Infrastructures, equipment, techniques and standardization

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Discipline and Research Practice

QualityNano Research Infrastructure

Infrastructure for Quality in nanomaterials safety testing.

EARLY REPORTS WERE CONTROVERSIAL, DISJOINTED, REPORTING (WRONGLY) EXTENSIVE ACUTE HAZARD-RESPONSE

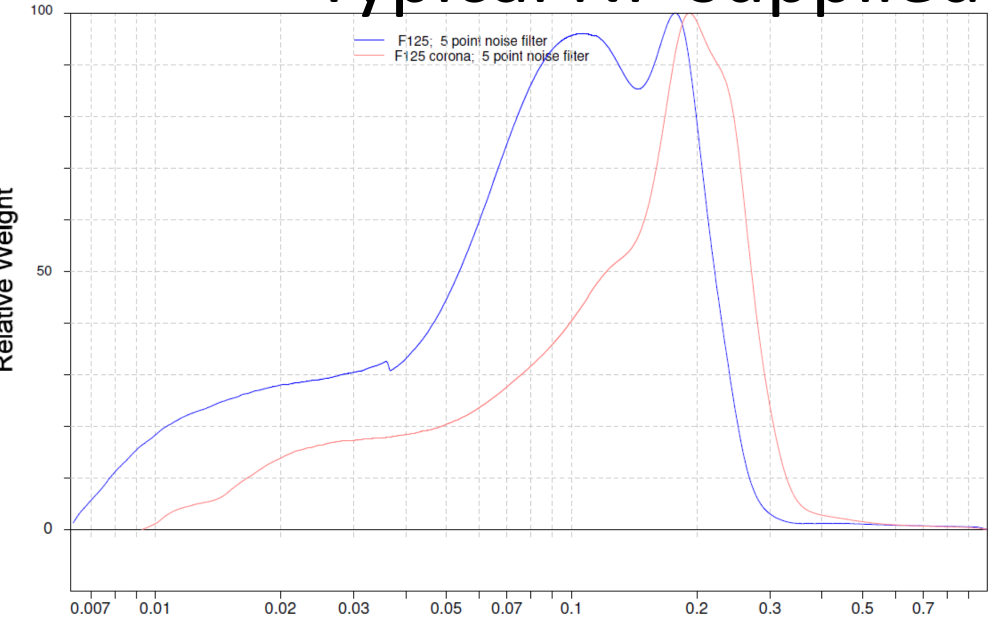
EARLY CONCEPT OF INFRASTRUCTURE WAS PLANNED TO TRY TO PREVENT THOSE ERRORS BY SHARING IDEAS, METHODS AND BENCHMARKING

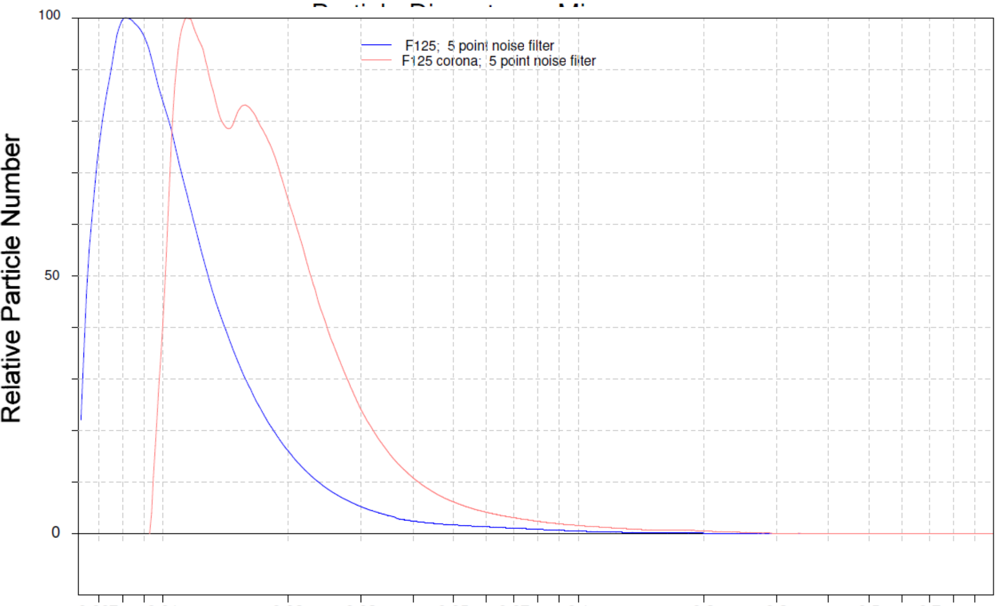
All we make is data-if it is not accurate AND meaningful, it is worthless

€1M spent to obtain acccurate reproducible data, is worth more than €100M spent on controversial conflicted irreproducible data.

Research Infrastructure QualityNano

Typical NP supplied within FP7 project





QUESTIONS TO BE ANSWERED NOTE YET AGREED

- SHOULD WE STUDY THIS MATERIAL?
- WHAT CONCLUSIONS CAN BE DRAWN FROM SUCH A STUDY?
- WOULD HIGH QUALITY JOURNALS (KNOWLINGLY) PUBLISH THE STUDY
- WILL FUNDERS WORLDWIDE RETAIN CONFIDENCE IN COMMUNITY WITH SUCH STUDIES

A HIGH LEVEL OF **AMBITION** FOR

AN **INFRASTUCTURE** MIGHT BE TO

GAIN **CONCENSUS** ACROSS COMMUNITY ON THE ANSWERS TO THOSE QUESTIONS

AND

TEACH/TRAIN/DEVELOP METHODS TO ENSURE FUTURE STUDIES ARE INDEED ENHANCED

CULTURES TAKES DECADES TO EVOLVE, DO BEST WE CAN TO AGREE SOME ISSUES AND LEAVE ROOM FOR INDIVIDUALS TO FOLLOW THEIR OWN OPINIONS

QualityNano Research Infrastructure

Infrastructure for Quality in nanomaterials safety testing.

Research

Develop novel analytical approaches and tools to enhance understanding of health and safety issues in nanotechnology and push beyond the state of the art in nanomaterials processing, labeling and identification and characterisation in situ.

