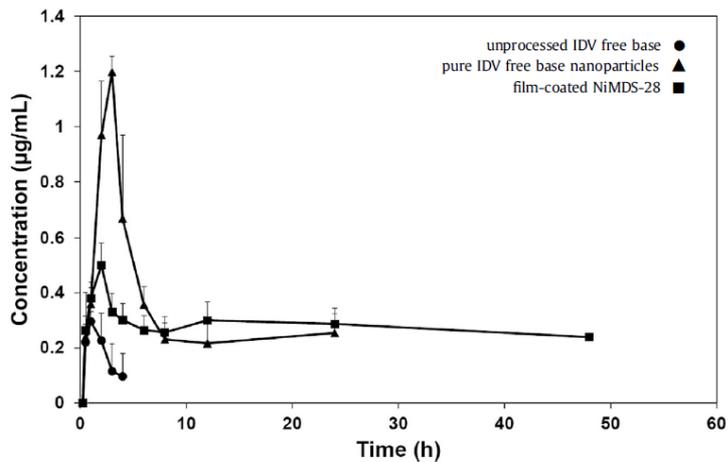
IMPROVED RELEASE RATE



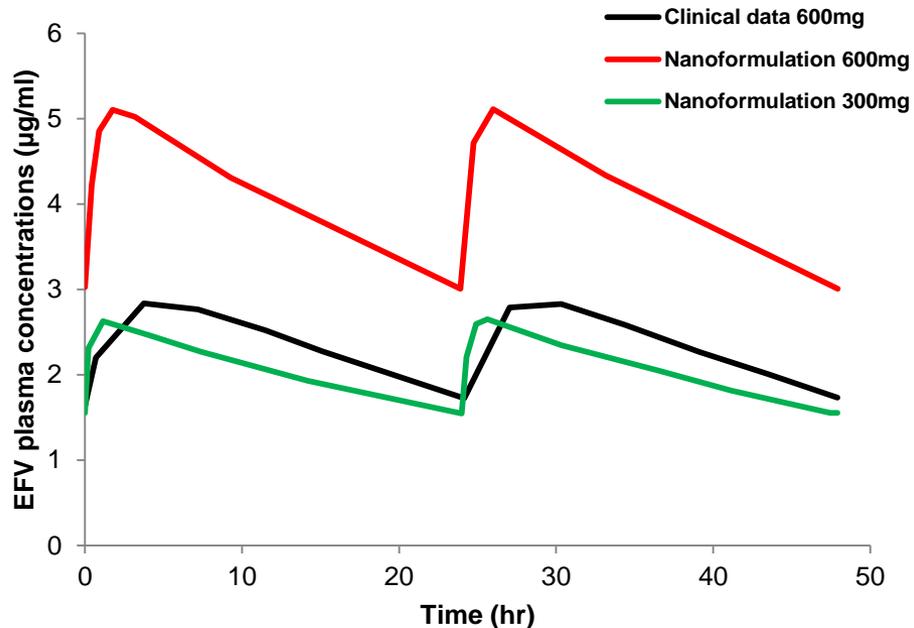
IMPROVED PERMEABILITY



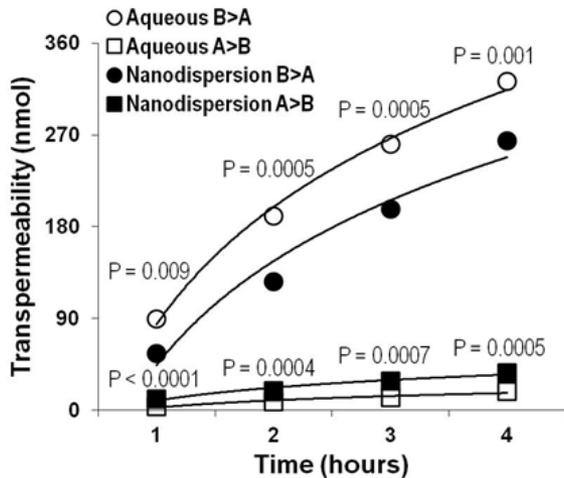
ENHANCED PHARMACOKINETICS IN ANIMALS

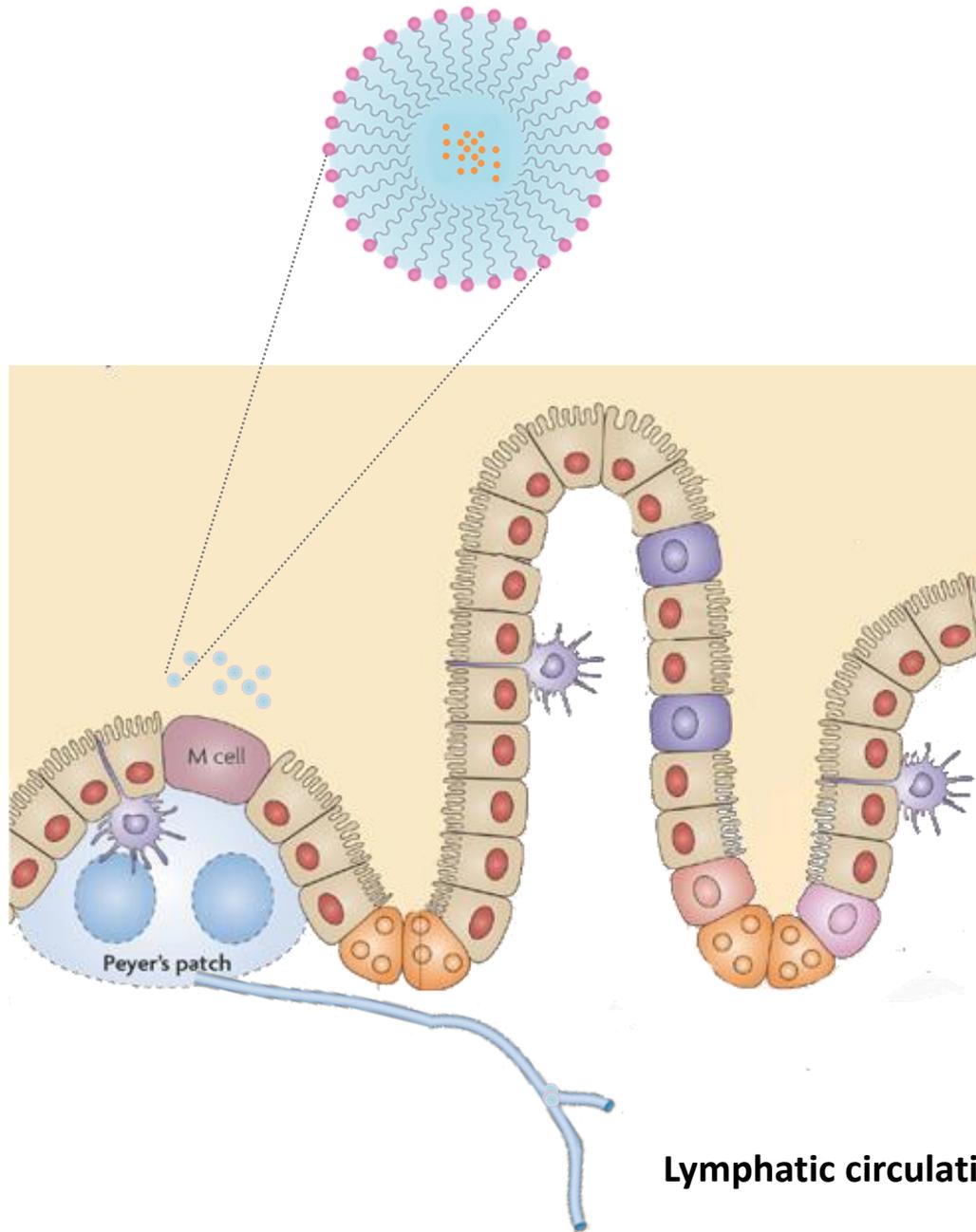


ENHANCED PHARMACOKINETICS IN HUMANS??



IMPROVED PERMEABILITY





