10th Anniversary
High Value Manufacturing Conference 2012

14 November 2012 Cambridge

www.cir-strategy.com/events/

GlobalAcorn
Advanced Therapeutics

Company Presentation

www.GlobalAcorn.com

10th Anniversary High Value Manufacturing Conference 2012

14 November 2012 Cambridge

Team

Name				Job Description
Prof	Andrew	Miller	GlobalAcorn	Chief Executive and Science Officer
Dr	Jeremy	Curnock-Cook	GlobalAcorn	Chairman
Dr	Shoona	Vincent	GlobalAcorn	Clinical Development/Regulatory Strategy
Prof	Luigi	Martini	King's College	Advisory Board Chairman
Dr	Nigel	Whittle	UK TI	Commercial Development
Dr	Matthew	Killeen	Consultant	Pharmaceutical Analyst
Ms	Joye	Leventhal	GlobalAcorn	Chief Business Development Officer
Mr	Steven	Allcock	GlobalAcorn	Chief Operating Officer
Mr	Stephen	Wright	GlobalAcorn	Finance Director

GlobalAcorn

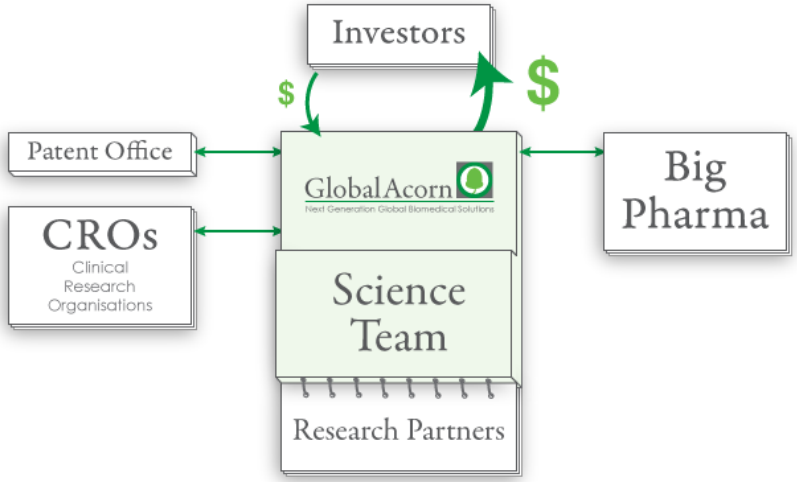
Advanced Therapeutics

- GlobalAcorn discovers and develops advanced therapeutics that address unmet medical needs in chronic, high burden diseases, including pain, diabetes, and dyslipidemia.
- GlobalAcorn is seeking an industry/ financial investor(s) partner to develop a pipeline of advanced therapeutics in a range of therapeutic areas.
- GlobalAcorn has a technology pipeline. First to be developed for commercialization is GA8 SMOL-PAIN, an analgesic for chronic nociceptive back pain.

J A · K E M P

Huntingdon Life Sciences

Working for a better future



GlobalAcorn's Pipeline

Product Development Pipeline

- **GA8 SMOL-PAIN** ←
- GA7 SMOL-DIAB
- GA6 NM-CAN
- GA5 NM-HBV
- GA4 NM-TB
- GA3 MEP-TB
- GA2 NM-MAL
- GA1 NP-MAL

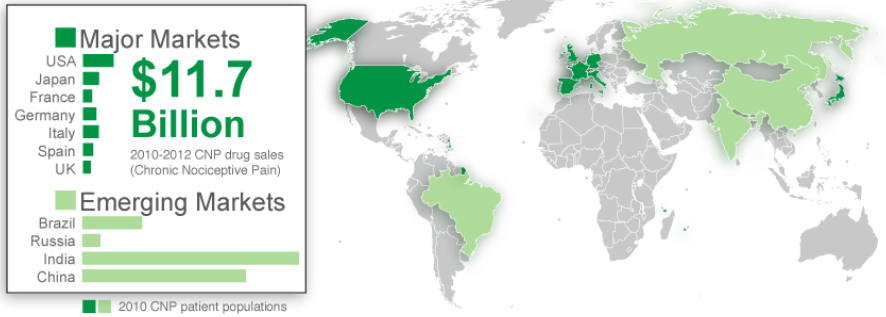
Developed around combinations of Nanotechnology and Bio-actives.

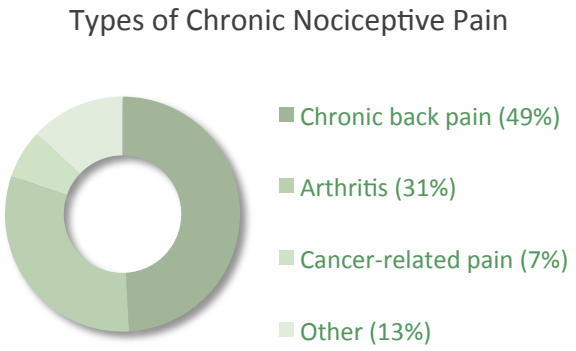
Development Network

- King's College London
- INSERM, Marseille, France
- Virtanen Institute, Kuopio, Finland
- Bergen Uni, Bergen, Norway
- IICT, Hyderabad, India
- Chula Uni, Bangkok, Thailand
- Wits Uni, Johannesburg, RSA
- Shanghai Jiaotong Uni, Shanghai

Science capability/ technology networks.