Networking

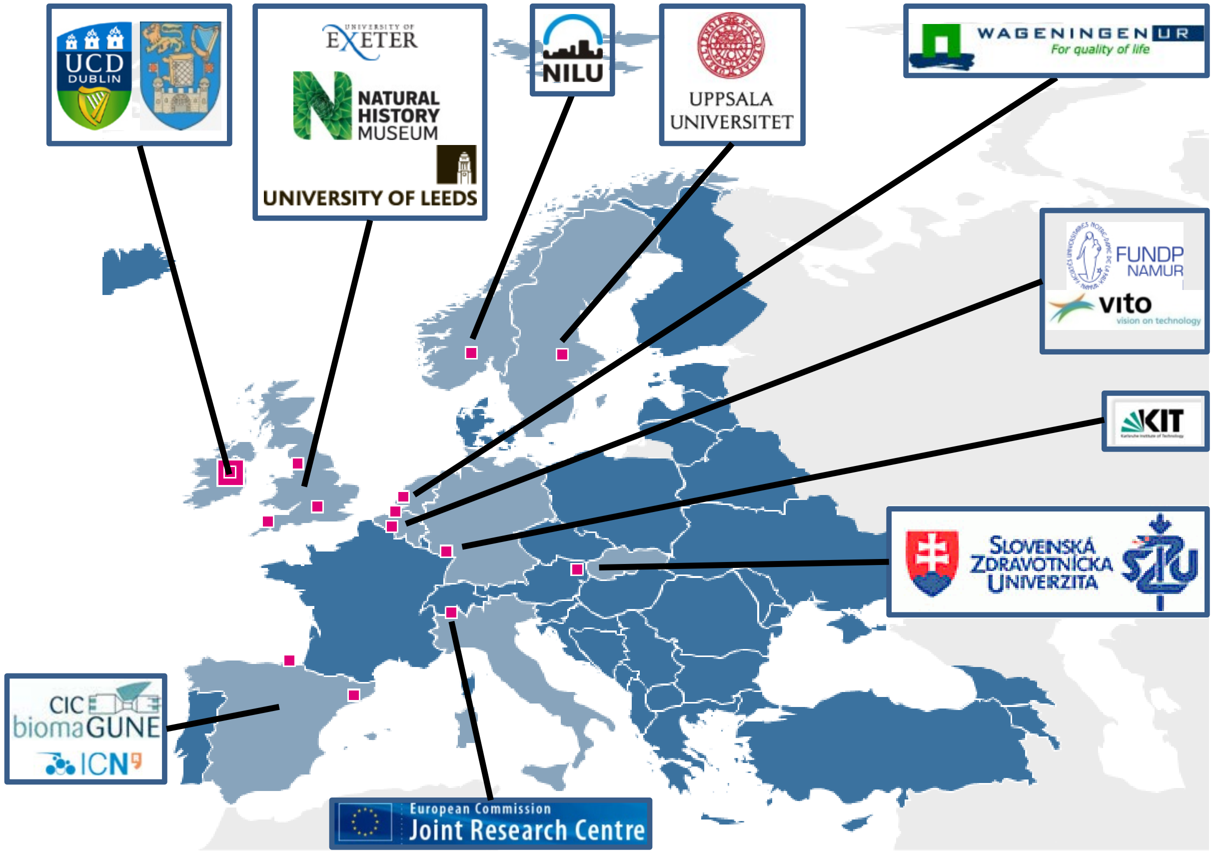
The Networking Activities (NA) component for QualityNano will aim to support and integrate the European nanosafety community.

Access

The Transnational Access (TA) component for QualityNano is dedicated to providing Users from the European nanosafety community access to nanomaterials processing, characterisation and exposure assessment facilities (TAFs).

TRAINING BASIC SKILLS

Transnational Access Sites



Italy
- Joint Research Centre - JRC - European Commission (JRC)

Belgium
- Facultés Universitaires de Namur (FUNDP)
- Vlaamse Instelling voor Technologisch Onderzoek NV (VITO)

Germany
- Karlsruher Institut für Technologie (KIT)

Ireland
- University College Dublin (NUID-UCD)
- Trinity College Dublin (TCD)

Netherlands
- Wageningen University (WU)

Norway
- Norsk Institutt for Luftforskning (NILU)

Slovakia
- Slovenská Zdravotnícka Univerzita v Bratislave (SMU)

Spain
- Centro de Investigación Cooperativa en Biomateriales (CIC)
- Institut Català de Nanotecnologia (ICN)

Sweden
- Uppsala University (UU)

United Kingdom
- Natural History Museum (NHM)
- University of Leeds (UNIVLEEDS)
- University of Exeter (UOE)

Transnational Access

Research Infrastructure
QualityNano

Welcome to QualityNano Transnational Access (TA)

Fully funded access to equipment & technical expertise at 15 nano-characterization laboratories in Europe

www.QualityNano.eu

QualityNano is funded by the European Commission
Grant Agreement No: FP7-262163

Applying is so easy…

1. Find your **technology of interest** at **www.QualityNano.eu**
2. Contact the TA expert and plan the experiments
3. Apply at www.QualityNano.eu
4. Peer review selection
5. Find a date for your visit
6. Visit your host laboratory
7. Publish the data acknowledging QualityNano TA

