Can magnetic NPs be of any help for stem cell delivery?

Dipartimento di Biotecnologie e Scienze Molecolari
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hst034

Toxicology of Engineered Metal Nanoparticles

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1 INTRODUCTION

Nanotechnology is a rapidly developing multidisciplinary field of science which offers the promise of generating new products which will revolutionize diverse areas of our life. Nanotechnology, therefore, is expected to have an enormous impact on economy and it is already so *a la page* to flaunt "nanotech" as a well-established nick name. It deals with materials of extremely small size that due to their high surface area, chemical and biological activities find a wide range of applications.

The fast growth of nanotechnology will undoubtedly be paralleled by an ever-increasing presence of nanomaterials in the environment. The peculiar and unique properties that make these nanomaterials in general and nanoparticles (NPs) in particular so attractive may be associated with potentially new and largely undefined risks (Di Gioacchino *et al.*, 2009) for the human health and for the environment. NPs, for example, are readily taken up by the cells (Gornati *et al.*, 2009; Papis *et al.*, 2009) and stored in cytoplasmic vesicles (Figures 1 and 2) from where they can exert their toxicity. In this context, a new discipline, nanotoxicology, is established to provide answers to the concern about the possible drawbacks of this technology.

In this chapter, after having examined the ecotoxicology of nanoparticles, we will focus on two main concerns that may arise for the human health, that is, cancer and allergy. Last but not least, we will give a glance to the other side of the coin by examining how medicine might take advantage from nanomaterials.

2 ECOTOXICOLOGY

The dispersal of engineered metal NPs in the environment can be accidental, unwanted but unavoidable, or intentional when, for example, used for bioremediation of contaminated sites. Accidental leakages from productive plants or during transport of refined products have never been reported, but exposure to airborne nanomaterials is well documented both at the workplace and in polluted sites. The accumulation of nanometals dispersed in water and soils from consumer products has been predicted to span between few ppt, for

Handbook of Systems Toxicology. Edited by Daniel A. Casciano and Saura C. Sahu
 ISBN 978-0-470-68401-6

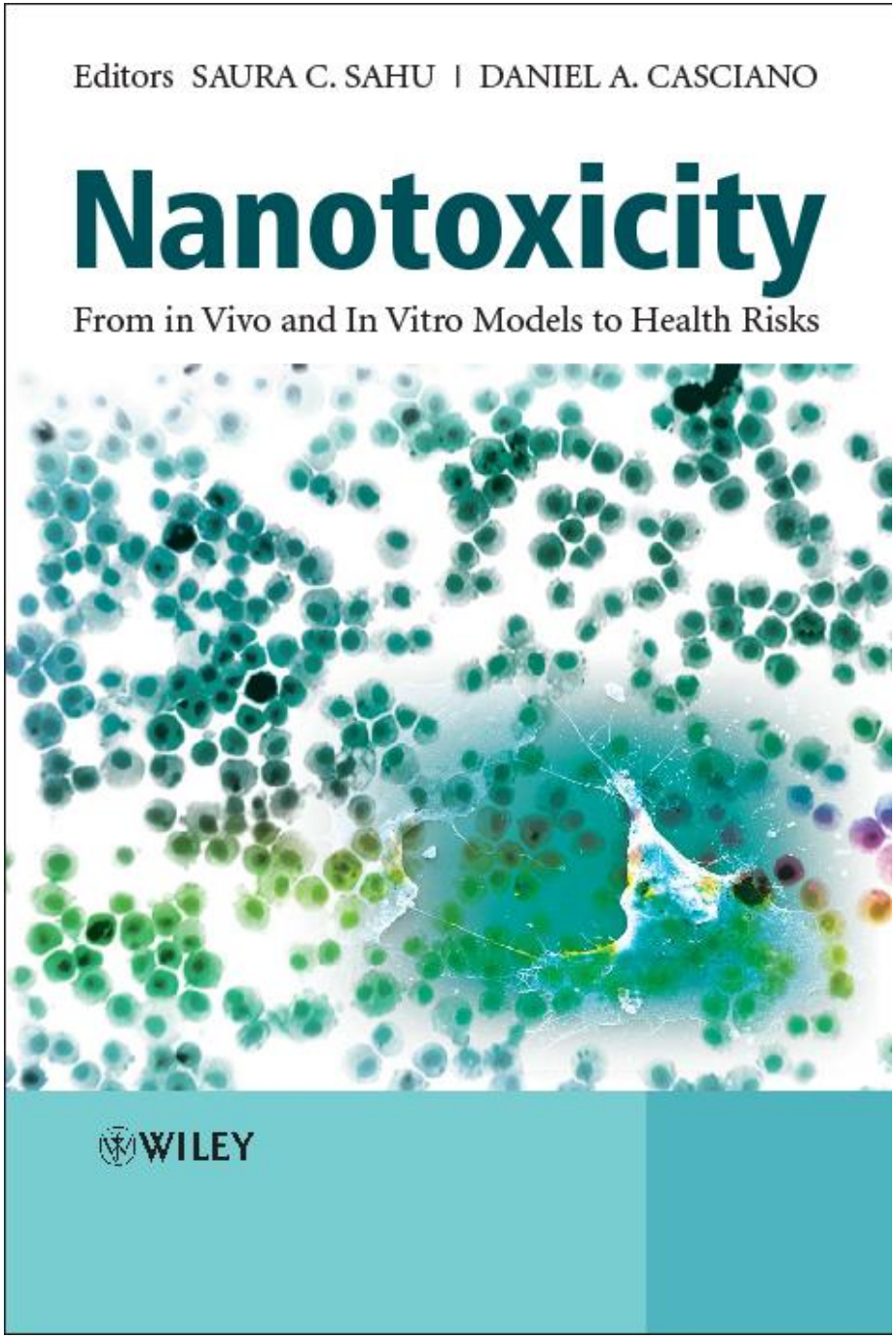
Nanotechnology is a rapidly developing multidisciplinary field of science which offers the promise of generating new products which will revolutionize diverse areas of our life.

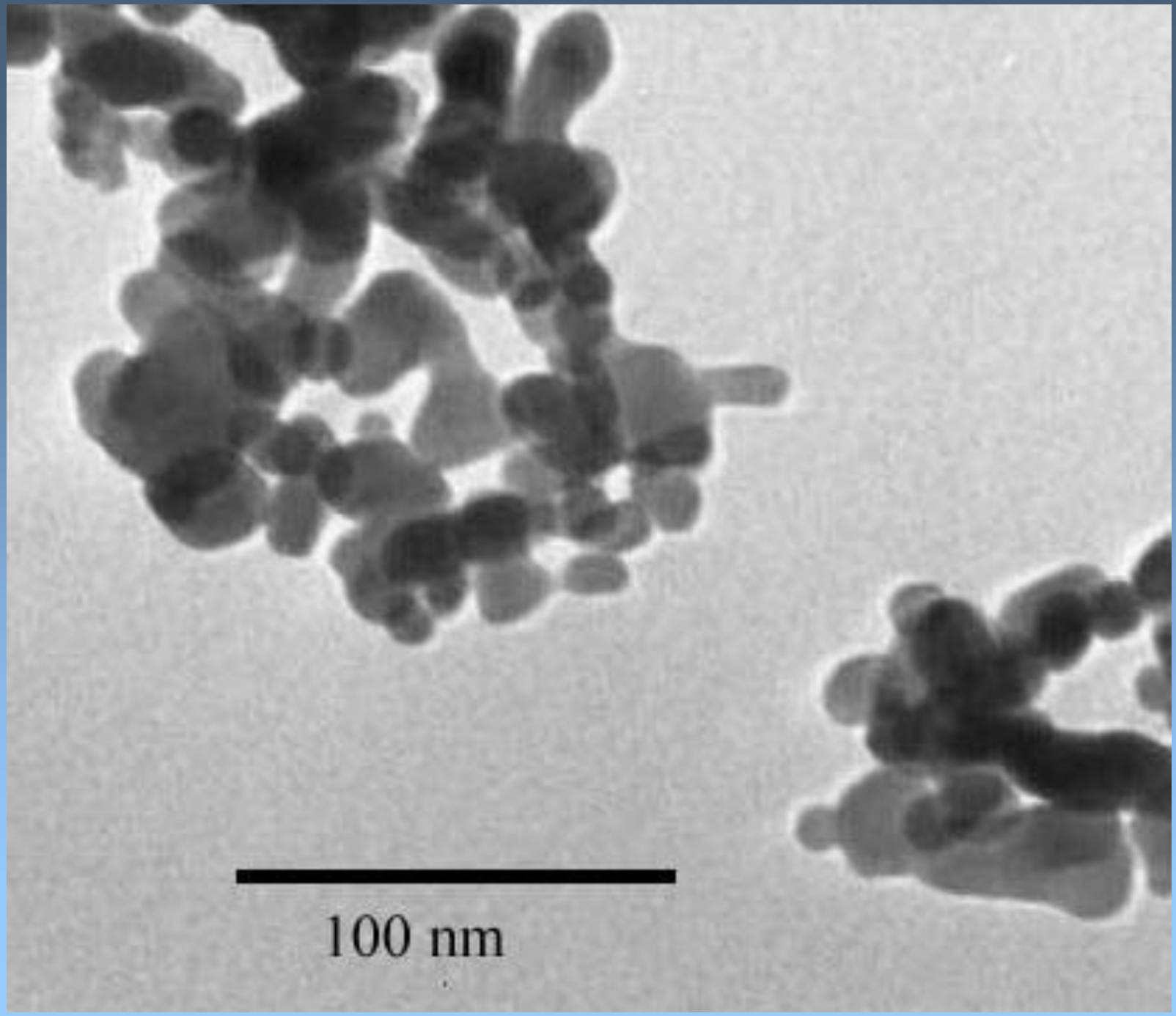
A **concern** on the possible drawbacks of this technology exists and, therefore, there is a **need** for accurate, reliable and unbiased information on the risks and benefits of this new technology.

