INTERACTIONS OF NANOPARTICLES
WITH LIVING ORGANISMS
HIGHLIGHTING SOME OUTSTANDING ISSUES

PROFESSOR KENNETH A. DAWSON
CENTRE FOR BIONANOINTERACTINS
UNIVERITY COLLEGE DUBLIN

FUNDING EU FP7, NEURONANO, QNANO, SFI RFP, ESF EPITOPE MAP
CEIN (NSF)
40 nm green ps particles inside cell
red lysosome

A549 cell and LysoTracker Red
30 min after 10 min pulse of 100 μg/mL
Same system-4 hours later-many particles have reached lysosomes
The engineered Nanoscale is written in our biology, and medicine.

Chemicals partition........ Nanoparticles processed.
Same particle and lysosomes-different cells, forming blood brain barrier

‘blood side of barrier’

‘brain side of barrier’

BBB crossing very rare unless particles specially engineered for it

nanomedicine
NANOSAFETY;

Ensuring safety of all nanotechnology products (congressional hearings, EU parliament-regulations emerging)

NANOMEDICINE

Capacity to delivery to organs, cell specific etc

NANODIAGNOSTICS

Capacity to access compartments for early biomarkers etc

FOOD AND NANOTECHNOLOGY-EG ADDRESSING CHRONIC DISEASE OR DEFICIENCIES
Uncertainty has been damaging

1st reports of Nanotoxicity

2015 One Trillion value chain-NSF

INVESTMENT
Worldwide – $13.8 billion in 2007

VC investment in nano

share of total VC investments


Confusion
Stabilisation
Resolution

Ad hoc, often irreproducible in vitro

Science and system (IANH, OECD, ISO) in vitro

Joining it all up.....
BIOLOGICAL PROCESSING OF THE NANOSCALE
Nanoparticles travel into cell via Existing \textit{energy dependent} pathways

\textbf{Recognition Motifs and ‘Identity’ Matters}

Salvati, A Time and space resolved uptake study of silica nanoparticles by human cells. Mol Biosyst, 7, 371-378

The Hypothesis
Biological Identity of Nanoparticle in situ

Cozzarelli Prize NAS 2008

PNAS, 2007, 104, 2050-2055
NATURE NANO, 2009, 4, 546
JACS, 2010, 2011,
ACS Nano 2011
‘Hard Corona’
Nanoparticles are surface covered by proteins

Lighter shell is a rudimentary visualization of the corona
Protein coatings persist in time, and do change
Washing the particles does not remove the corona

NANOPARTICLES ENGAGING WITH CELLS
Overall Interaction determined by Adsorbed Proteins, not by Size

PROTEIN ABSENT

No protein present

PROTEIN PRESENT

Signal proportional to amount of nanoparticles in cell

Time (hours)

0 2 4 6

0

300

600

900

1200

CELLS/BARRIERS ‘SEE’ LONG LIVED OUTER COATING?
Emergent Biological identity
The Particles surface is only a scaffold
Tracking the Original Corona through cellular processing machinery

**2h pulse**
- **Lysosomes**: Green+red = yellow
- **Particles**: Green, on the way
- **Corona**: Yellow, just arrived
- **Lysosomes**: Red, not filled yet

**2h pulse + 4h chase**
- **Particles**
- **Corona**: In endosomes
- **Being processed**

**2h pulse + 7h chase**
- **Totally degraded**

**Protein corona**

Fluorescent intensity of protein corona vs. Chase time, hours
NANOPARTICLES
FUNCTIONAL IMPACTS CELLS

From Corona
After Corona stripped
Interactions with Lysosomes

Long term accumulation of Nanoparticles can be lysosomes
Primary target for safety studies

See upcoming papers in JACS, Nature Nano 2011
• Many early claims of nanoparticle toxicity were based on poorly understood science, and have not proven correct

• Interaction with biological systems is new, so caution and examination are legitimate

• Mechanistic understanding key-otherwise, ‘needle in a haystack’

• Well-managed and executed, such studies will ensure not just safety in nano, but future generations of nanomedicines and nanodiagnostics