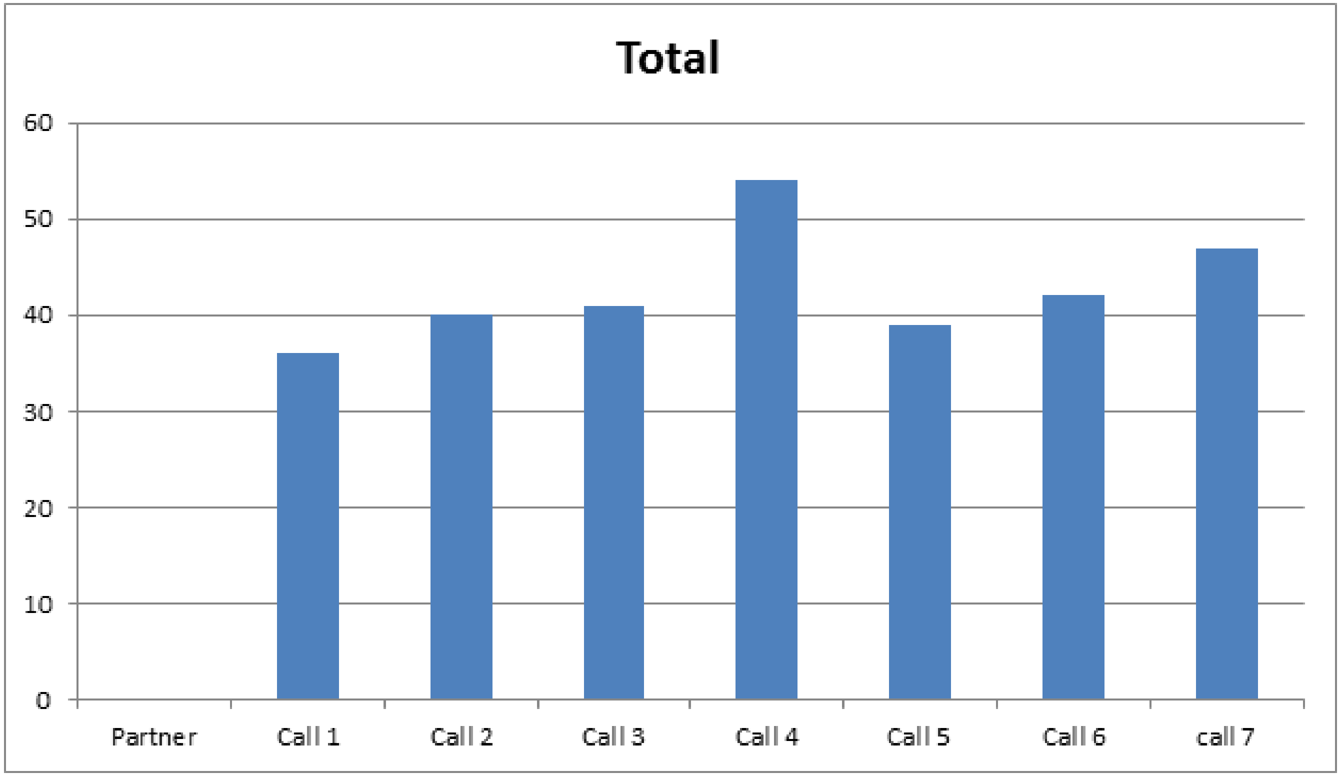
4 TA Technological categories:

- ✓ A) Nanomaterial synthesis
- ✓ B) Nanomaterial labelling & pre-processing
- ✓ C) Nanomaterial characterization *in situ* & *ex situ*
- ✓ D) Nanomaterial exposure assessment

www.QualityNano.eu

Transnational Access

Overall visit submitted



Transnational Access

Overall visits performed

Partner	Actual Number of visits	User days Granted
NUID-UCD	35	427
NHM	4	45
JRC	16	157
KIT	17	155
FUNDP	10	164
UNIVLEEDS	2	15
NILU	23	395
CIC	7	67
UU	5	65
ICN	14	130
WU	1	10
VITO	11	155
SMU	16	285
TCD	17	159
UOE	4	48
UoB	1	5
	183	**2282**

OTHER NETWORKING APPROACHES TO IMPROVING DATA QUALITY

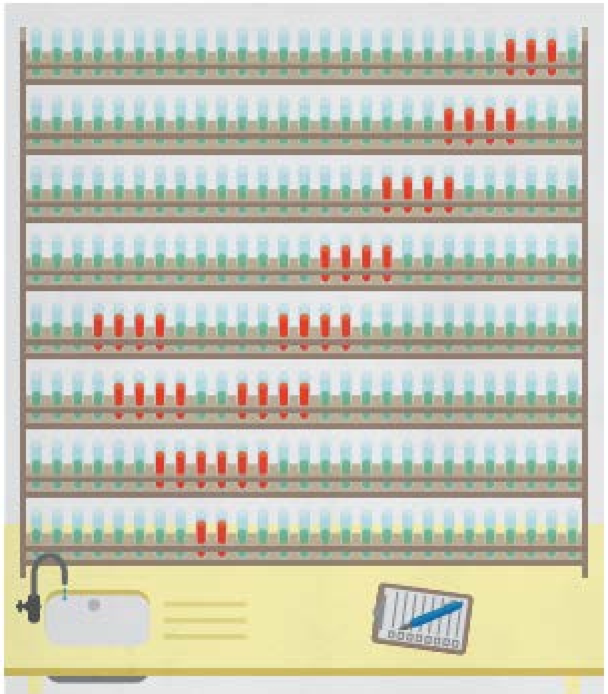
IF THE DATA IS NOT OF HIGH QUALITY-RELEVANT, REPRODUCIBLE AND TRANSPARENT
IT CAN DO MORE HARM THAN GOOD-WRONG DIRECTIONS

ANNOUNCEMENT

Reducing our irreproducibility

Over the past year, *Nature* has published a string of articles that highlight failures in the reliability and reproducibility of published research (collected and freely available at go.nature.com/huhbyr). The problems arise in laboratories, but journals such as this one compound them when they fail to exert sufficient scrutiny over the results that they publish, and when they do not publish enough information for other researchers to assess results properly.

From next month, *Nature* and the Nature research journals will introduce editorial measures to address the problem by improving the consistency and quality of reporting in life-sciences articles. To ease the interpretation and improve the reliability of published results we will more systematically ensure that key methodological details are reported, and we will give more space to methods sections. We will examine statistics more closely and encourage authors to be transparent, for example by including their raw data.



NIH plans to enhance reproducibility

Francis S. Collins and **Lawrence A. Tabak** discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

Guest Director's Letter: NIH Initiative on Enhancing Research Reproducibility and Transparency

Dear Colleagues:

In rare circumstances, scientific breakthroughs happen quickly and unexpectedly. More often, the scientific enterprise is an incremental process with new discoveries based upon the foundation of previous findings. Recently, a growing number of studies examining biomedical and behavioral research have drawn attention to a lack of methodological transparency and reproducibility of results in published research, which can affect this process. This issue may stem from a number of factors, including:

- deficiencies in reporting the experimental methodology and a lack of core standards that should be reported,
- bias in the randomization and blinding of experimental subjects,
- insufficient numbers of study participants to detect meaningful differences between the treatment and control groups, and
- problems in data handling and analysis which can lead to false positive results.