Public perception and the consequent attitudes toward nanotechnology is likely to be influenced by the correctness of the provided information on risks and benefits and, **in turn**, is likely to influence the realization of further technological advances.

But are the needed information on risks of this emerging technology really available? Although the answer to this question is probably negative, several efforts have been made to study the toxicology of nanomaterials and, in this context, **a new discipline, nanotoxicology, is emerging**.

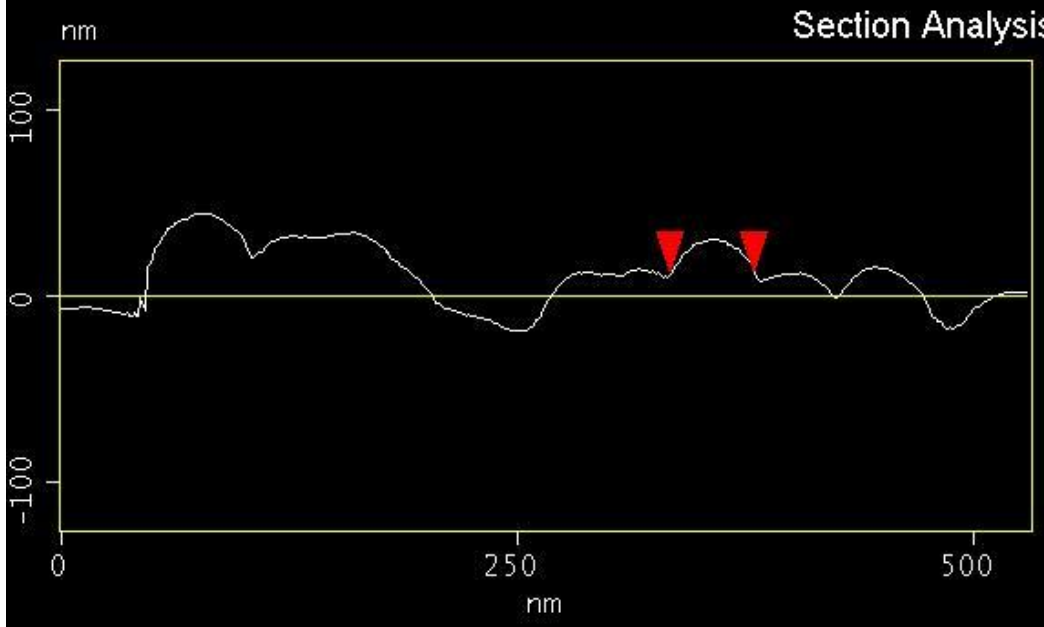
Gornati et al Chapter 15
Di Gioacchino et al Chapter 24



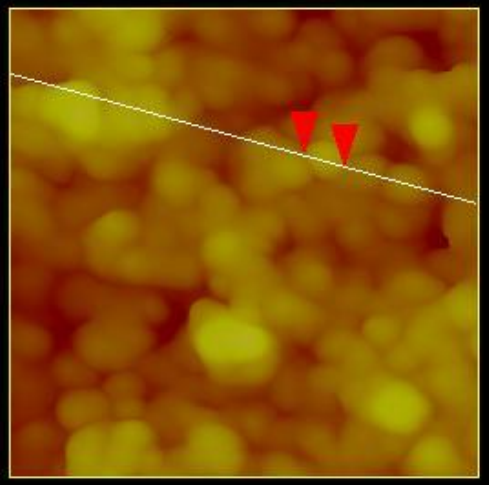

100 nm

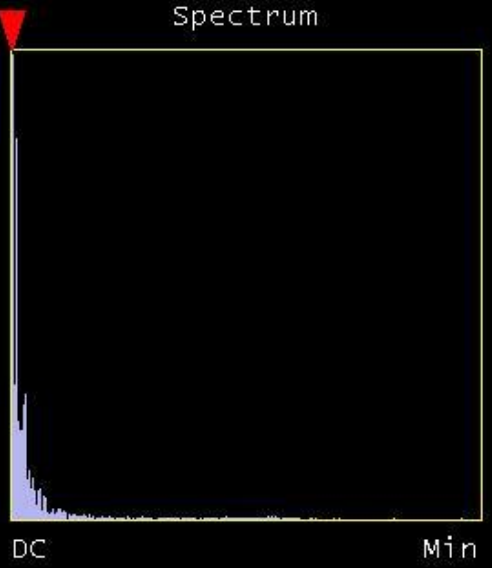
Cursor Marker Spectrum Zoom Center Line Offset Clear

Fig. 2



L	46.000 nm
RMS	5.307 nm
lc	DC
Ra(lc)	4.249 nm
Rmax	18.828 nm
Rz	18.122 nm
Rz Cnt	2
Radius	22.849 nm
Sigma	0.461 nm





Surface distance	63.682 nm
Horiz distance(L)	46.000 nm
Vert distance	0.165 nm
Angle	0.206 °
Surface distance	
Horiz distance	
Vert distance	
Angle	
Surface distance	
Horiz distance	
Vert distance	
Angle	
Spectral period	DC
Spectral freq	0 Hz
Spectral RMS amp	0.016 nm