Lymphatic circulation - GALT

Lopinavir loaded solid lipid nanoparticles (SLN) for intestinal lymphatic targeting

M.R. Aji Alex^a, A.J. Chacko^a, S. Jose^a, E.B. Souto^{b,c,*}

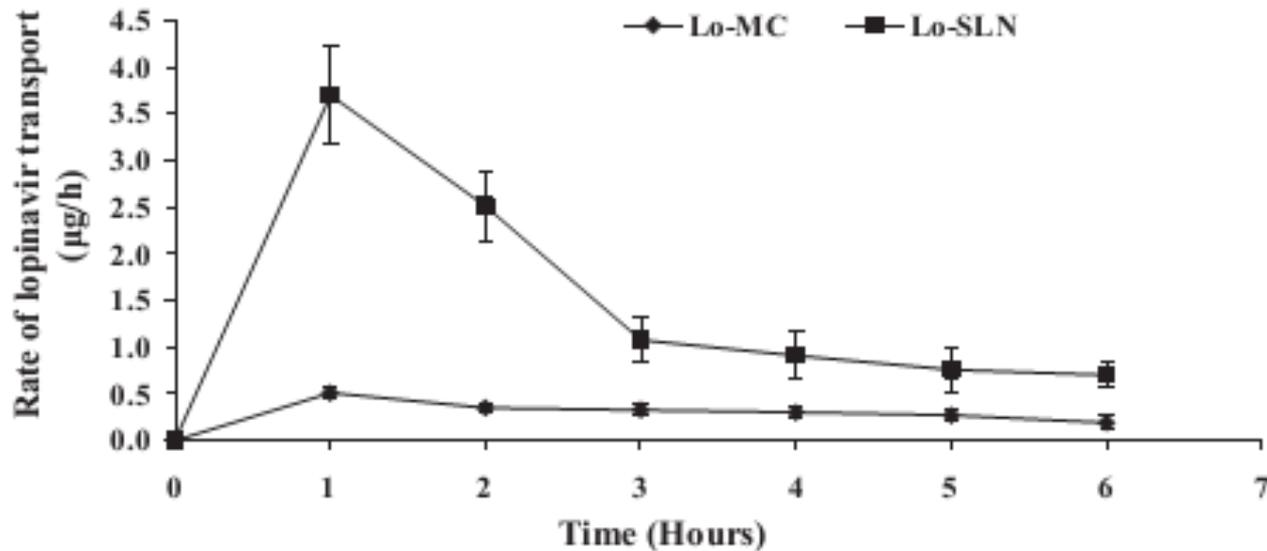


Fig. 7. Rate of intestinal lymphatic uptake of lopinavir. The *p* value of Lo-SLN versus Lo-MC was <0.001.