GA8 SMOL-PAIN Business Opportunity





- Market dominant chronic nociceptive pain drug is (opioid-based) Oxycontin with annual sales of **$3bn.** Oxycontin patent due to expire in 2013.

- GA8 SMOL-PAIN represents a novel, first-in-class, P2X3 receptor antagonist for the treatment of chronic low back pain. Through its mechanism of action, GA8 SMOL-PAIN has been developed to address overwhelming medical unmet needs for safer pain therapies lacking abuse potential:

- non-opioid based
- locally administered
- locally acting
- P2X3 focused mechanism

GA8 SMOL-PAIN

- Indication: Chronic nociceptive pain
- IP Status: Filings completed
- Project Status:
  - Pre-clinical, lead optimization
  - Two advanced lead candidates identified
  - IND/NME development strategy in place
- Partner Profile:
  - Expert in clinical development
  - Expert in manufacture and marketing

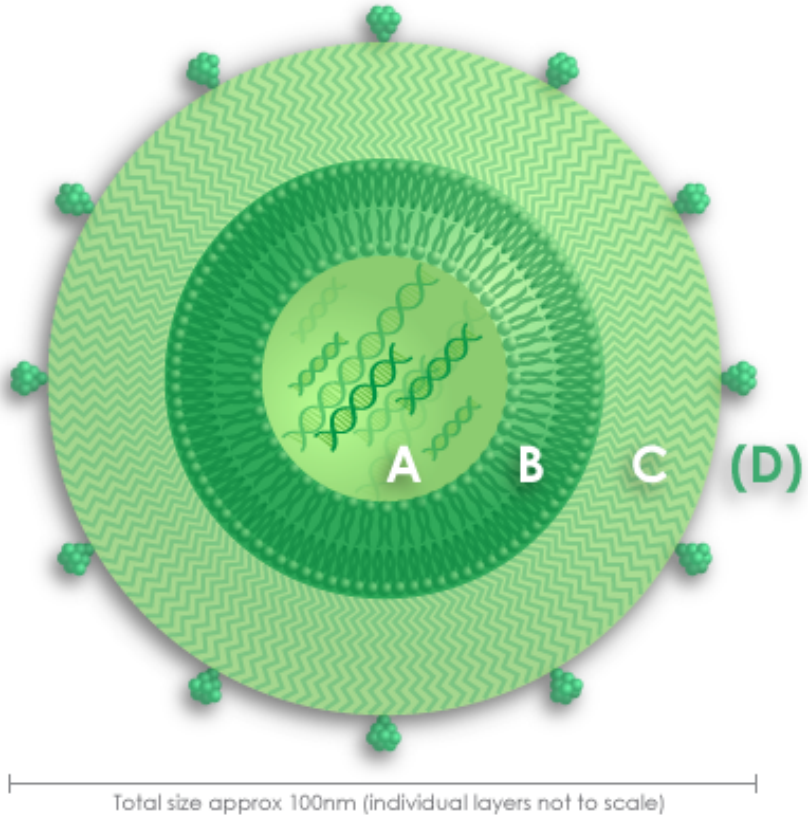
GA8 SMOL-PAIN Target Product Profile

- First-in-class “P2X3 receptor antagonist”
- Block pain locally without entering the brain
  - Fast acting
  - Potential for fewer side effects
- Administered by:
  - Injection, local under-the-skin injection
  - Cream, oil or lotion
- Prepared for sale to the Pharmaceutical Industry

GA7 SMOL-DIAB Target Product Profile

- First-in-class broad band “bioactive lipid”
- Modulates dyslipidemia, accelerates fat burning
  - Fast acting
  - Potential for treatment of metabolic syndrome disorders
  - Minimal side effects anticipated
- Administered:
  - Per-oral, gut adsorption for direct transport to liver
- Prepared for sale to the Pharmaceutical Industry