08_002b.005

Cursor: fixed Zoom: 2:1 Cen line: Off Offset: Off

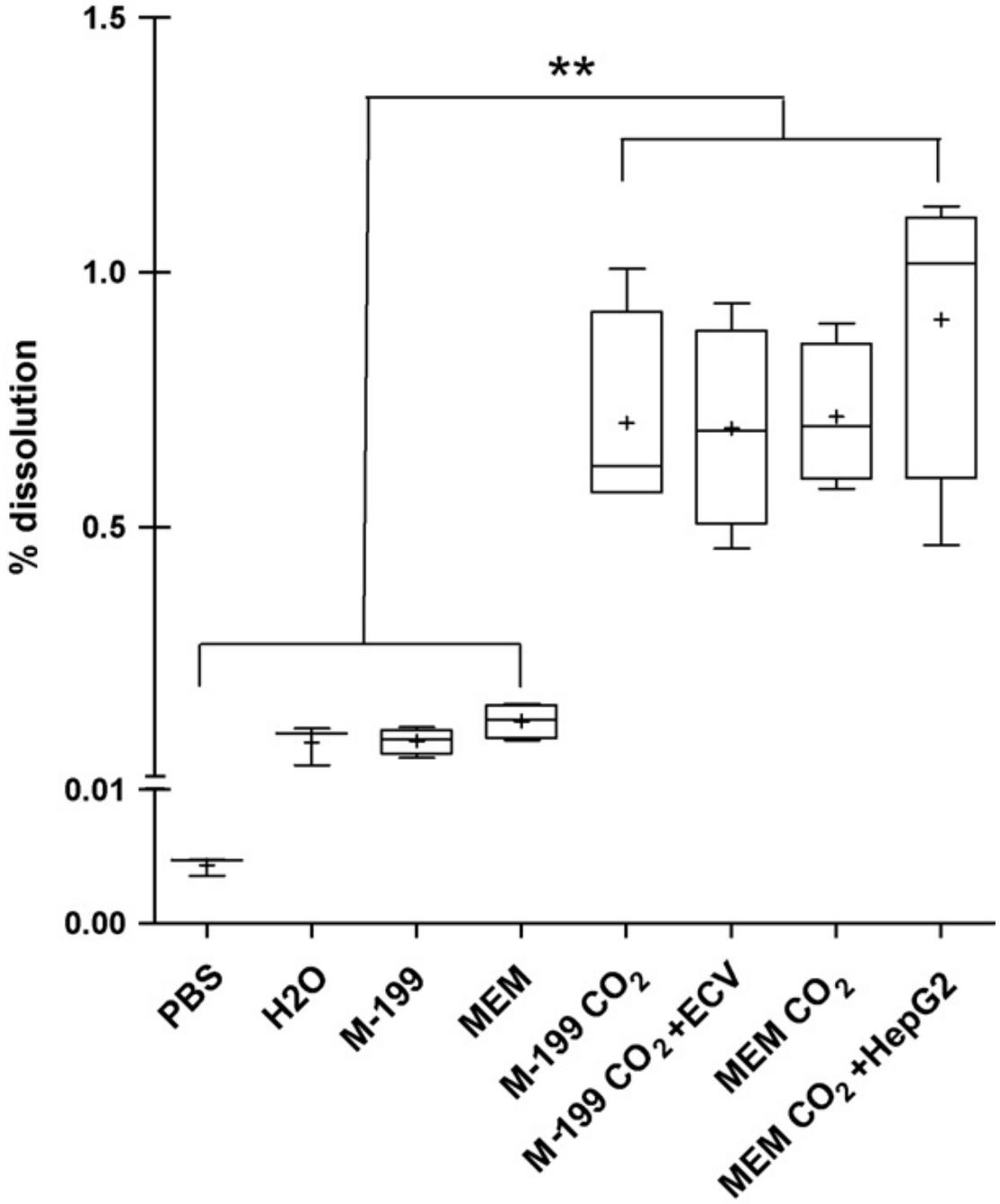
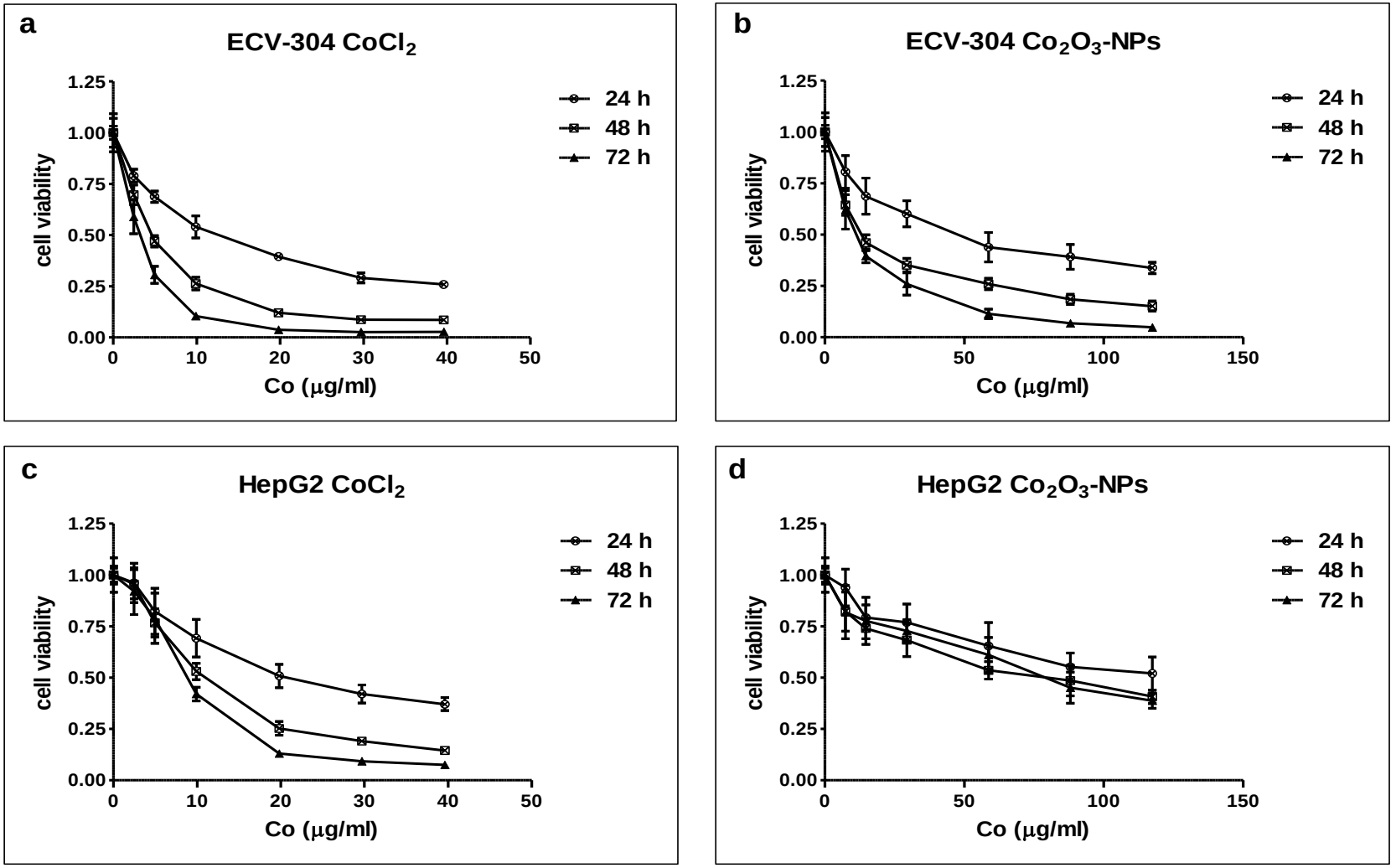
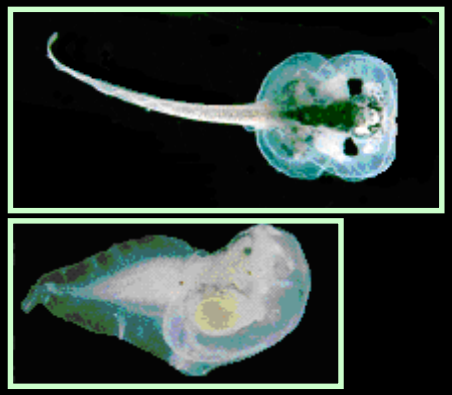


Fig. 2. Box and Whiskers plot of Co3O4-NP dissolution in different media. Dissolution values are indicated as percentage of the pristine content of cobalt: +mean, **statistically significant differences between the samples ($0.01 > p > 0.001$).



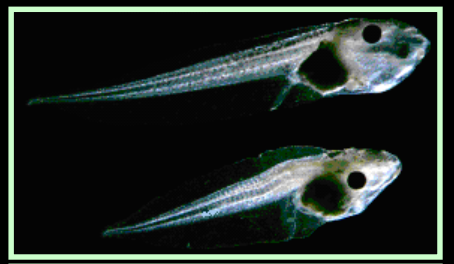
ECV-304 and HepG2 viability after exposure to Co3O4-NPs (b, d respectively) and CoCl2 (a, c respectively) for 24, 48 or 72 h. Viability values were normalized versus control samples and plotted against cobalt content (μg/ml) of Co3O4-NP and CoCl2 test solutions.