Table 2

Cumulative lymph flow and cumulative amount of lopinavir secreted in lymph.

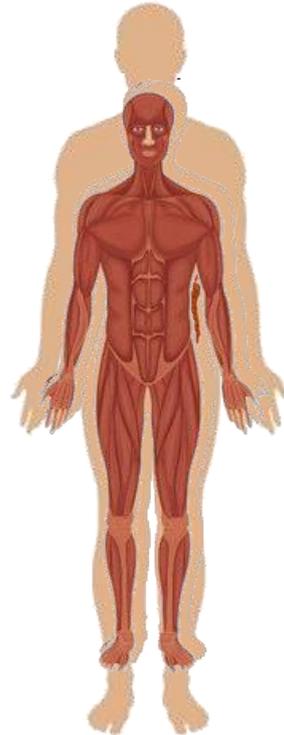
| Formulation | Cumulative amount of drug found in lymph after 6 h (μg) \pm SD | Cumulative percentage dose of lopinavir transported in lymph \pm SD |
|-------------|---|---|
| Lo-SLN | 9.68 \pm 0.88 | 0.32 \pm 0.03 |
| Lo-MC | 1.97 \pm 0.42 | 0.066 \pm 0.01 |

“There are no safe molecules nor toxic ones. The dose makes the poison.”

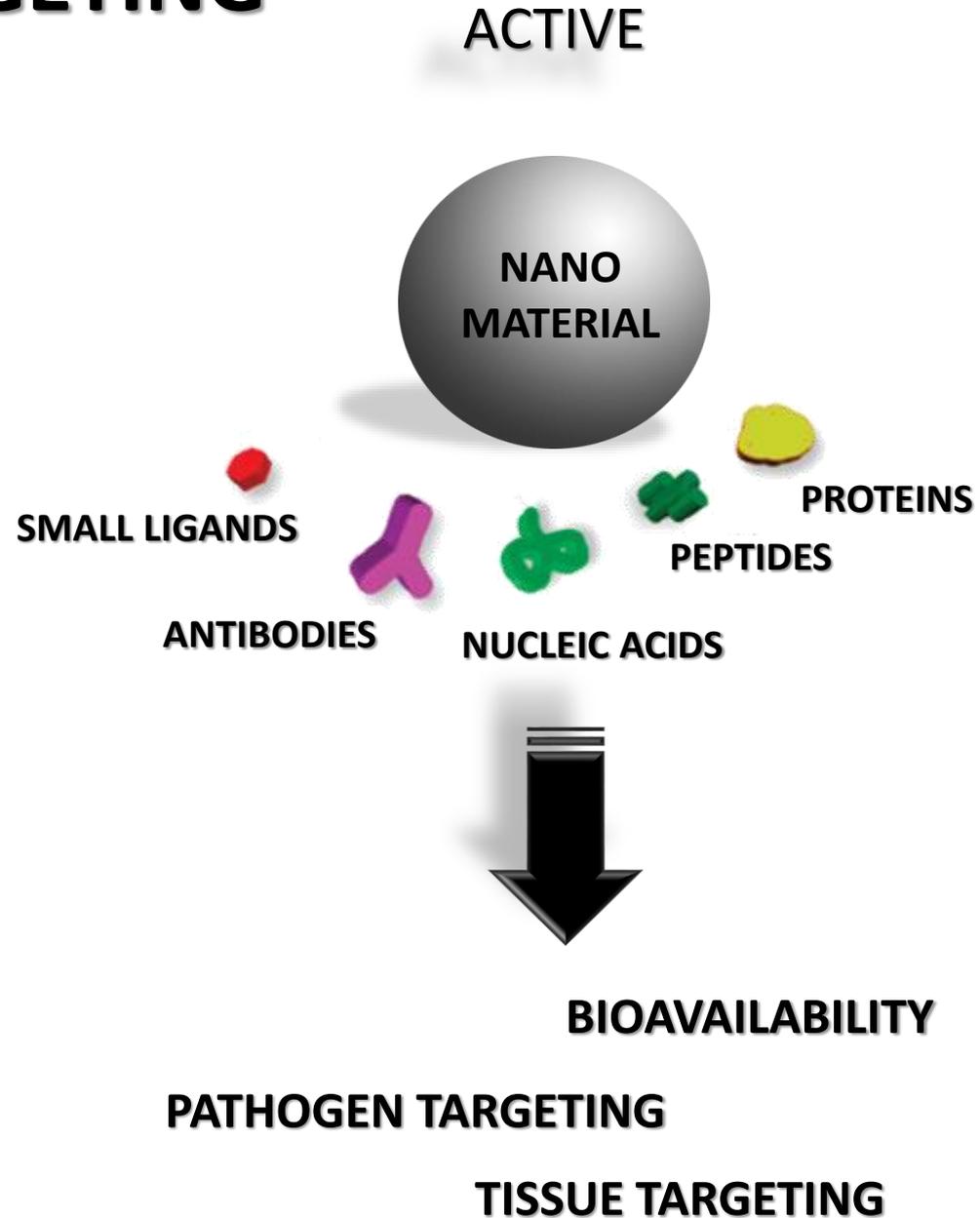
*Philippus Aureolus Theophrastus
Bombastus von Hohenheim (1493 –1541)*