Bio-Nano Approach to Advanced Therapeutics



ABCD Nanoparticle

A Payload API
siRNA / pDNA / drug agent

B Protective Envelope
Lipid layer

C Stealth/Biocompatibility
Polymer layer

D Biological Recognition
Target-matching Ligands

Off-the-Shelf Synthetic Chemical ComponentTool-Kits

↓

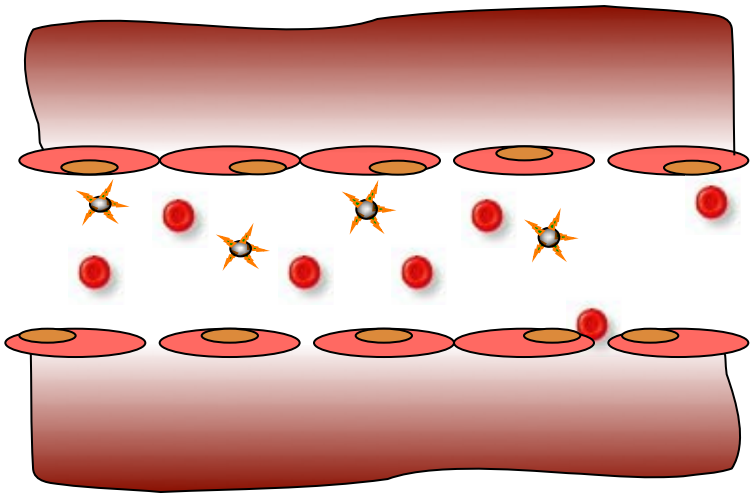
Bespoke ABCD Nanoparticles

↓

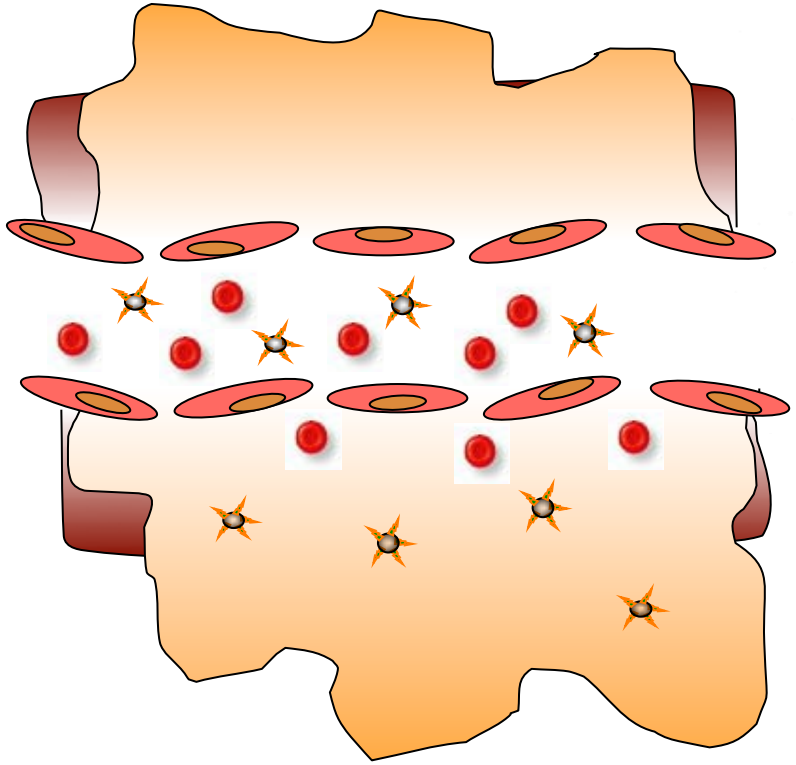
Tailor-Made Delivery Solutions

Enhanced Permeability and Retention

EPR Effect – leads to accumulation of nanoparticles in the tumour tissue



Normal tissue



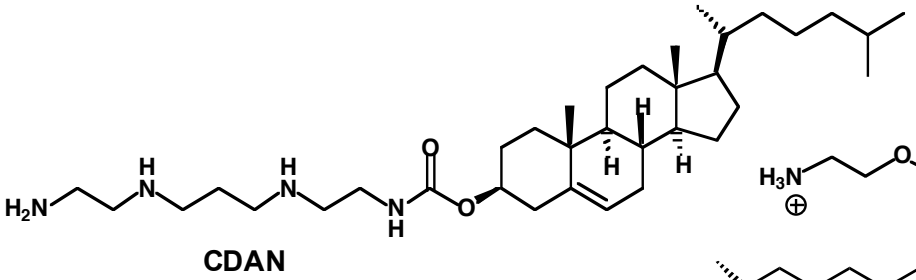
Tumour tissue

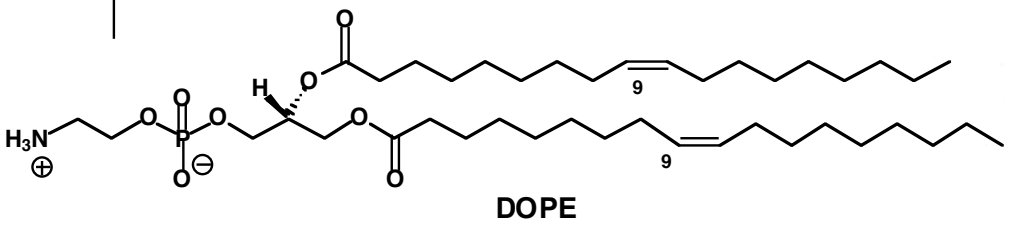
Erythrocyte

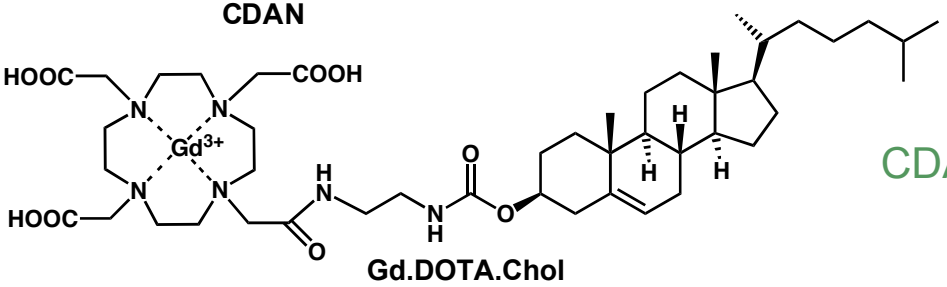