MALFORMATIONS



plurimalformed

Tail kinking

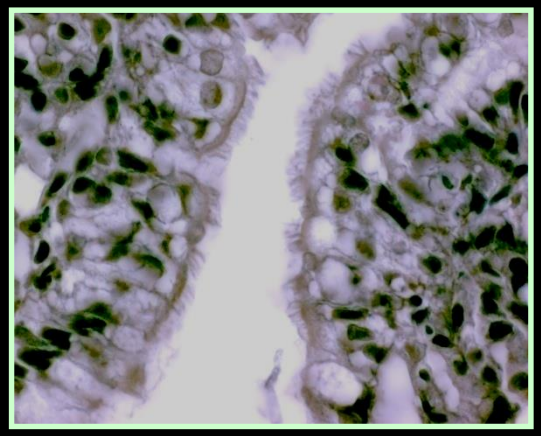


gut coil defects

rounty

hypognathia

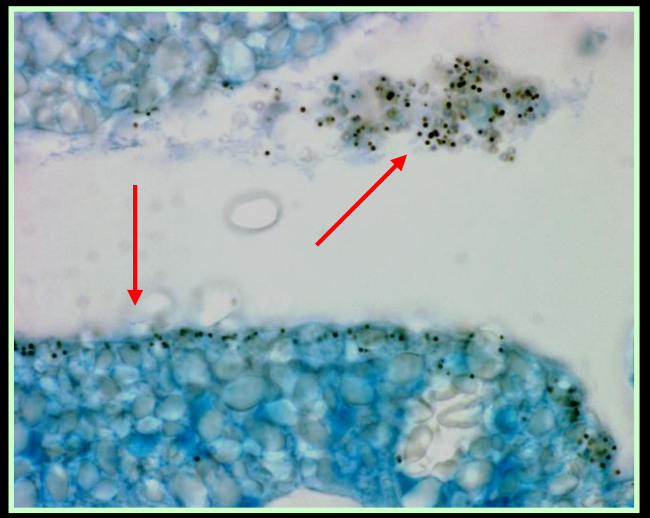
120 h tadpole



control

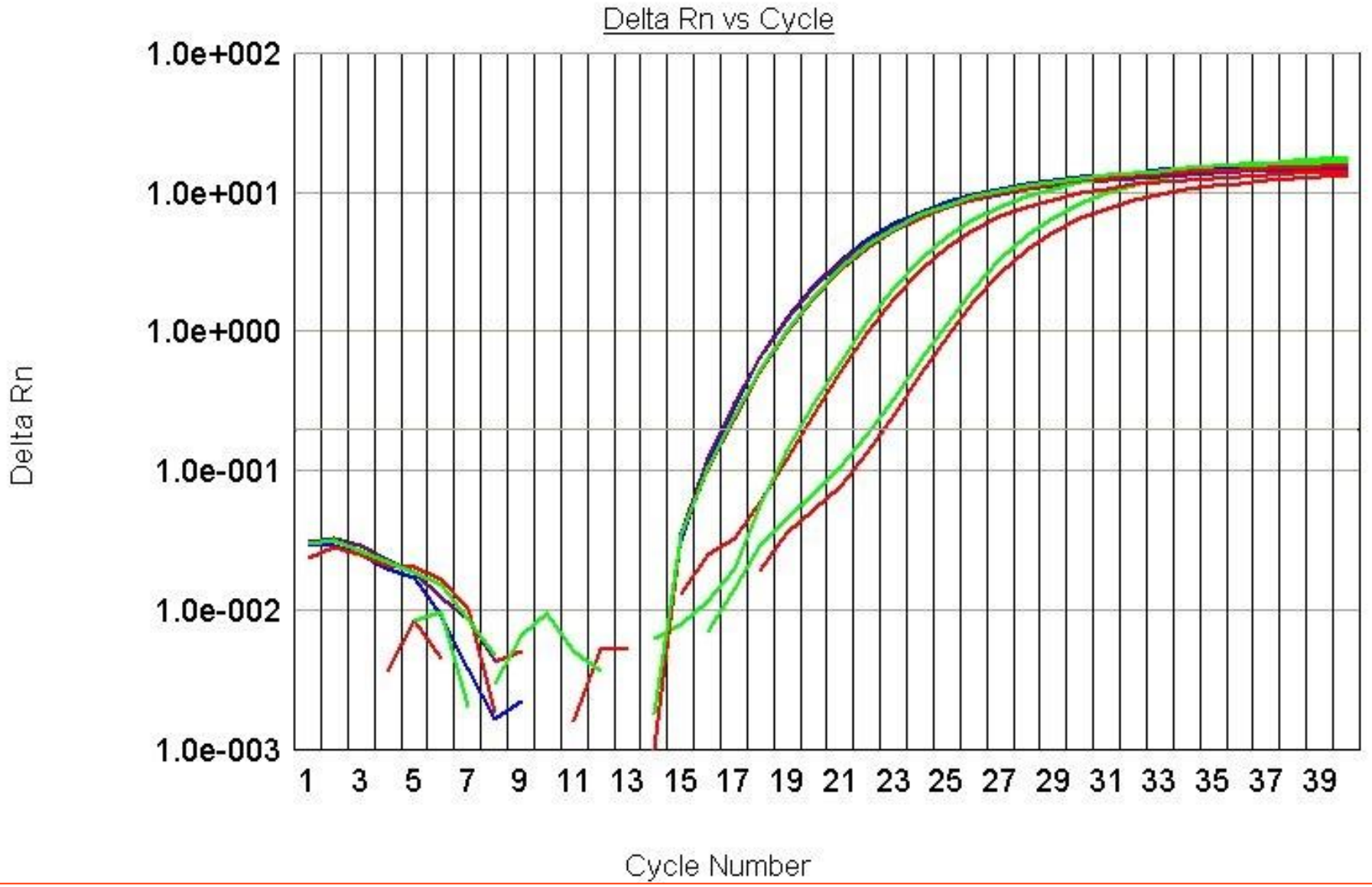
200μmol/L

720μmol/L



Nanoparticles modify gene expression

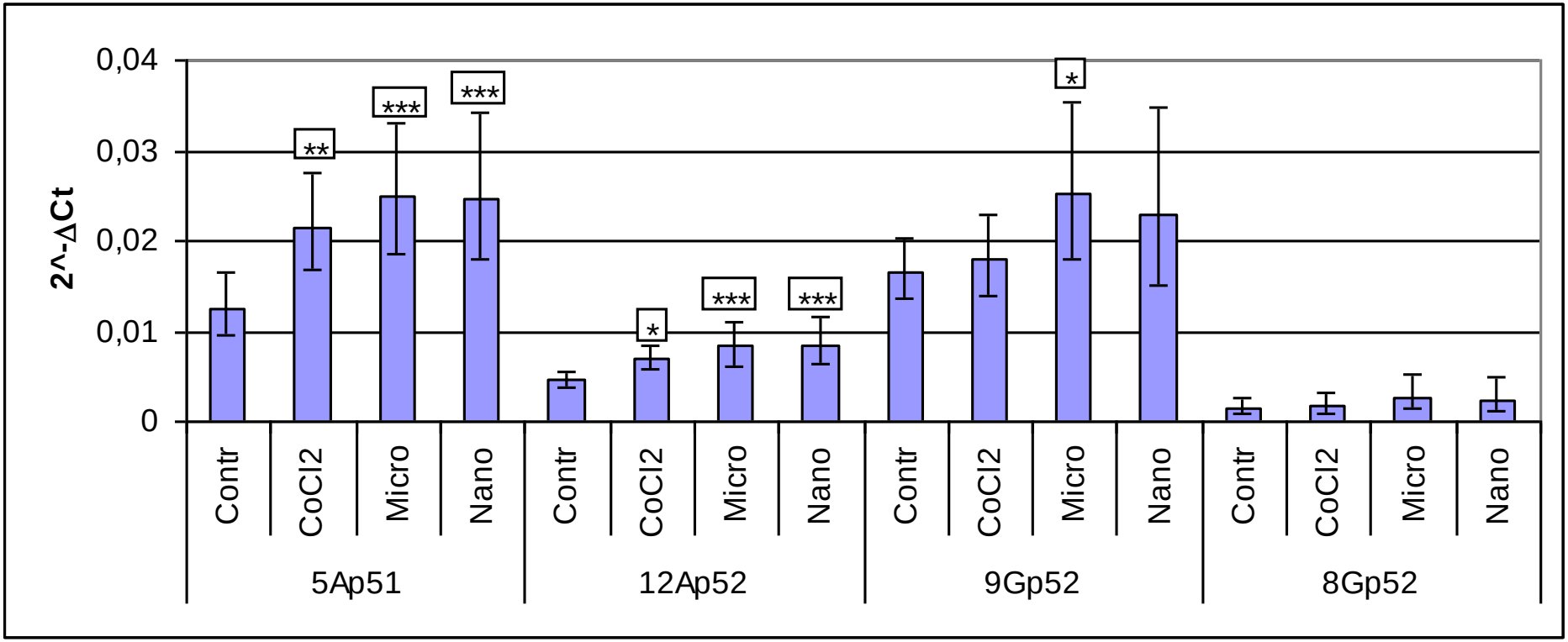
BALB/3T3


Delta Rn vs Cycle
1.0e+002
1.0e+001
1.0e+000
1.0e-001
1.0e-002
1.0e-003
Delta Rn
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39
Cycle Number