DRUG DISTRIBUTION



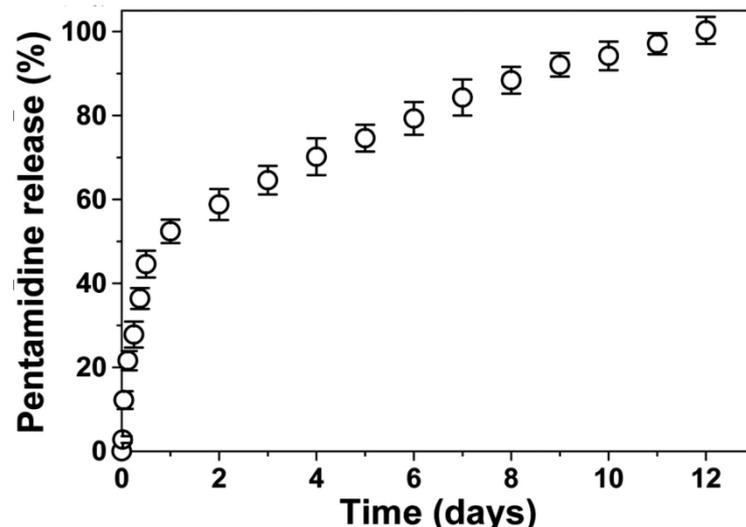
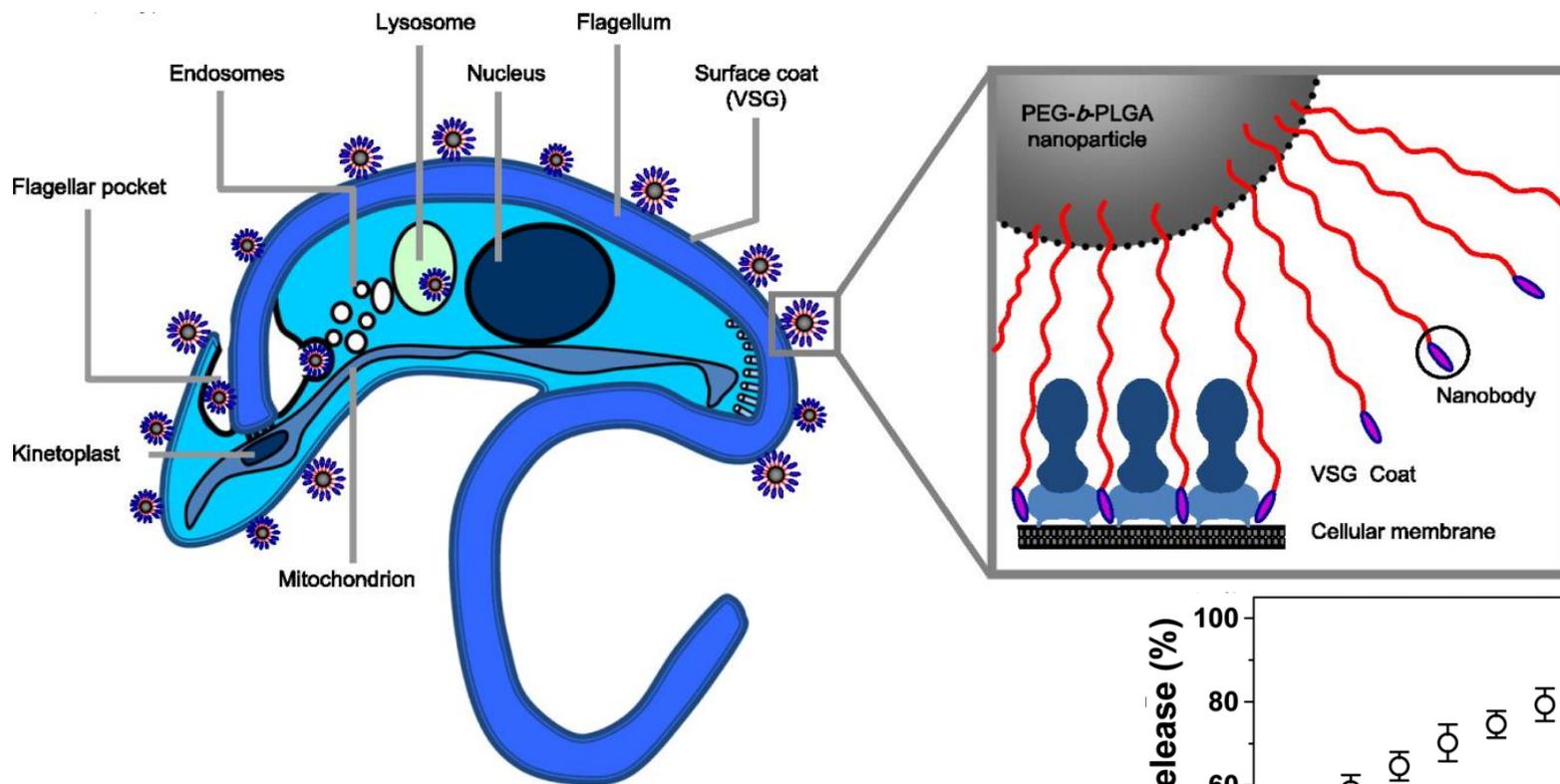
TARGETING