Macromolecules/nanoparticles

MAGfect™ for Gd *in vitro* delivery

- Launched in 2007
- "Diagnostics" delivery

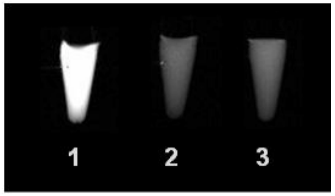


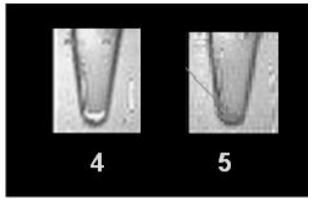




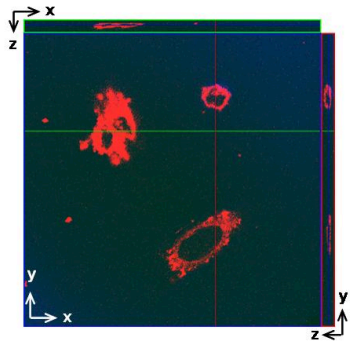
CDAN:DOPE: Gd.DOTA.Chol 4:3:3 m/m/m ratio cationic liposomes

Synthetic vector for Gd^{3+} (and pDNA or siRNA) delivery to cells





MRI images: 1. MAGfect™; 2.Control liposomes; 3. PBS
4. Cells post MAGfect treatment; Cells post control liposome treatment

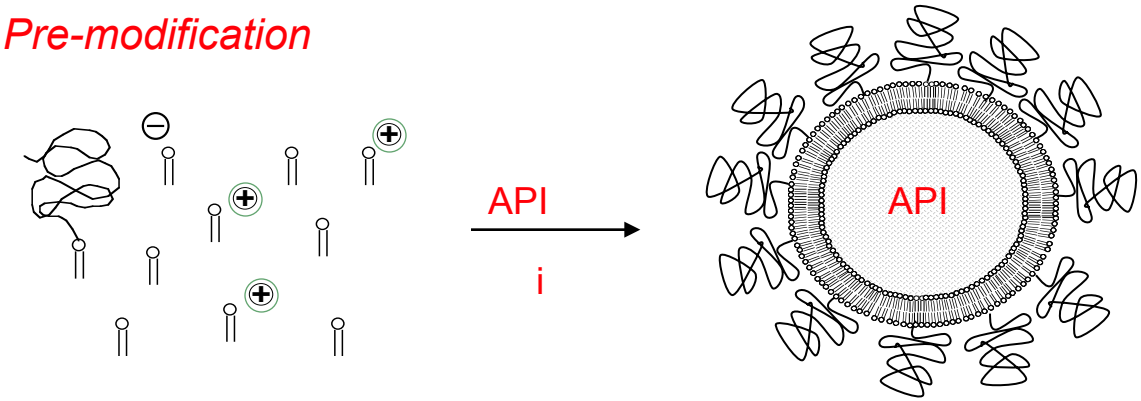


MAGfect™ Cell entry (DSPE-Rhoda)

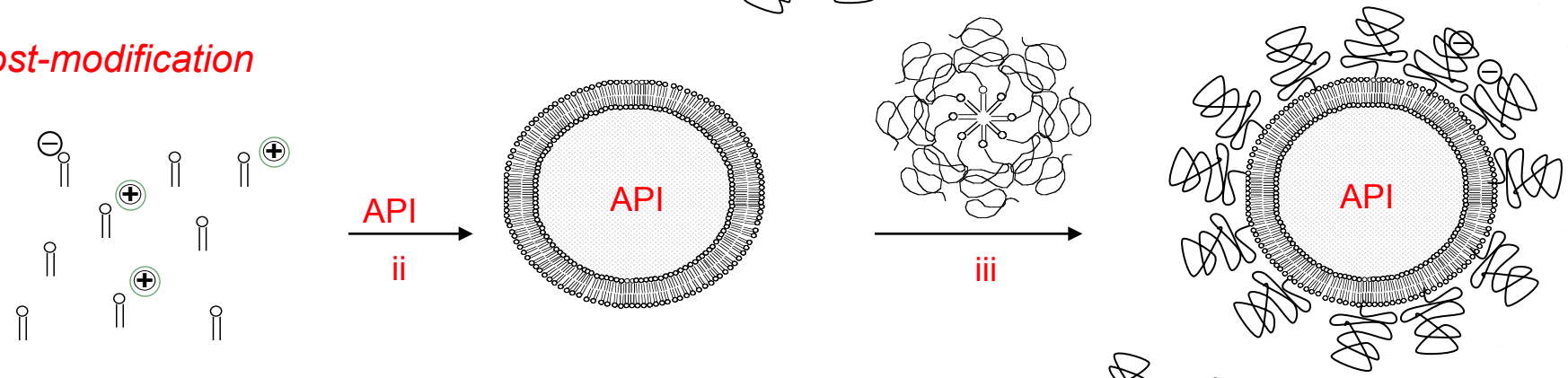
M. Oliver, *et al., Org. Biomol. Chem.* 2006, *4*, 3489-3497.