* 5%>p>1%

** 1%>p>0.1%

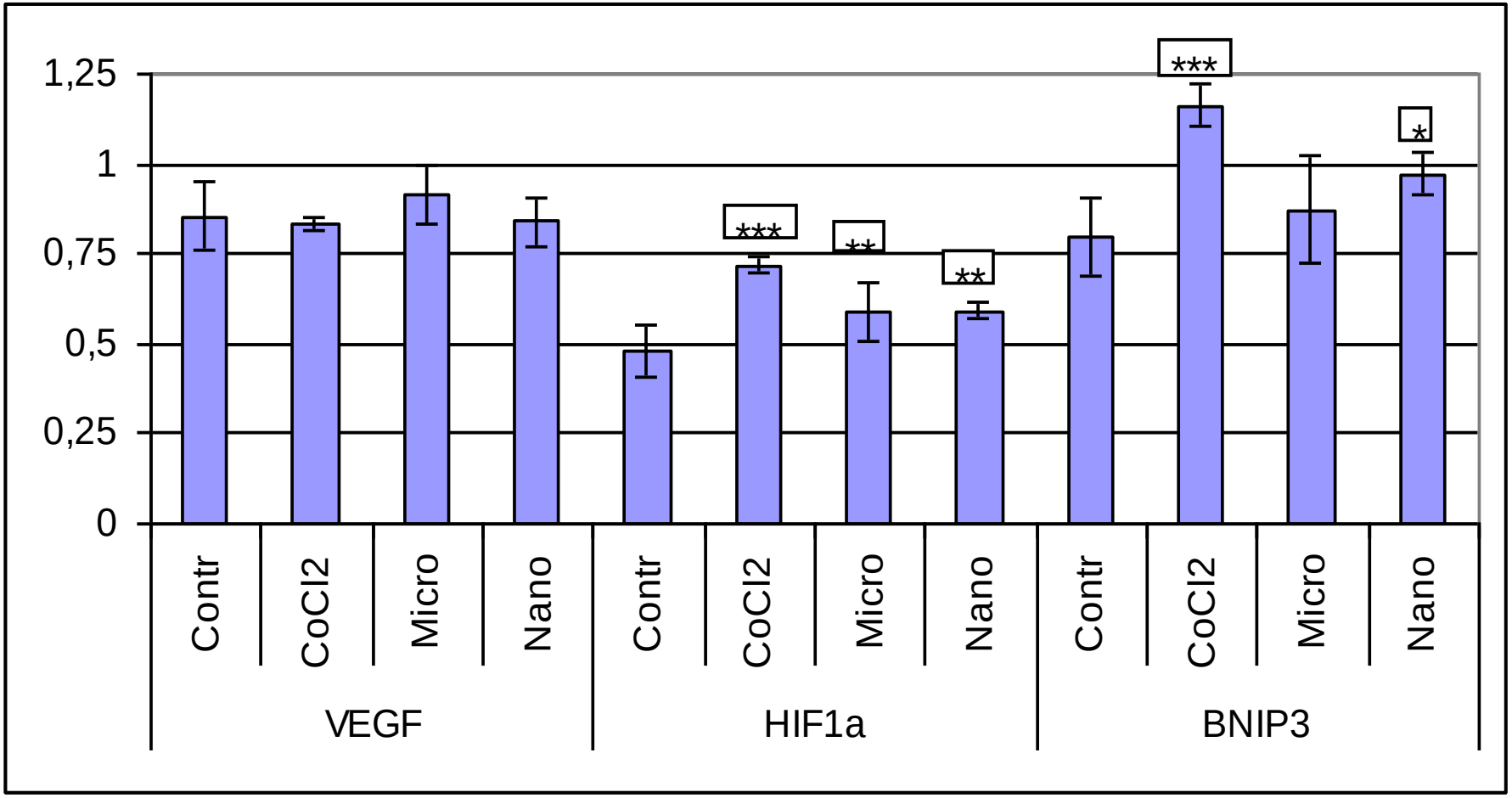
*** p<0.1%

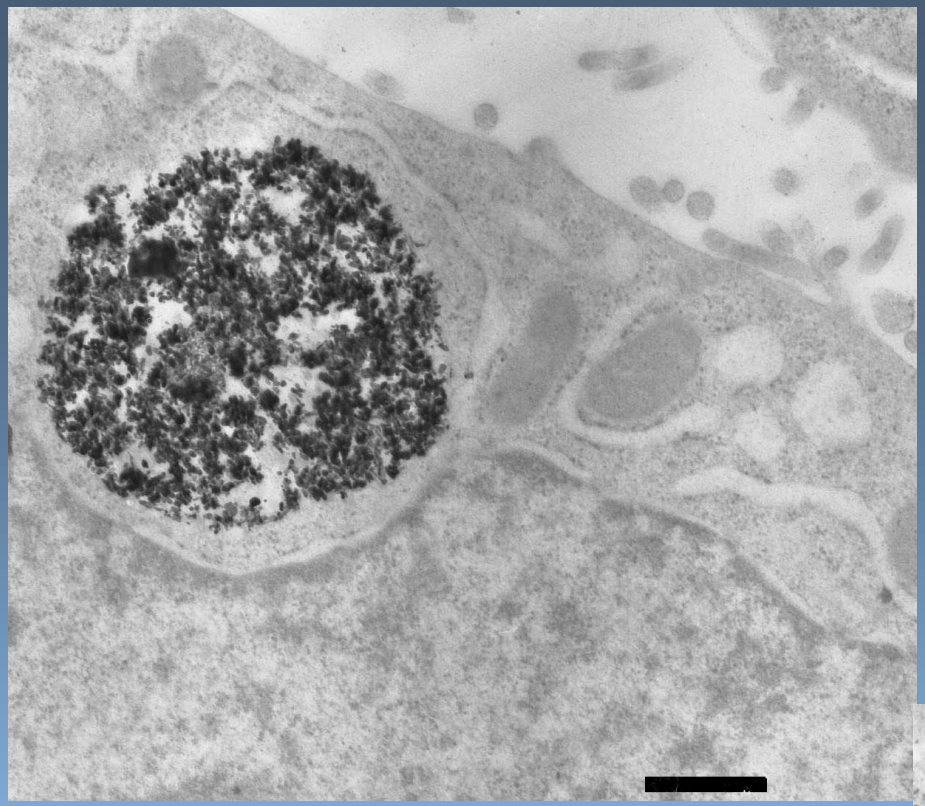

2^-ΔCt
0,04
0,03
0,02
0,01
0
**
***
***
*
***
***
*
Contr
CoCl2
Micro
Nano
5Ap51
12Ap52
9Gp52
8Gp52