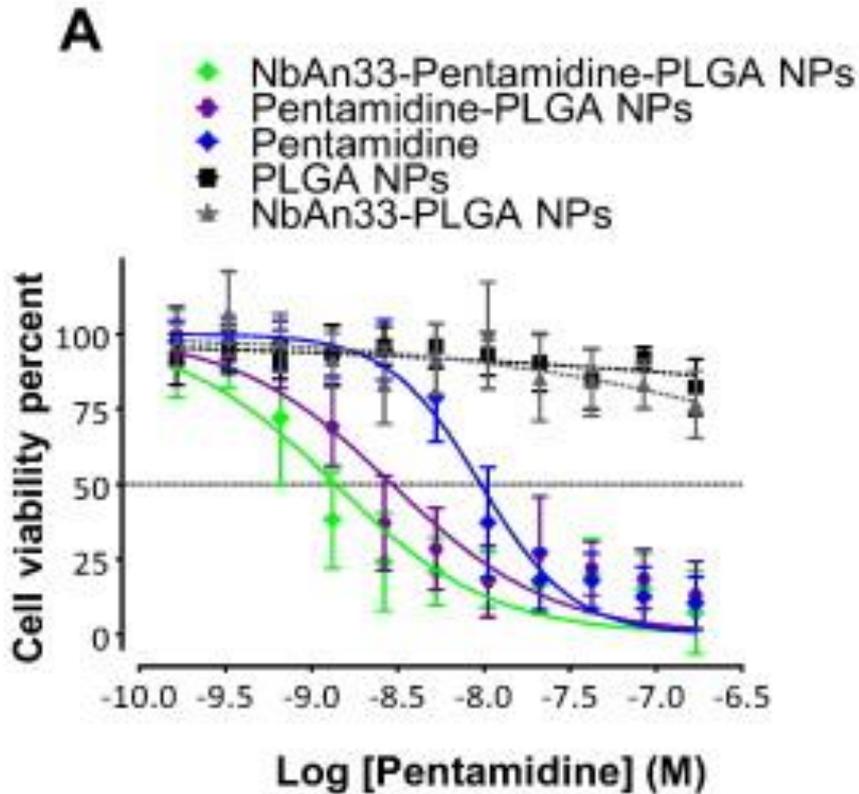
Nanobody conjugated PLGA nanoparticles for active targeting of African Trypanosomiasis

Journal of Controlled Release 197 (2015) 190–198

José L. Arias^a, Juan D. Unciti-Broceta^{b,c,d}, José Maceira^{b,c,d}, Teresa del Castillo^{b,c,d}, José Hernández-Quero^b, Stefan Magez^{e,f}, Miguel Soriano^{d,g,1}, José A. García-Salcedo^{b,c,d,*}