API-ABC nanoparticle assembly

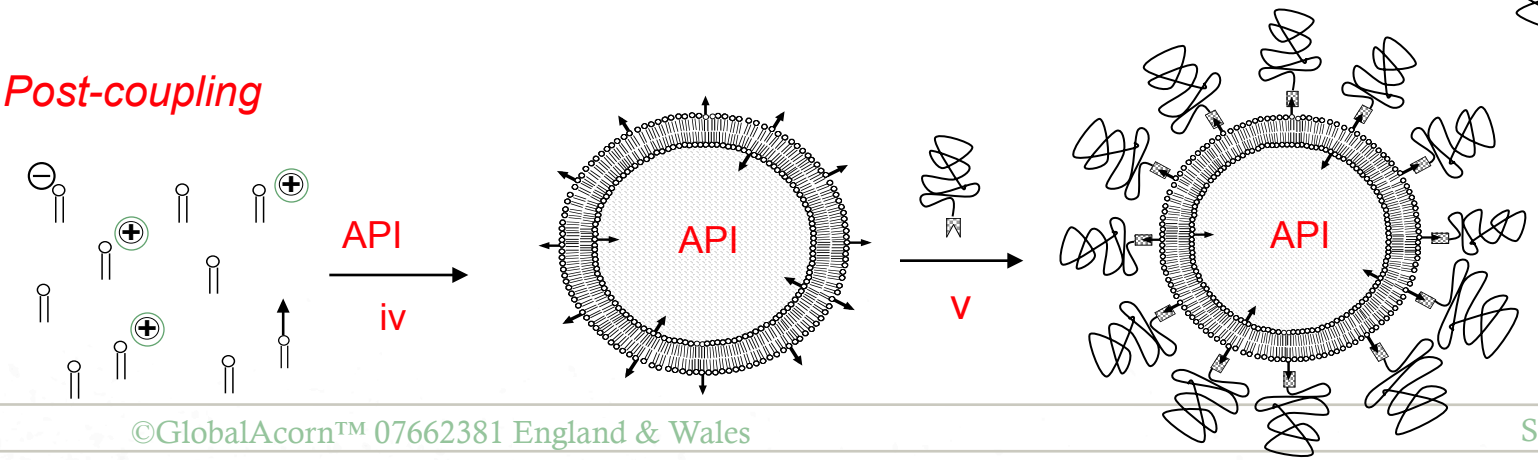
Pre-modification



Post-modification

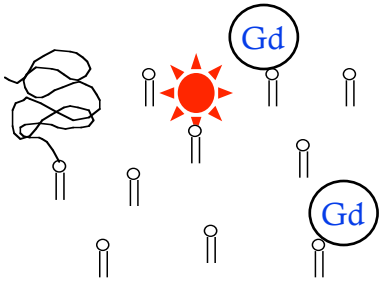


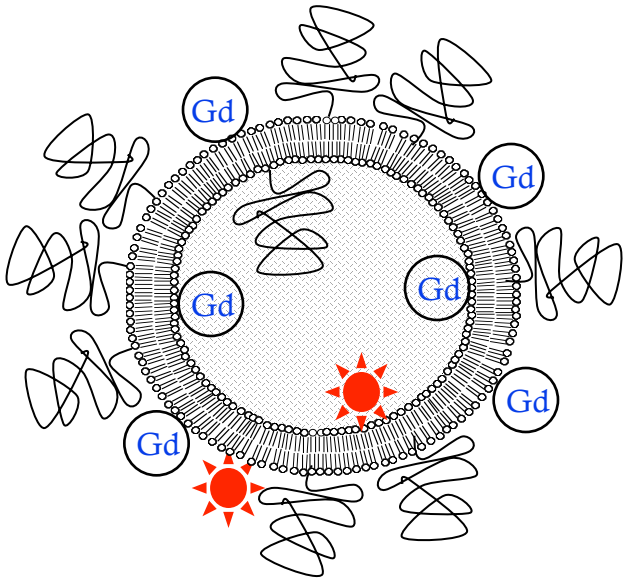
Post-coupling

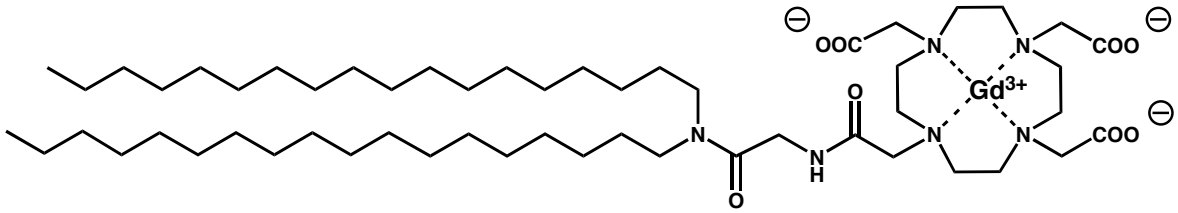


Gd-ABC nanoparticles; *in vivo* delivery