Dr. Lawrence A. Tabak,
Principal Deputy Director,
National Institutes of Health.

JOURNALS ACT
RECENT REVIEW FROM PLOS ONE

Journal requirements:

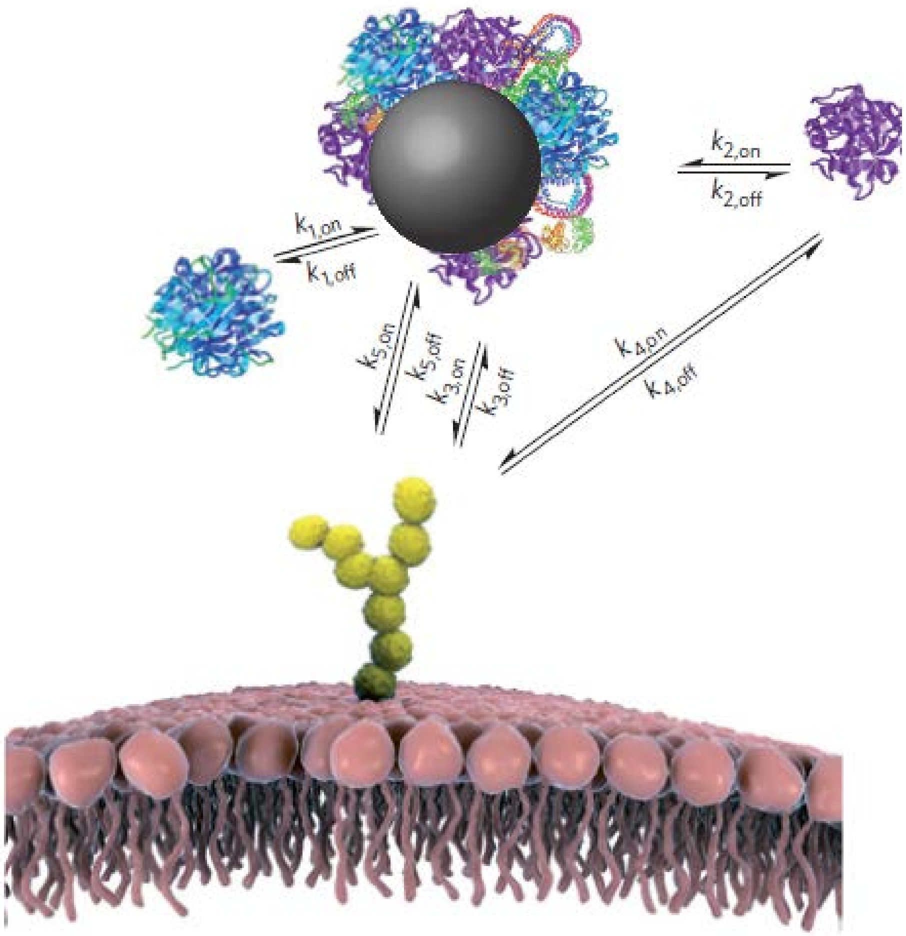
- When submitting your revision, we need you to address these additional requirements.
- PLOS ONE has updated its data sharing policy. For more information, you may refer to: www.plosone.org/static/publication#datareport. The information you have provided in the submission form will accompany your article should it be accepted for publication.
- *We noticed that you did not deposit your data to a publicly available database, or include it in the submission form. All PLOS journals now require raw data underlying the findings described in the manuscript to be freely available to other researchers, either in a public repository, or in the manuscript itself.*
- This policy applies to all data except where public deposition would compromise patient privacy or where there might be other ethical concerns.

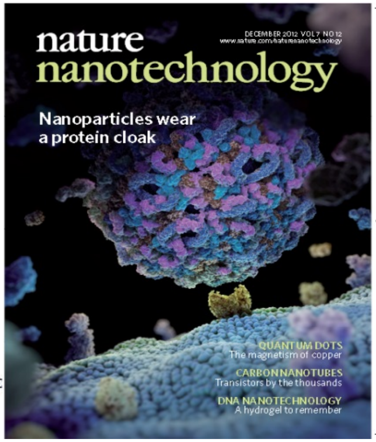
Salik Hussain,
D.V.M., M.S., Ph.D.,
Academic Editor PLOS ONE

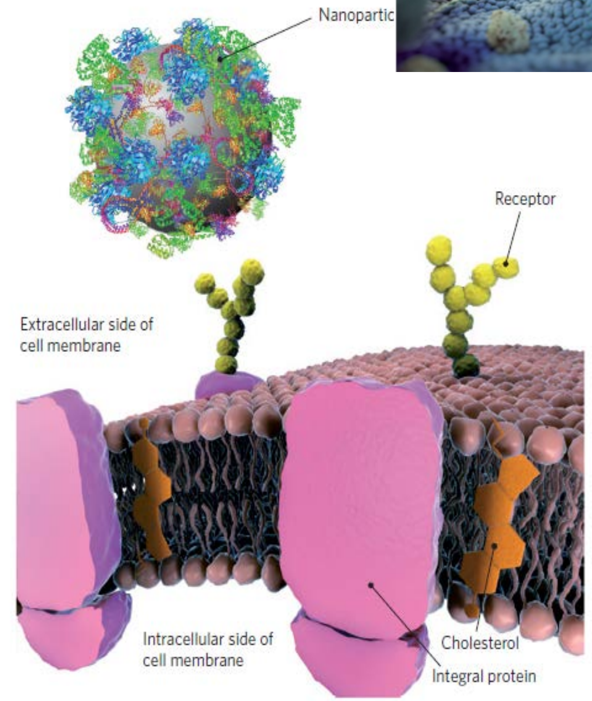
IDENTIFYING SOURCES OF ERROR, MISUNDERSTANDINGS

IF RAW DATA IS NOT AVAILABLE, HOW CAN WE TRUST THE CONCLUSIONS?