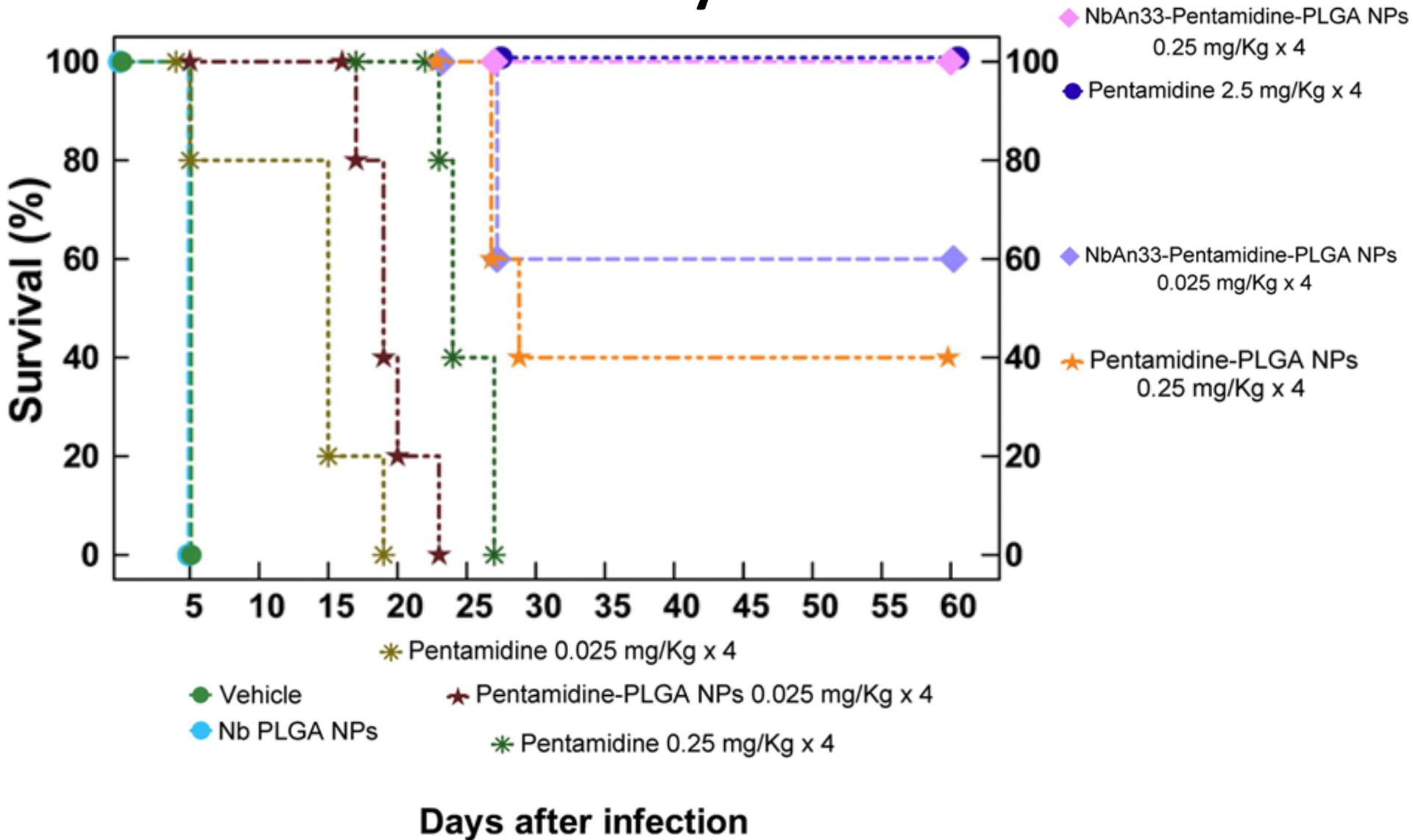


Activity in vitro

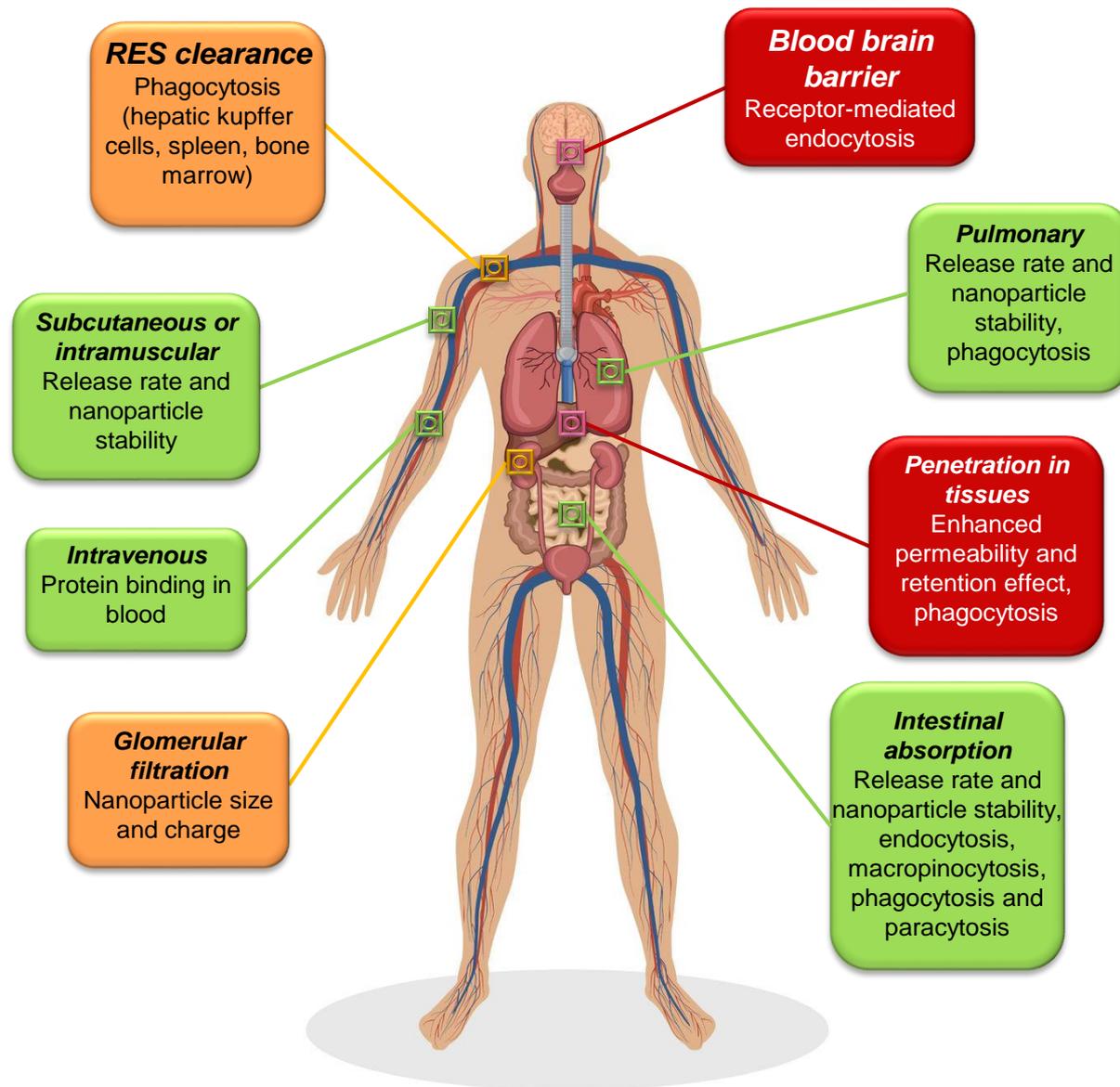


In vitro effectiveness study. A) Dose–response curve (% cell viability versus pentamidine concentration). B) IC 50 values. Blue column: IC 50 value for free pentamidine. Purple column: IC 50 value for pentamidine-PLGA NPs..