Pre-modification







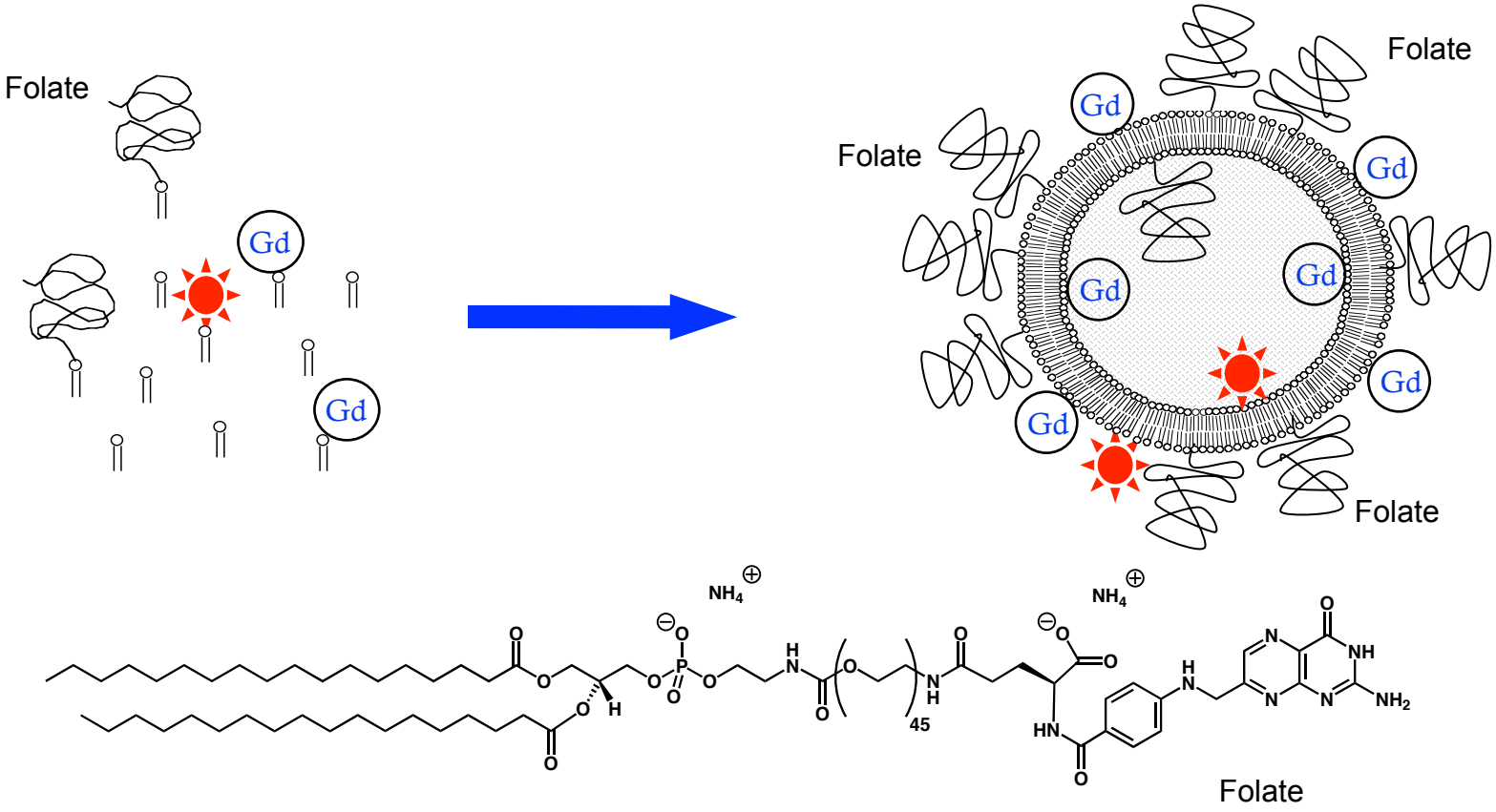
LTC Gd-ABC nanoparticles (Gadonano) for MRI and fluorescence imaging

Gd.DOTA.DSA/DOPC/Chol/DSPE-PEG^{2000}/DOPE-Rhoda (30:32:30:7:1, m/m/m/m/m)
size: ~ 100 nm (PCS and cryo-EM); net charge ~ neutral