PARTICLES SHARE THEIR IDENTITY WITH ENVIRONMENT-SEEMS SUBTLE BUT…





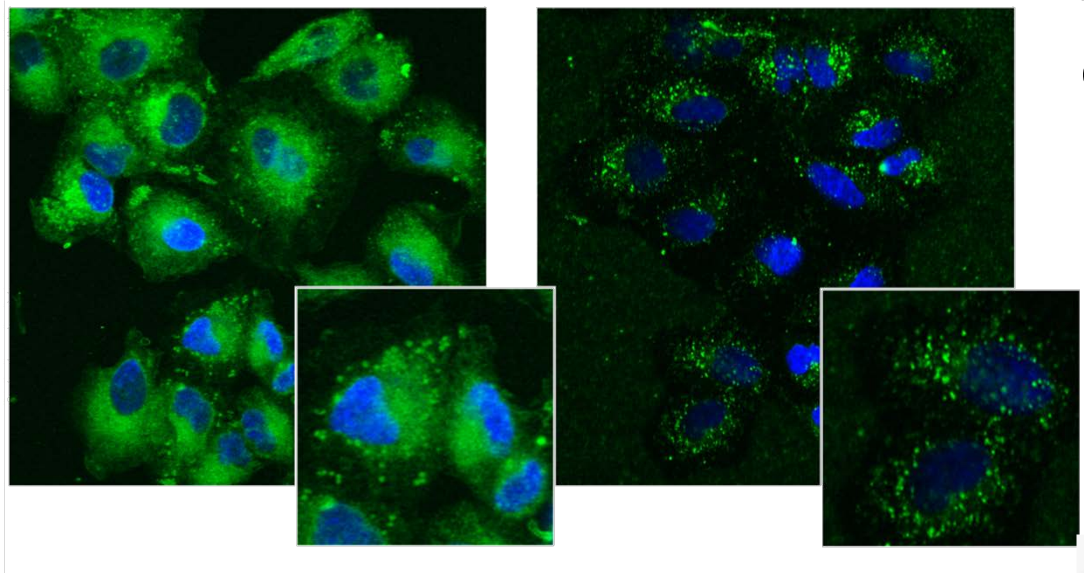


Monopoli MP, et al Nat Nanotechnol. 2012 Dec;7(12):779-86.

Example: Dye Leaking

"Leaky" particles

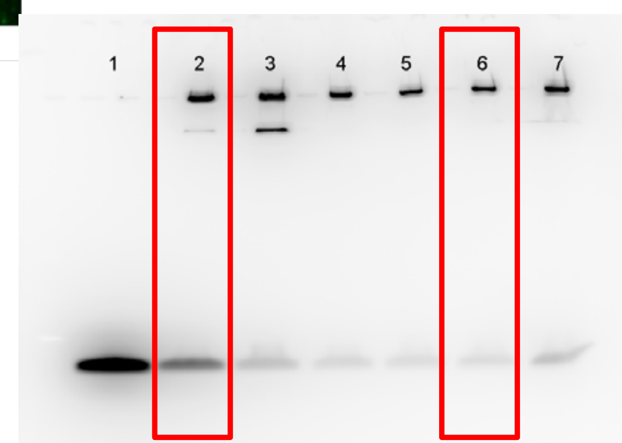
"Good" particles



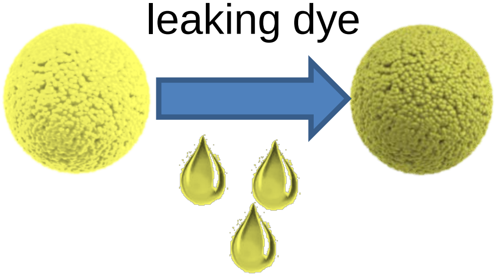
Some nanoparticles loose their fluorescent label in contact with cells

"Leaky" particles

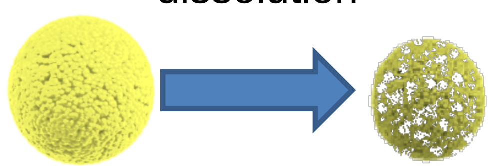
"Good" particles



Polystyrene
leaking dye



Silica
dissolution



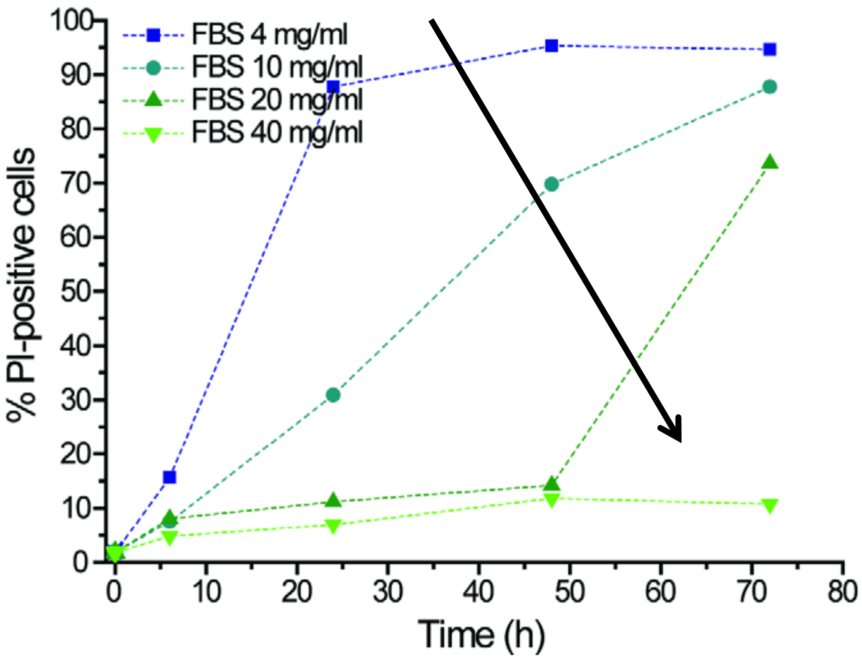
A. Salvati *et al*. *Nanomedicine* **7,** 818-826 (2011)