Activity in vivo

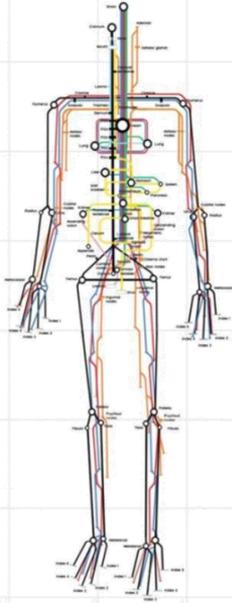
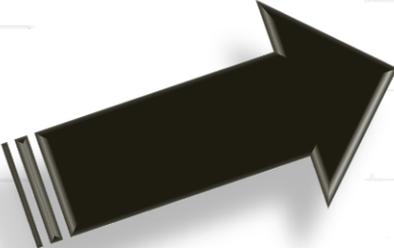
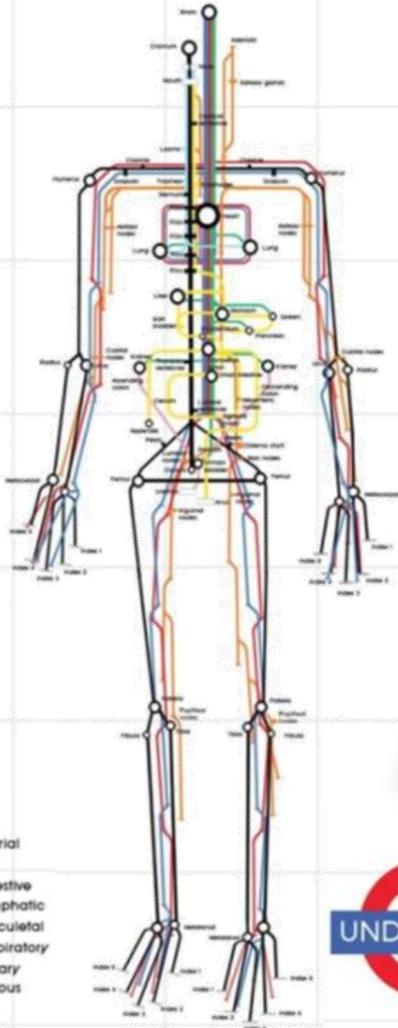


Nanoparticle ADME

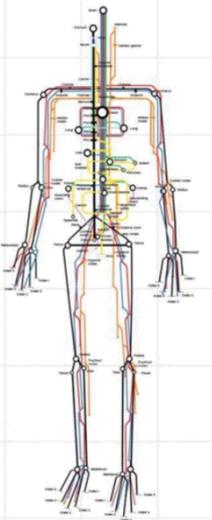
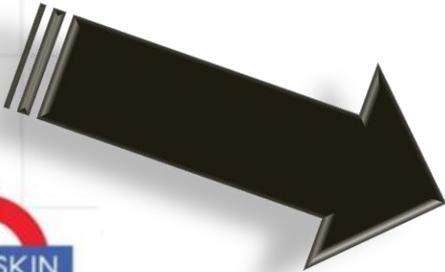


RELEASED DRUG

NANOPARTICLES



NANOPARTICLE COMPONENTS



© Transport for body

Created by: Sam Loman

© Transport for body

Created by: Sam Loman

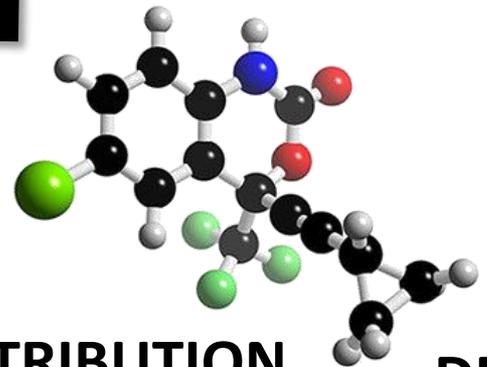
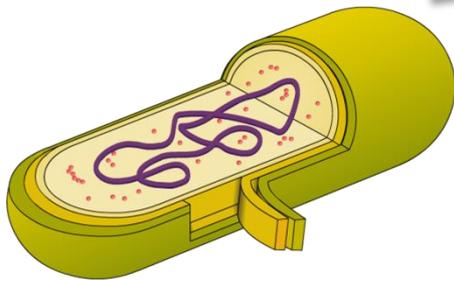
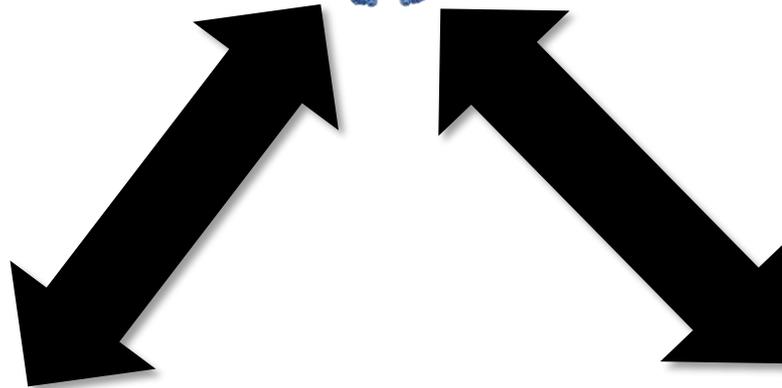