Gd-ABCD nanoparticles; *in vivo* delivery

Pre-modification

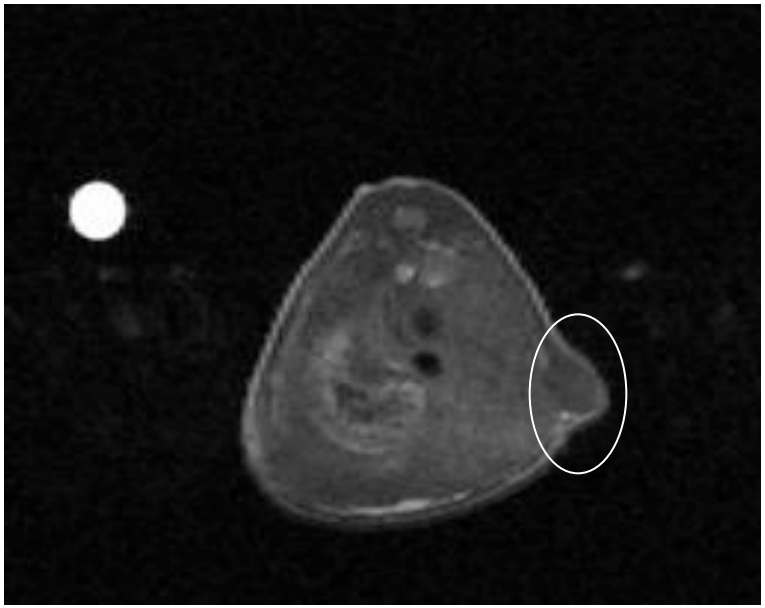
LTC enabled



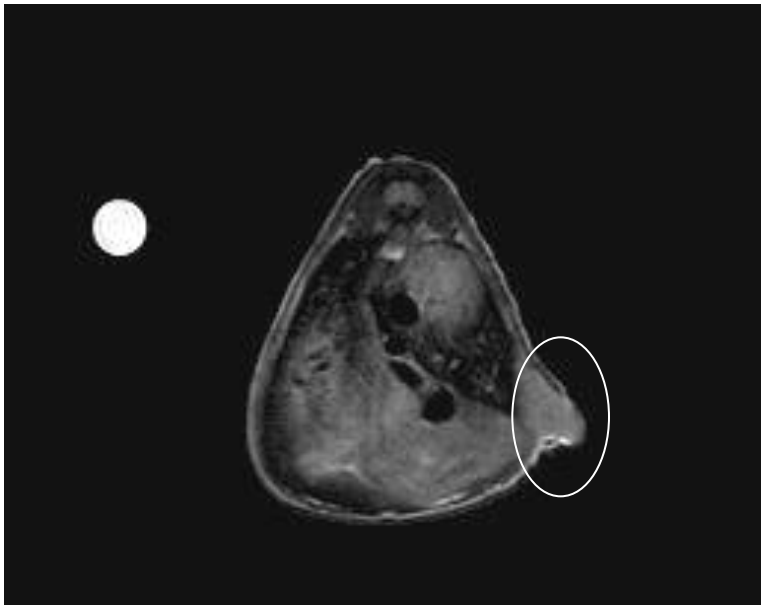
LTC Gd-ABCD nanoparticles

MRI scans of xenograft tumour

- MRI scans of transversal IGROV xenograft tumour in Balb/c nude mice pre- and post- i.v. injection of LTC Gd-ABC nanoparticles.
- Tumour shows positive contrast enhancement from decrease in T_1 values owing to the presence of Gd.



Pre-injection

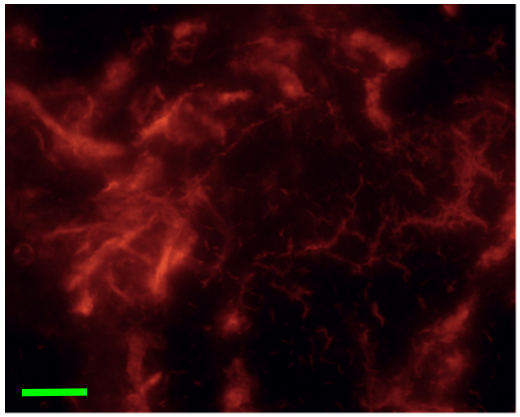


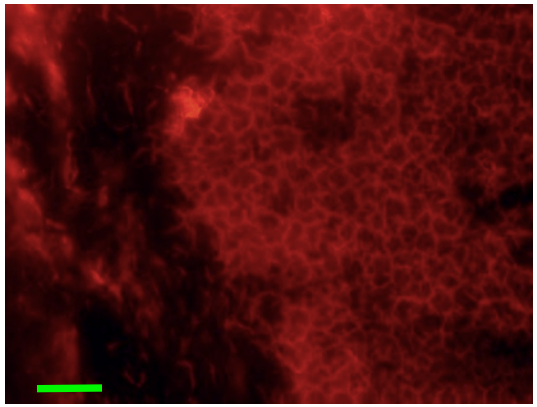
Post-injection 24 h

TR 2800, TE 10, FOV: 45 x 45, Avg: 1, 2 μm, 20 slices

N. Kamaly, *et al., Bioconjugate Chem.* 2008, *19,* 118-129.

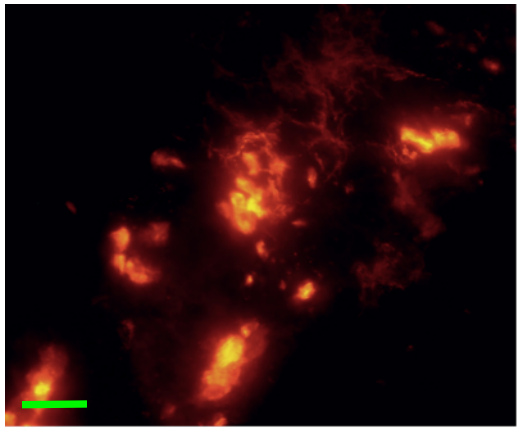
Fluorescence imaging of tumour slices

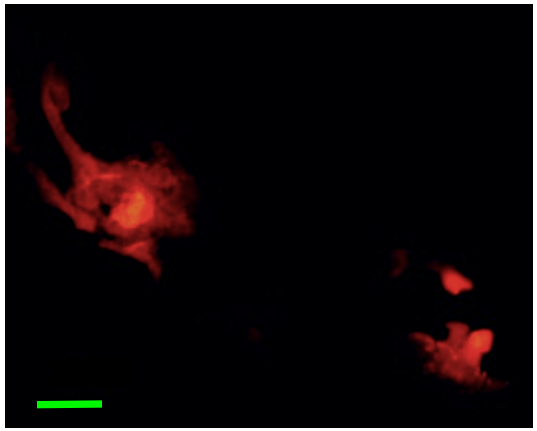




LTC Gd-ABC nanoparticles

bar 50 μm





LTC Gd-ABCD nanoparticles

surface-section

mid-section

- Fluorescent micrographs of tumour sections (10mm) embedded in OCT
- Tumour fluorescence distribution is the same as for "ghost" nanoparticles
- Fluorescence missing from necrotic regions of tumour