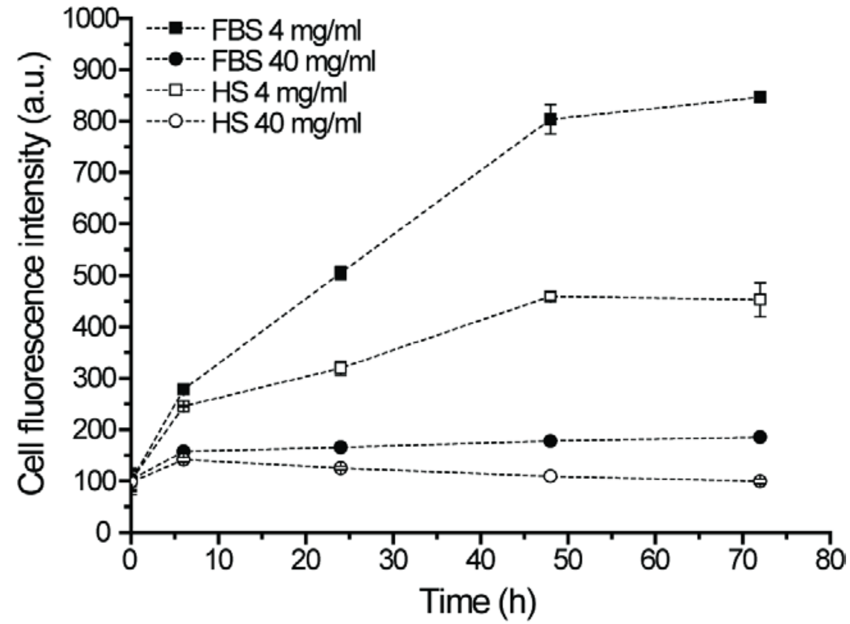
is the experiment meaningful?

Relevant exposure conditions

Suppression of nanoparticle cytotoxicity approaching in vivo serum concentrations; usually publish ‘wrong’ serum, ‘wrong’ concentration of serum-is it meaningful?

Increasing
[protein]





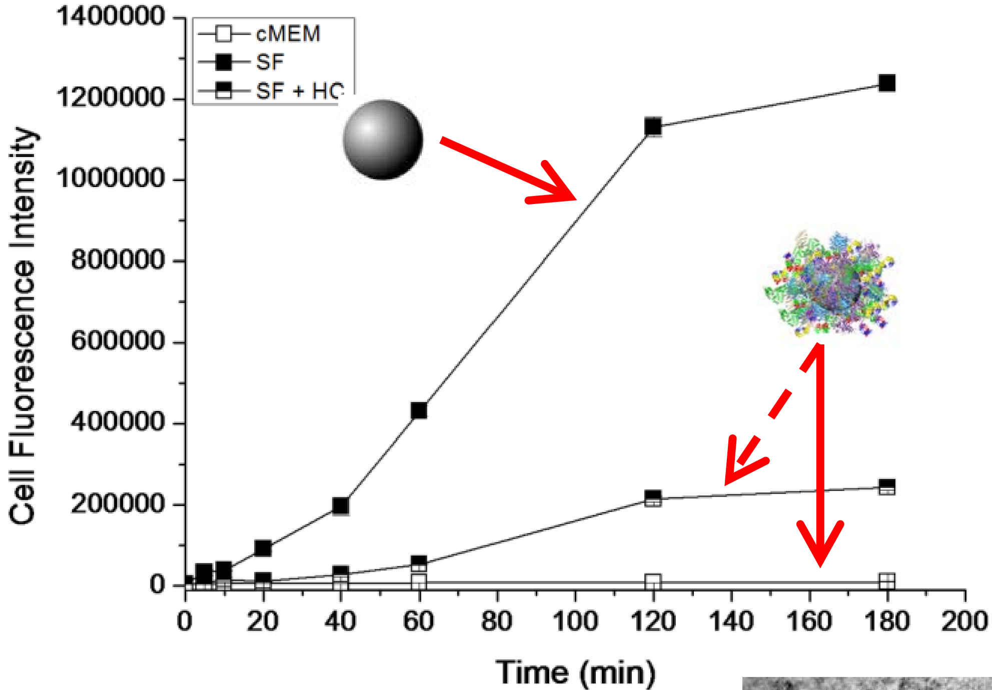
In vitro conditions: massive cell death
In vivo conditions: completely benign

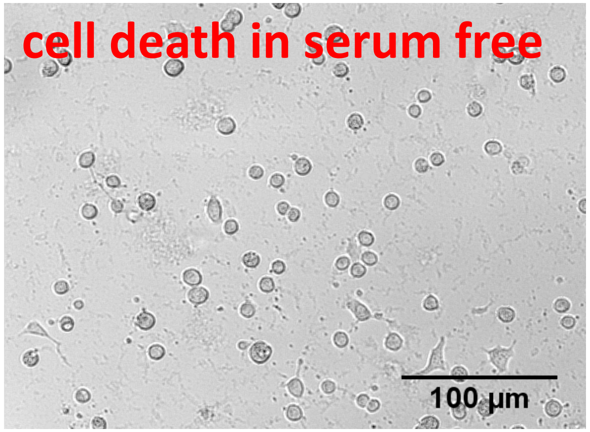
Correlated to decreased uptake

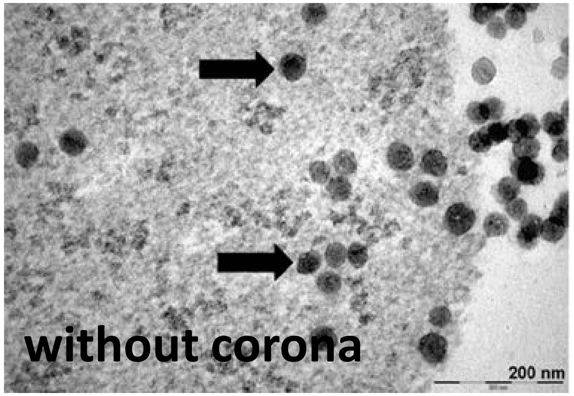
Kim, J.A., Nanoscale (2014), **6**, 14180-14184.