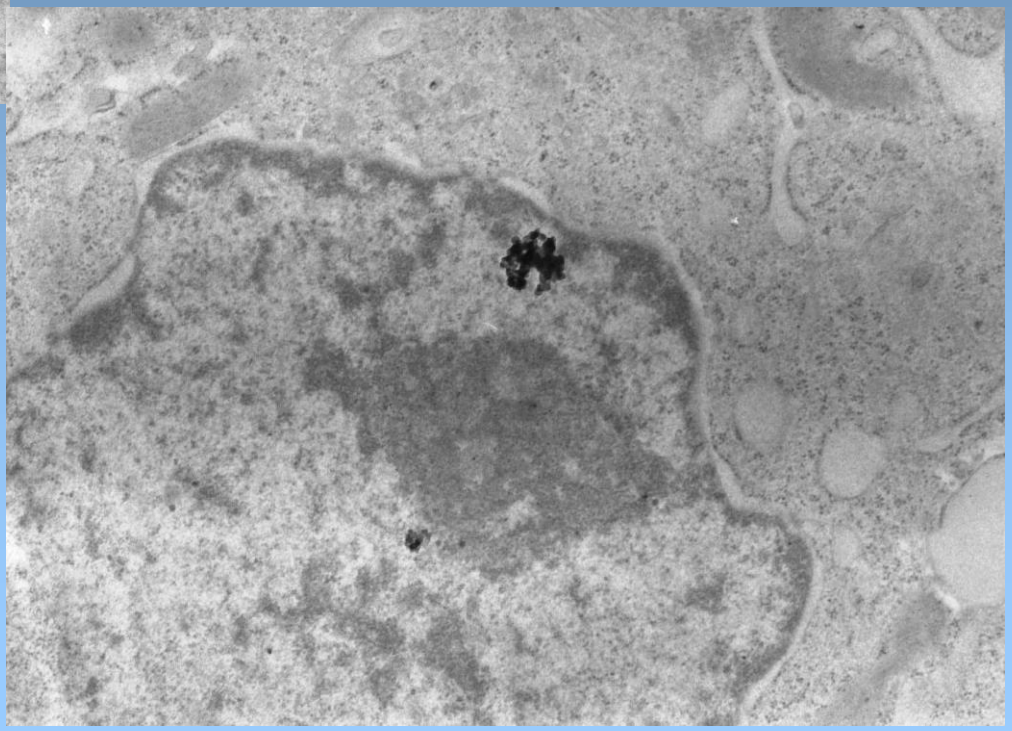
* 5%>p>1%

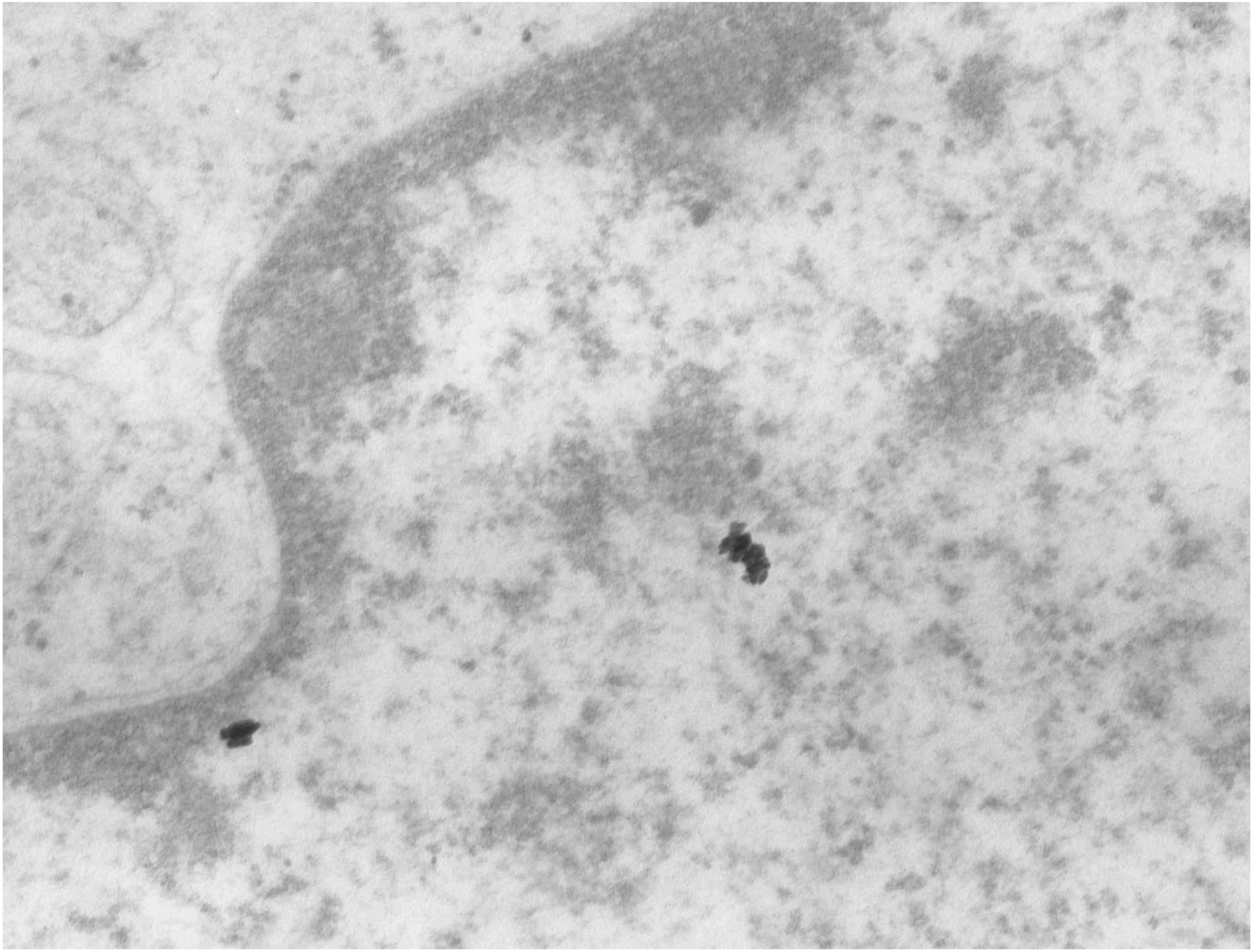
** 1%>p>0.1%

*** p<0.1%

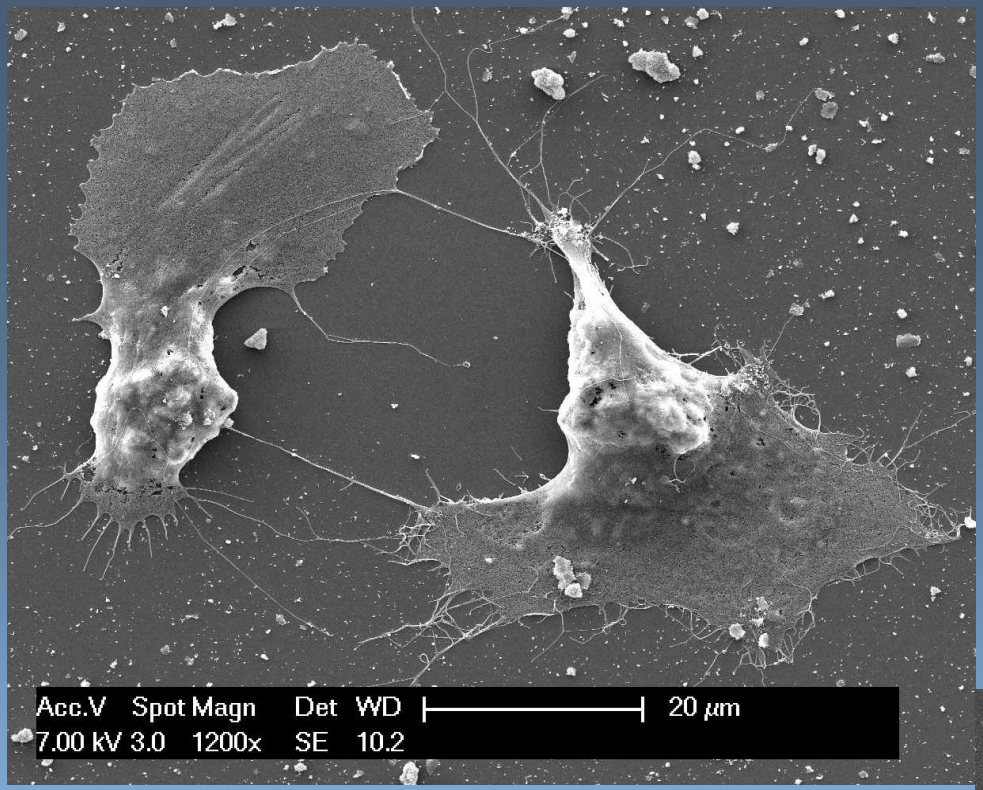

1,25
1
0,75
0,5
0,25
0
***
**
**
***
*
Contr
CoCl2
Micro
Nano
Contr
CoCl2
Micro
Nano
Contr
CoCl2
Micro
Nano
VEGF
HIF1a
BNIP3