N. Kamaly, *et al*., *Bioconjugate Chem.* 2009, *20*, 648-655; N. Kamaly, et al., *Mol. Imaging Biol.* 2010, *12*, 361-366; N. Kamaly, *et al*., *Org. Biomol. Chem.* 2010, *8*, 201-211.

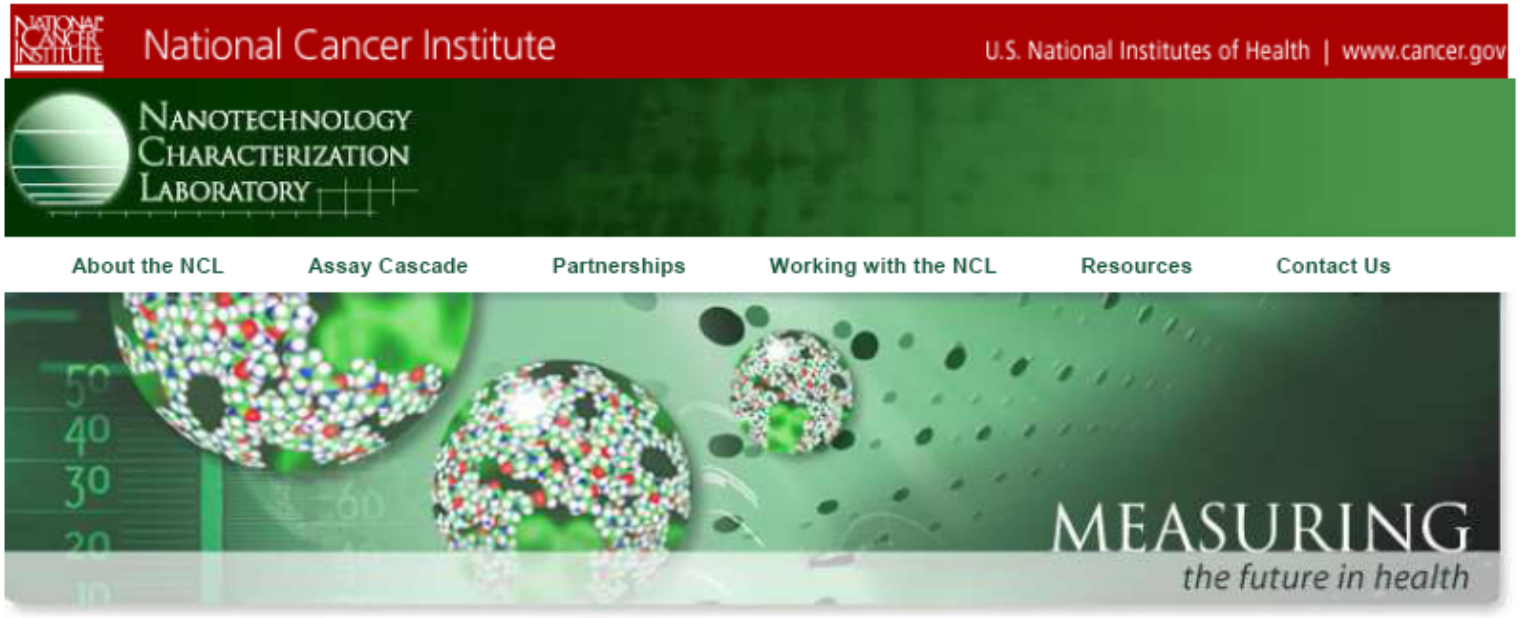
MRI and fluorescence conclusions

- LTC Gd-ABC/D nanoparticles formulations accumulate in tumours and enhance contrast
- "Ghost" LTC ABC/D nanoparticles have very similar tumour accumulation behaviour
- Folate bearing LTC Gd-ABCD nanoparticles appear to accelerate T_1 reductions in tumour tissue leading to accelerated image intensity

LTC Gd-ABC nanoparticle systems	% T_1 reduction		
	2 h	16 h	24 h
folate-LTC Gd-ABCD nanoparticle @ 0.5 non-targeted dose	62	71	66
LTC Gd-ABC nanoparticle	5	23	66

N. Kamaly, *et al*., *Bioconjugate Chem.* 2009, *20*, 648-655.

Progress with the NCL



- LTC Gd-ABC nanoparticles, “Ghost” LTC ABC nanoparticles and Folate bearing LTC Gd-ABCD nanoparticles selected by NCL for toxicology tests
- First non-US, European lab to be selected for this privilege
- Fast track through FDA for IND equivalent filing - early entry to clinical trials Companion diagnostic for metastatic cancerous lesions