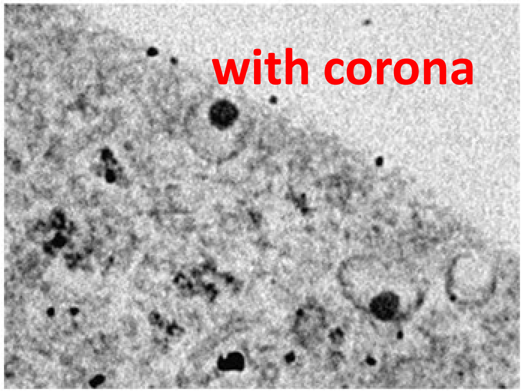
Learning from the past

Relevant exposure conditions







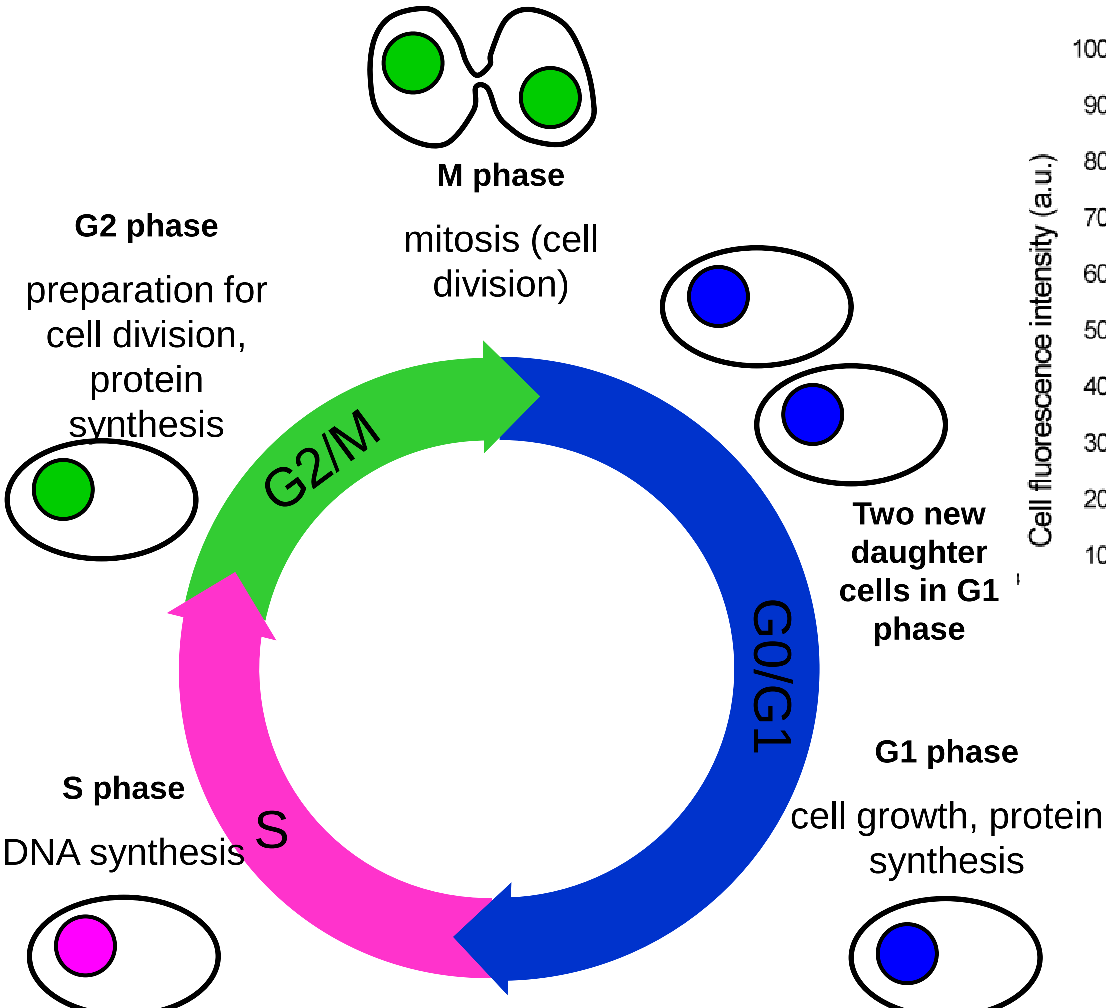


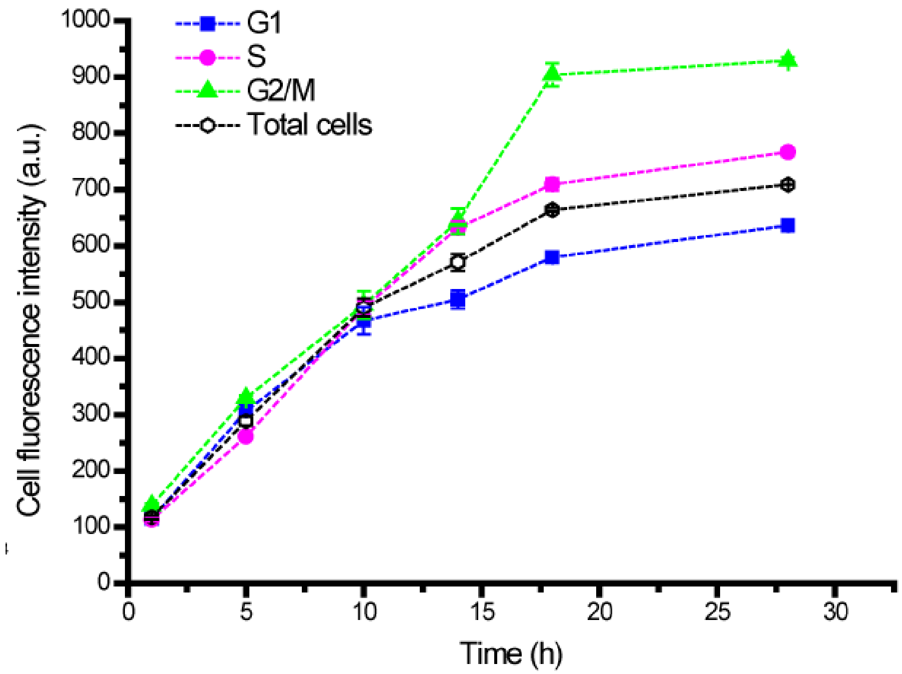
Different uptake efficiency
Different particle location
Cell damage in SF!