SPECIAL POPULATIONS

GENETICS

ADHERENCE

DEMOGRAPHICS



RESISTANCES

RESERVOIRS

DISTRIBUTION

DDIs

FITNESS

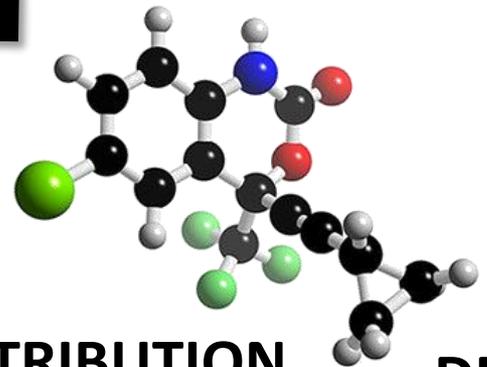
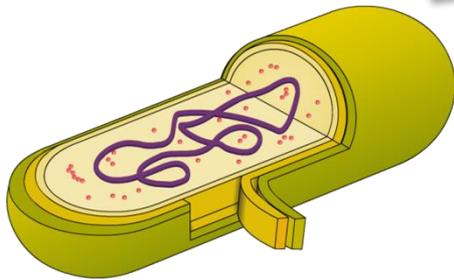
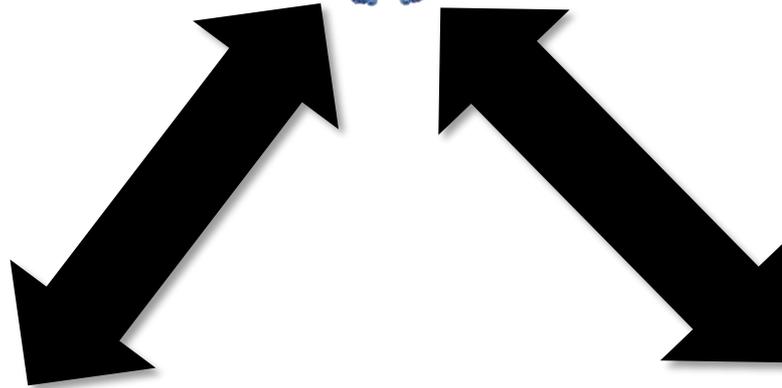
TOXICITY

SPECIAL POPULATIONS

GENETICS

ADHERENCE

DEMOGRAPHICS



RESISTANCES

RESERVOIRS

DISTRIBUTION

DDIs

FITNESS

TOXICITY

COMPOSITION

SPECIAL POPULATIONS

GENETICS

SIZE

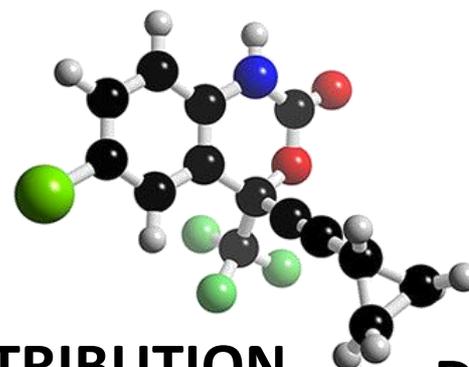
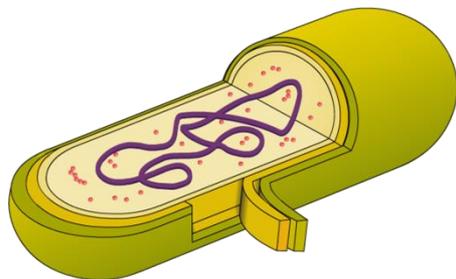
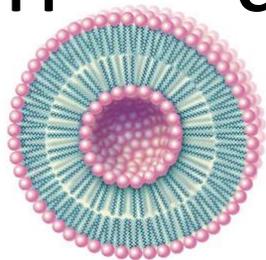
LIGANDS

ADHERENCE

DEMOGRAPHICS

STABILITY

CHARGE



DISTRIBUTION

DDIs

TOXICITY

RESISTANCES

RESERVOIRS

FITNESS

Nanoparticle design

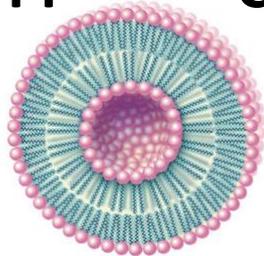
COMPOSITION

SIZE

LIGANDS

CHARGE

STABILITY



Pharmacological priorities

ORAL BIOAVAILABILITY

LOW TOXICITY

PATHOGEN
TARGETING

SUSTAINED RELEASE

PENETRATION IN
TISSUES

Challenges

ANIMAL MODELS IN VITRO MODELS

UNKNOWN MECHANISMS

LOW LOADING

NANOTOXICITY NONSPECIFIC LIGANDS

IMMUNE RESPONSE

Acknowledgments

Andrew Owen

David Back

Saye Khoo

Rajith Rajoli

Neill Liptrott

Lee Tatham

Phil Martin

Darren Moss

Paul Curley

James Hobson

Owain Roberts

Alessandro Schipani

Laura Dickinson

Sharon Murphy

Adny Henrique Silva

Adeniyi Olagunju

Christina Chan

Steve Rannard

Tom McDonald

Marco Giardiello

Tamara Alhilfi

Fiona Hatton

Sam Auty

Hannah Rogers

Andy Dwyer

Maude Le Hellaye

Helen Caulbeck

Jane Ford

Pierre Chambon



National Institute
of Allergy and
Infectious Diseases



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LIVERPOOL