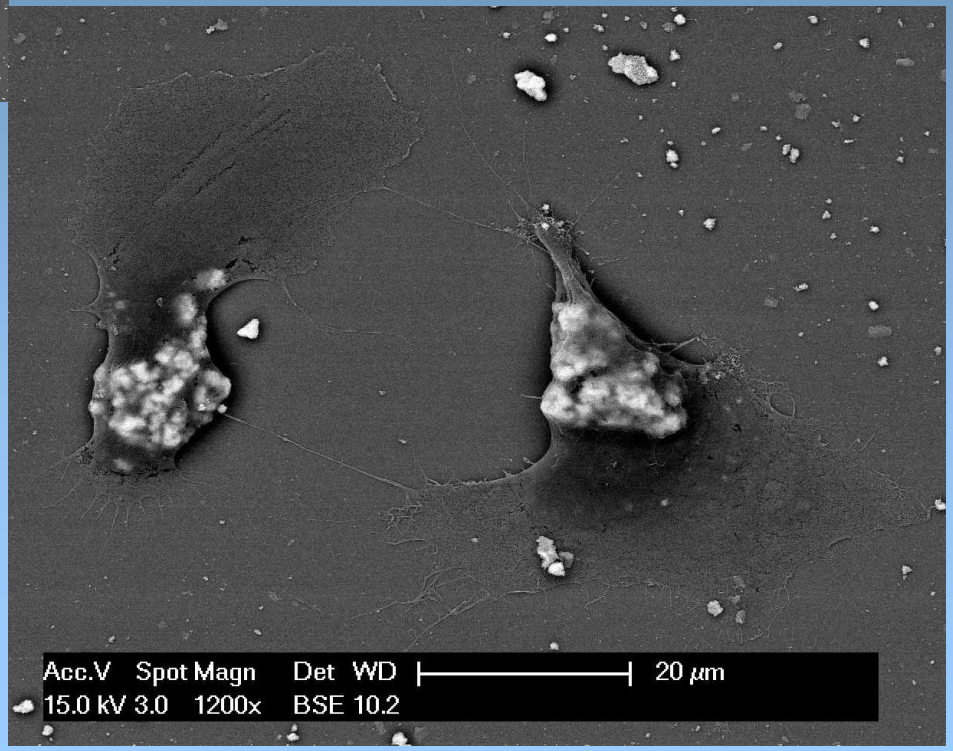


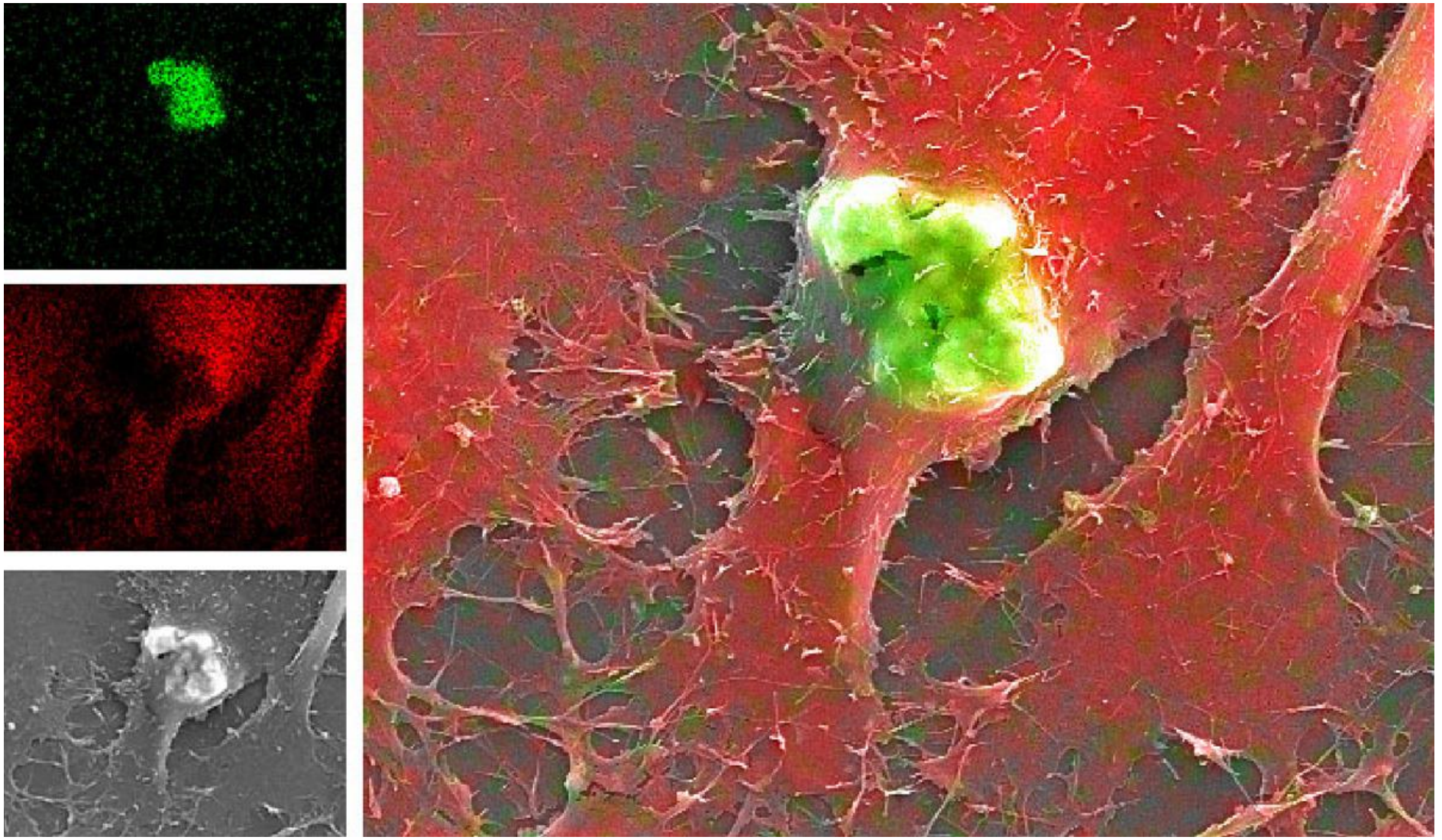




ECV-304


Acc.V Spot Magn Det WD 20 µm
7.00 kV 3.0 1200x SE 10.2


Acc.V Spot Magn Det WD 20 µm
15.0 kV 3.0 1200x BSE 10.2



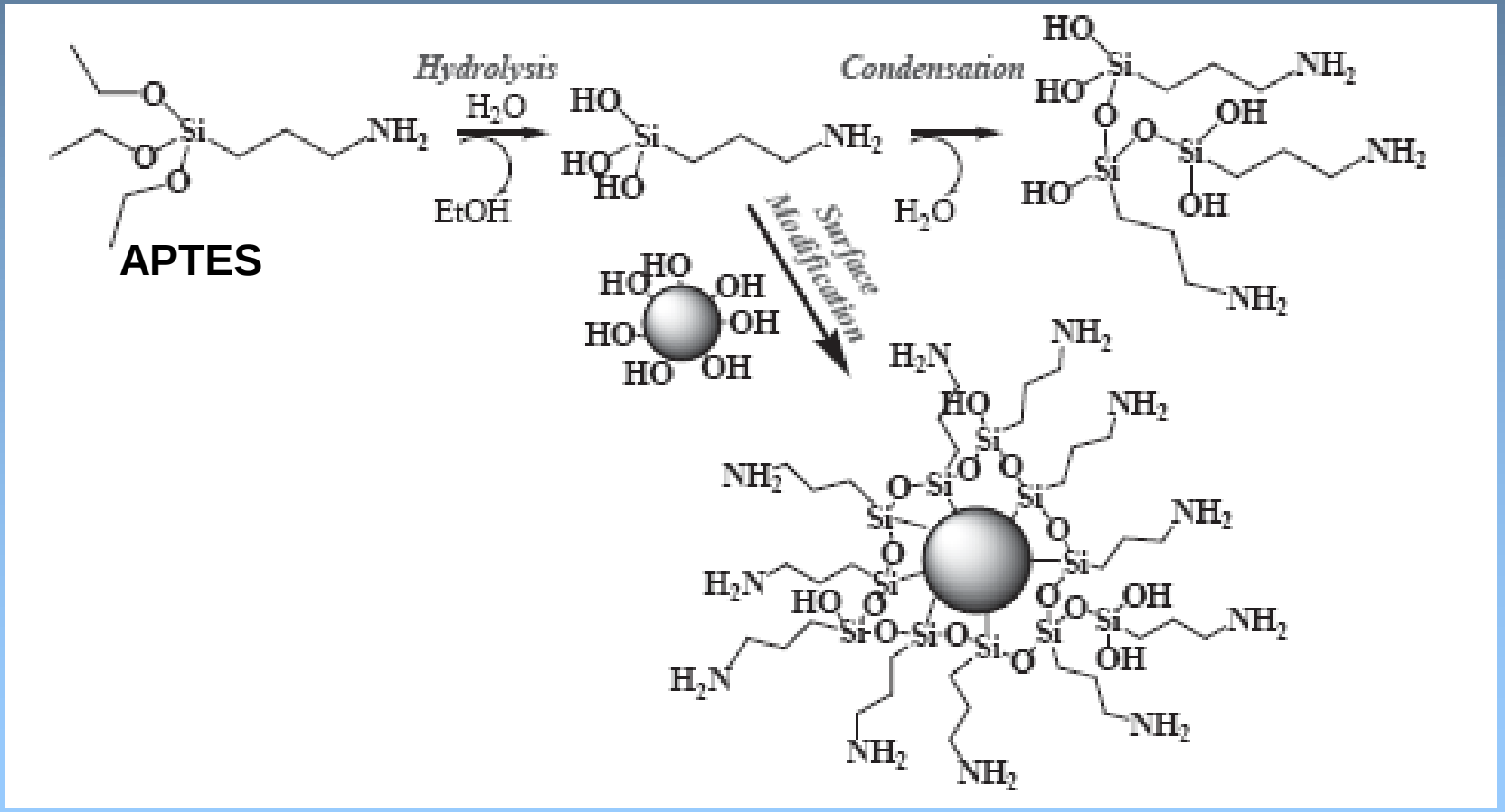
X-ray spectroscopy of cells exposed to Co3O4-NPs. On the left the distribution of cobalt (green) and carbon (red) is shown in false colors in the field of view shown on the SEM image at the bottom left. On the right the elemental mapping has been superimposed onto the micrograph. The horizontal field of view spans approximately 50m.

Magnetic NPs have a great potential for possible applications in medicine

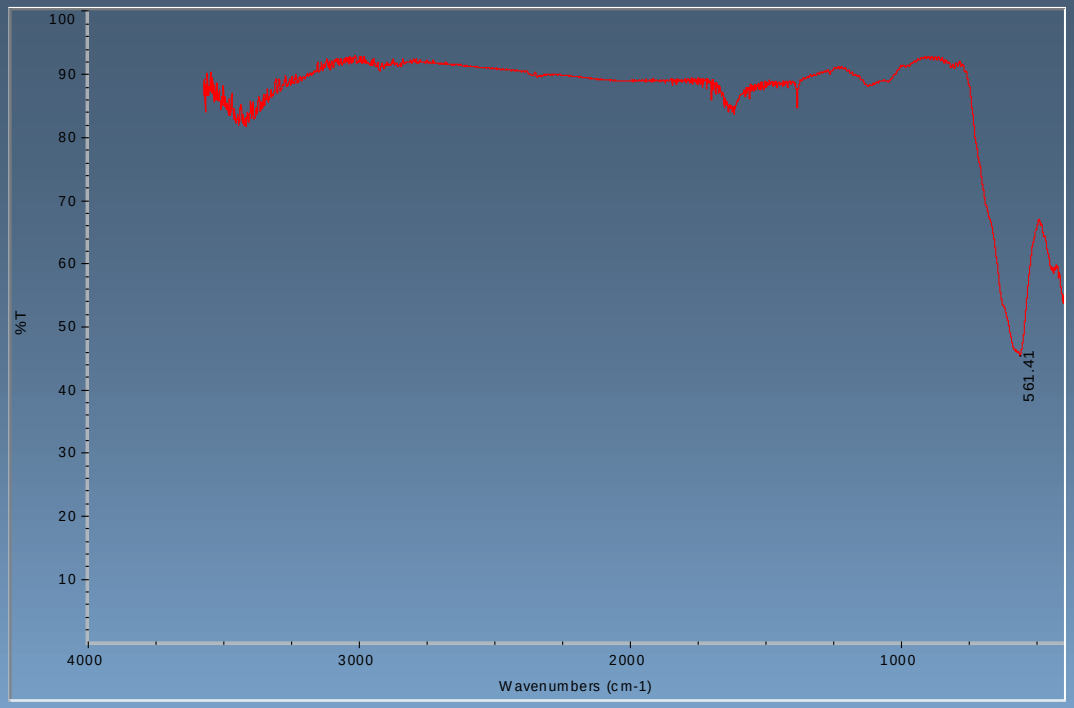
- Magnetism allows manipulation by means of an external magnetic field.

- Therefore, MNPs can be synthesized for the delivery of a drug in a determined area of the body.

- To this aim, however, we need to coat them...

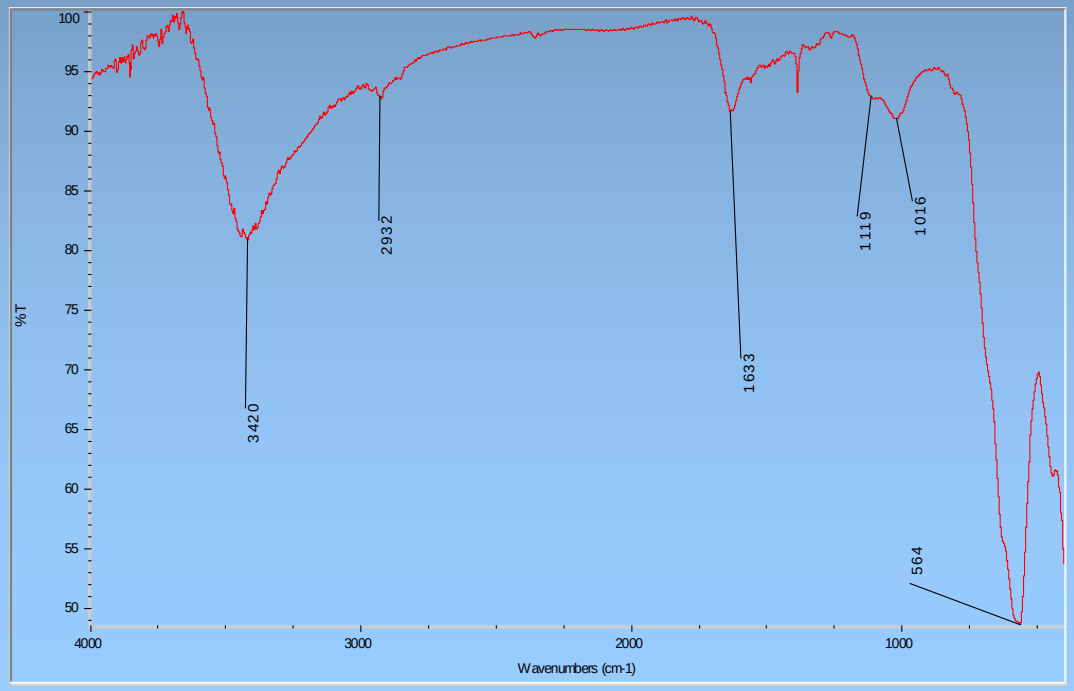

APTES
Hydrolysis
H_2O
EtOH
Condensation
H_2O
Surface Modification

FT-IR spectra



A)Fe-NP :