Lesniak *et al*. ***ACS Nano*** (2012)

Learning from the past

Cell cycle and cell populations





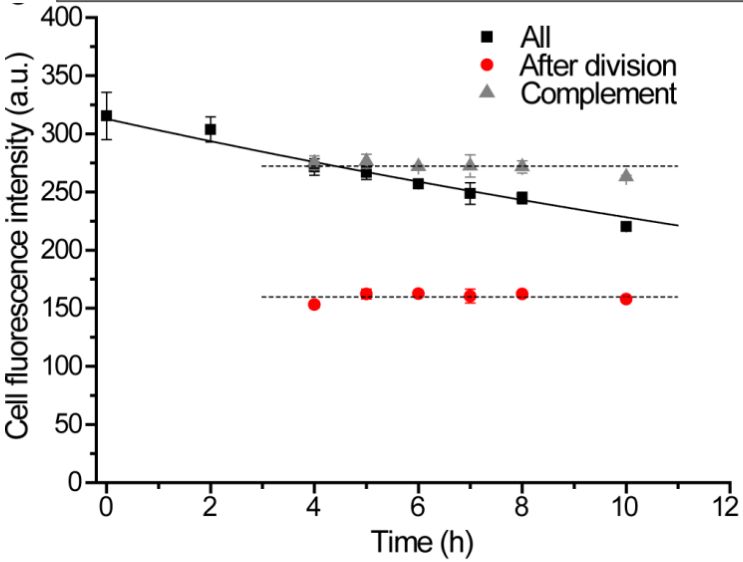
Nanoparticles enter in all phases of cell cycle!
Uptake rates similar for all phases

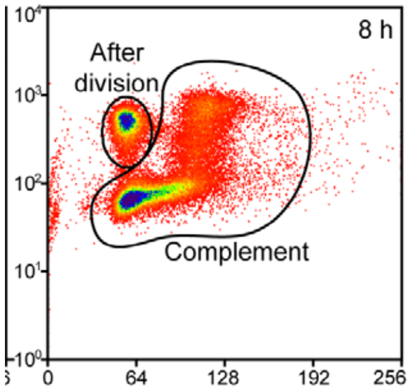
Kim *et al.*, ***Nature Nanotech.***(2012)

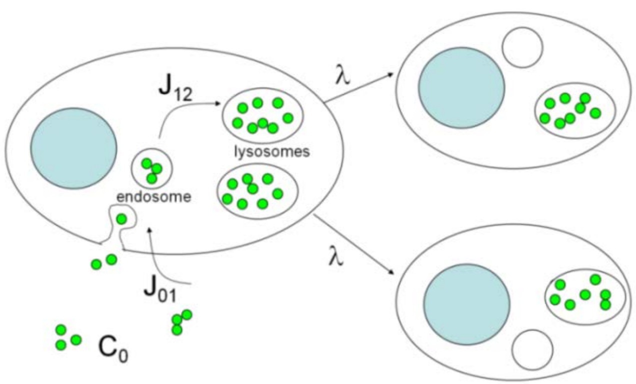
Learning from the past

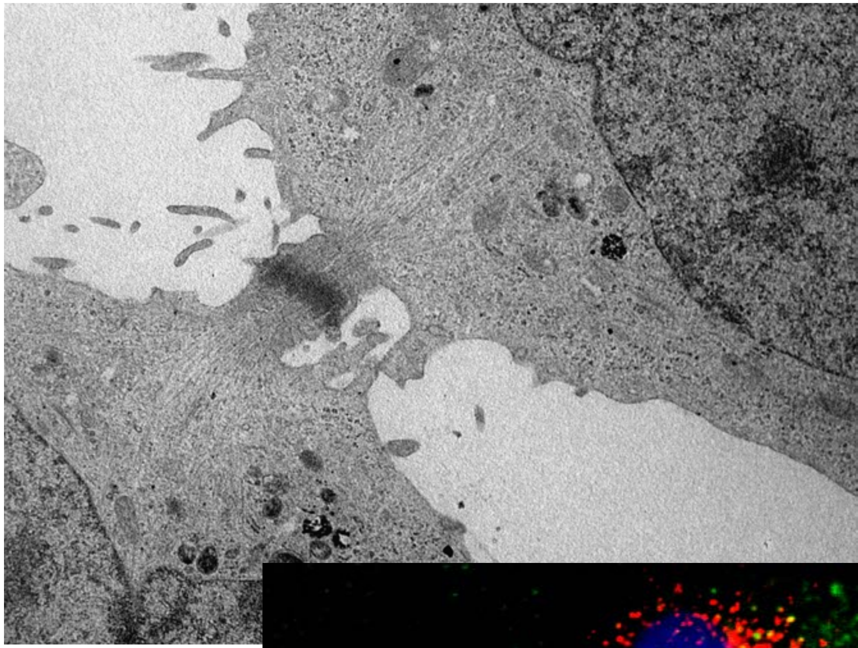
Discrimination of export, degradation, cell division effects?

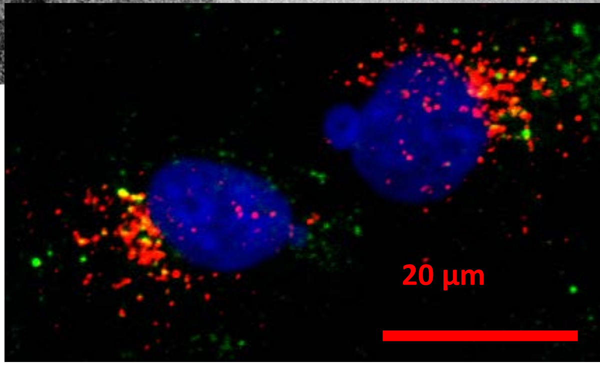
Fluorescence decrease due to cell division – no export or degradation!











Salvati et al., ***Nanomedicine*** (2011)
Kim et al. Nature Nanotech. (2012)

WE ARE ONLY AT THE BEGINNING

THERE IS SO MUCH TO BE DONE……

AGREE WHAT WE CAN

LEAVE ROOM FOR INDIVIDUAL CHOICES

Thanks

Research Infrastructure
QualityNano