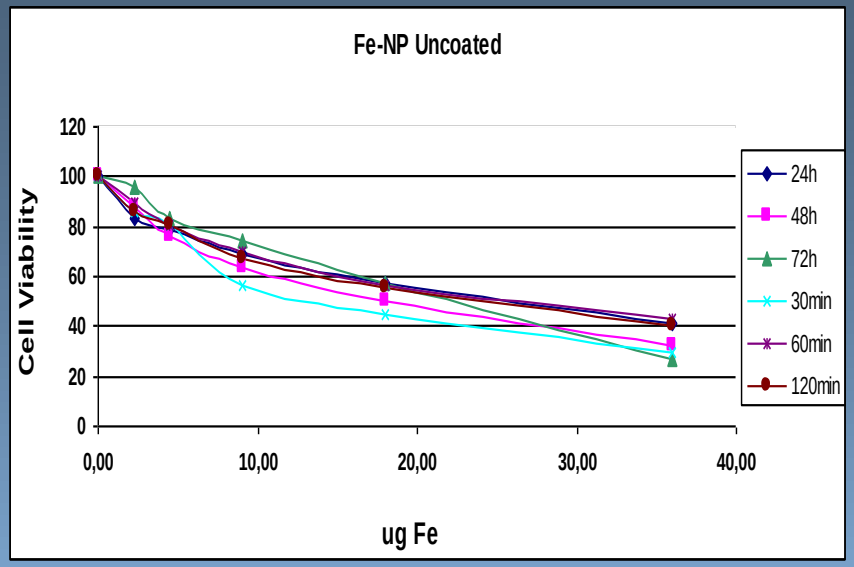
561 nm peak
indicates Fe-O bond

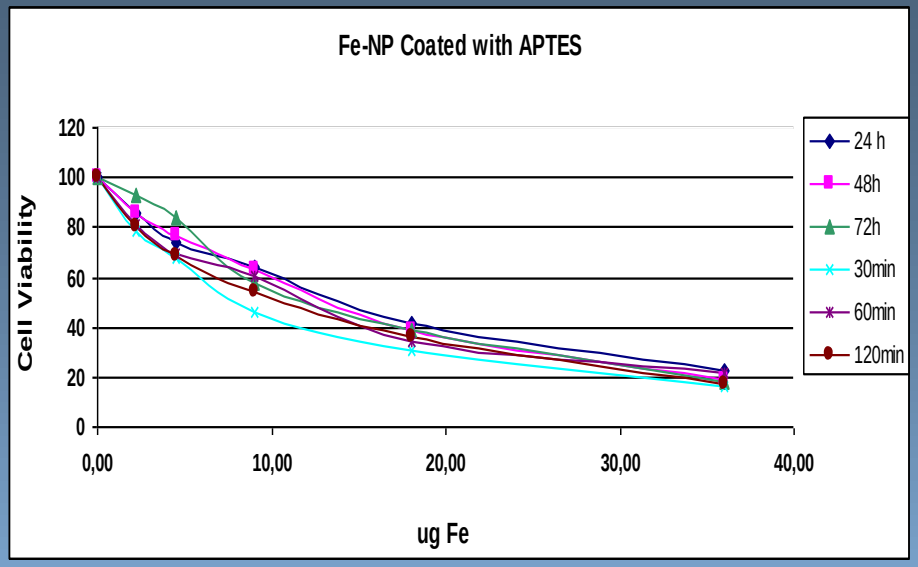


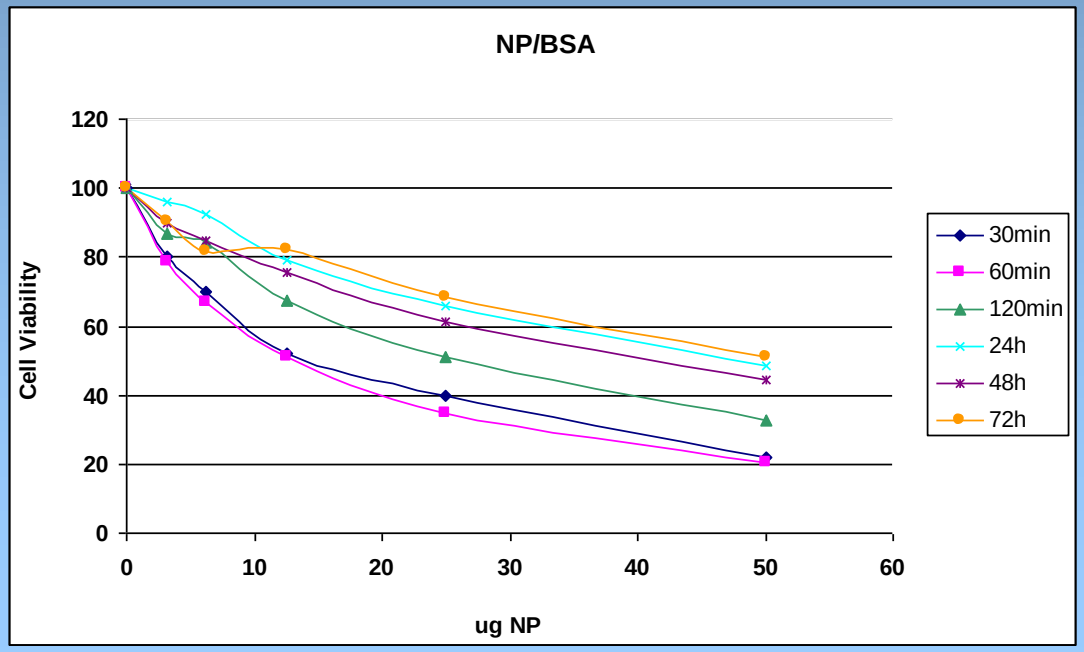
B) Fe-NP and APTES:

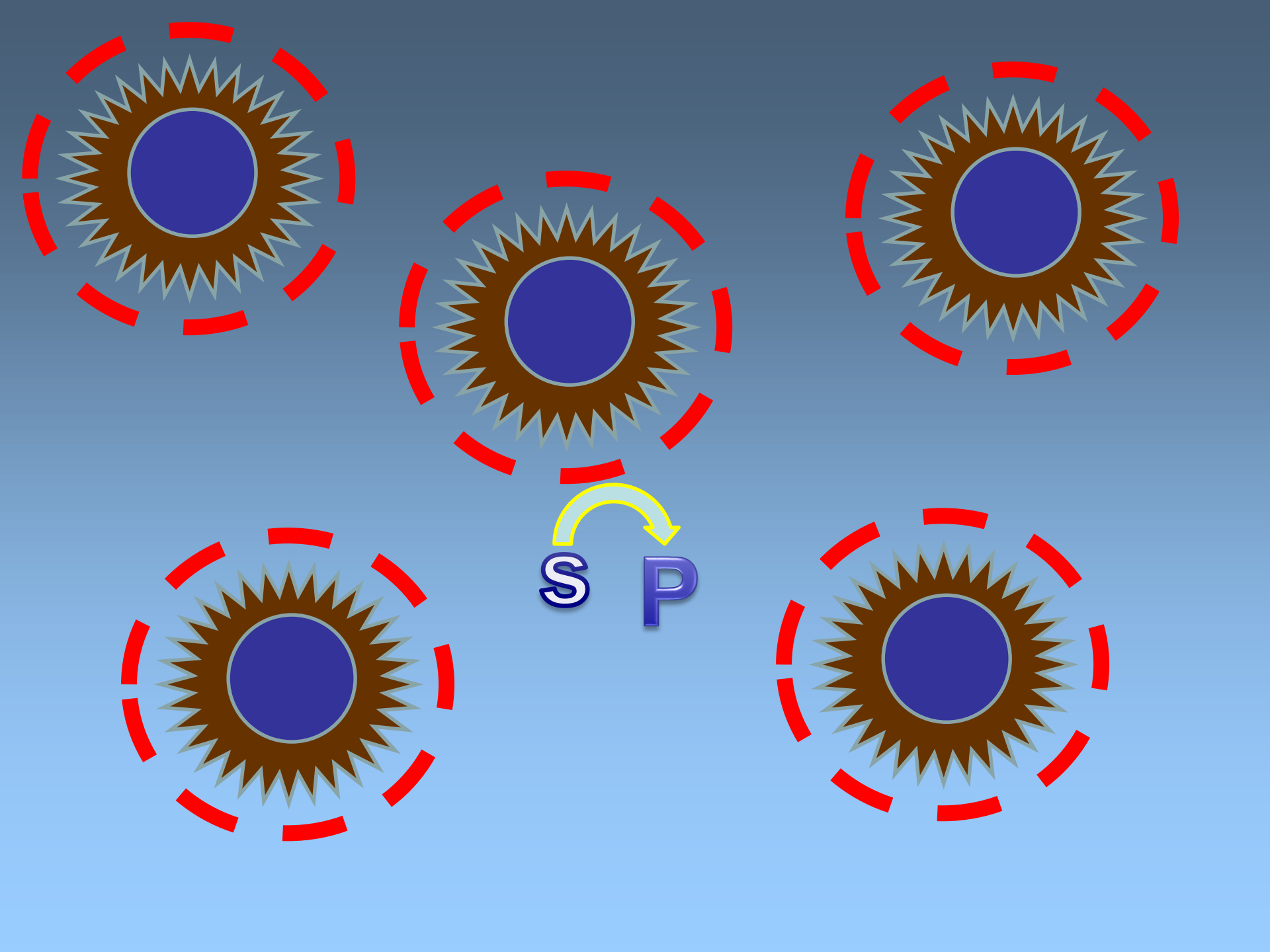
1016 nm peak
indicates O-Si bond

Cell viability tests: SKOV-3





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