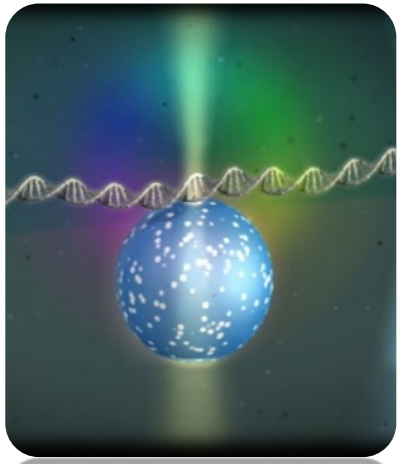
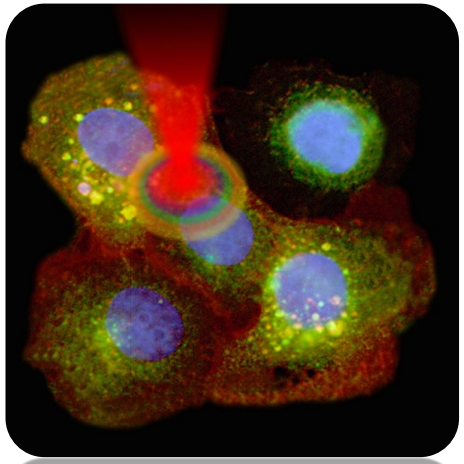
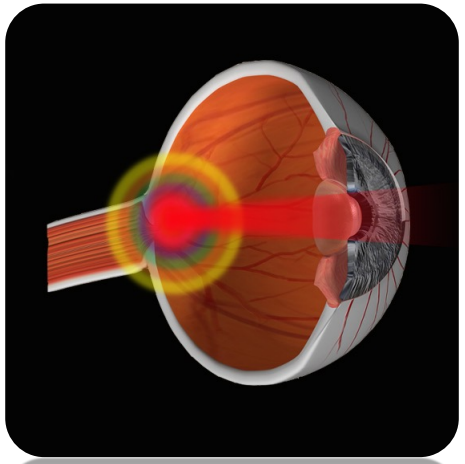
ICFO

Institut
de Ciències
Fotòniques







Raman spectroscopy for Cancer diagnosis: adding a new molecular dimension

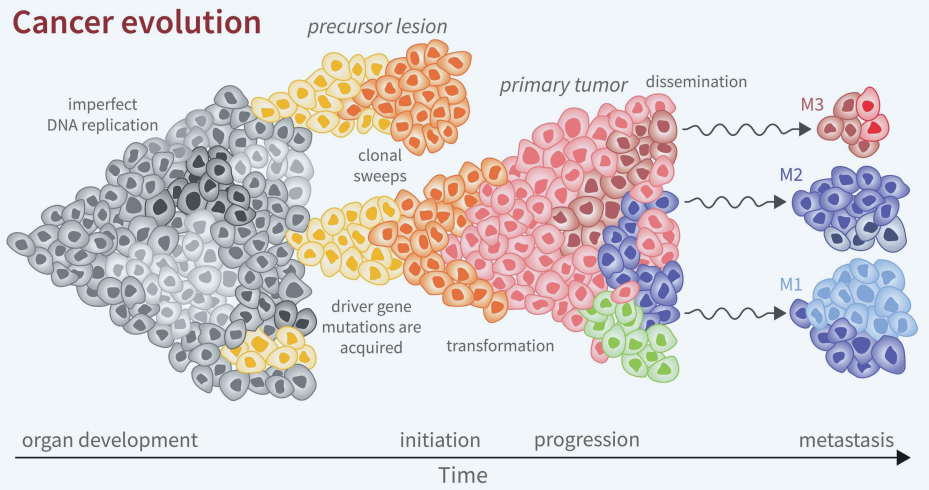
Dr. Monica Marro

Cancer diagnosis needs new tools:

Personalised medicine

Cancer
response to therapies

New biomarkers



To understand disease initiation and progression

Non-invasive,
(label-free)

Rapid diagnosis,
easy to implement,
no sample preparation

Cost-effective and portable

Raman spectroscopy

Cancer diagnosis needs new tools:

Non-invasive,
(label-free)

Rapid diagnosis,
easy to implement,
no sample preparation

Cost-effective and portable

Raman spectroscopy

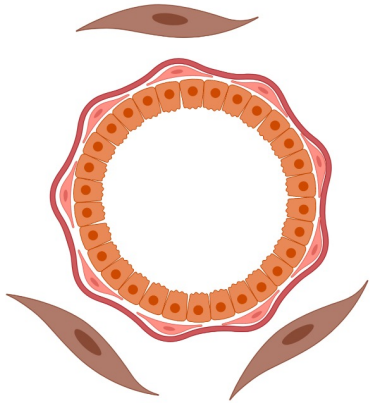
High spatial resolution: confocal resolution.

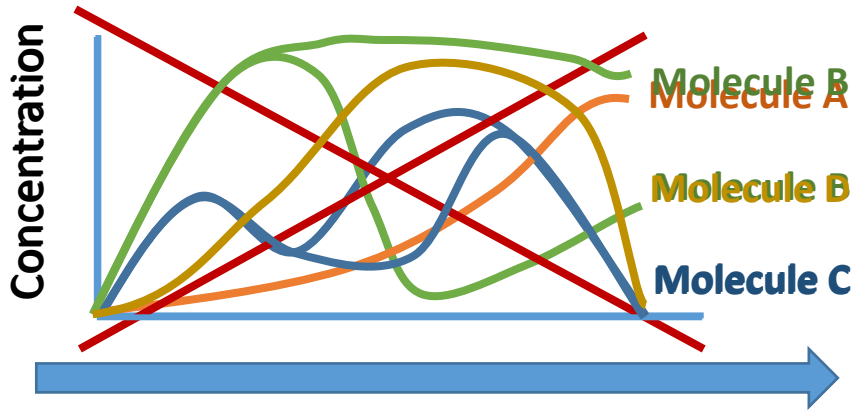
Chemical specificity: image multiple molecules simultaneously,
monitor molecular content,
classify samples with high specificity.

In-vivo (water insensitive)

Raman spectroscopy to disentangle new molecular information

Healthy breast



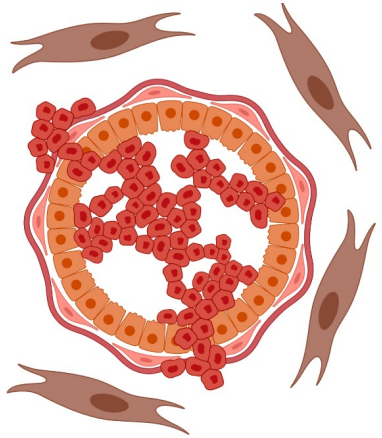


Time

External variable: force, drugs, lack of oxygen

Biological process

Breast cancer



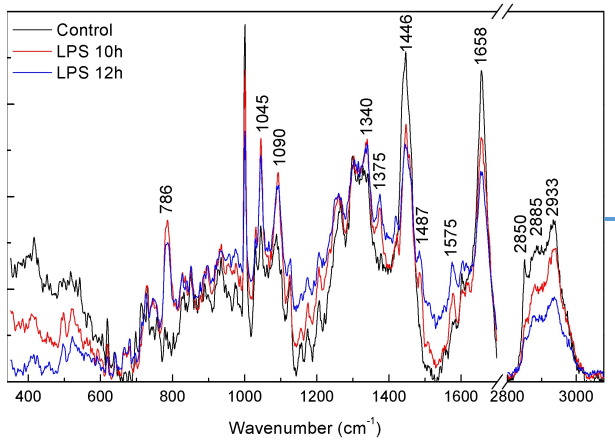
Elucidating how the different molecular makeup change, allow to:

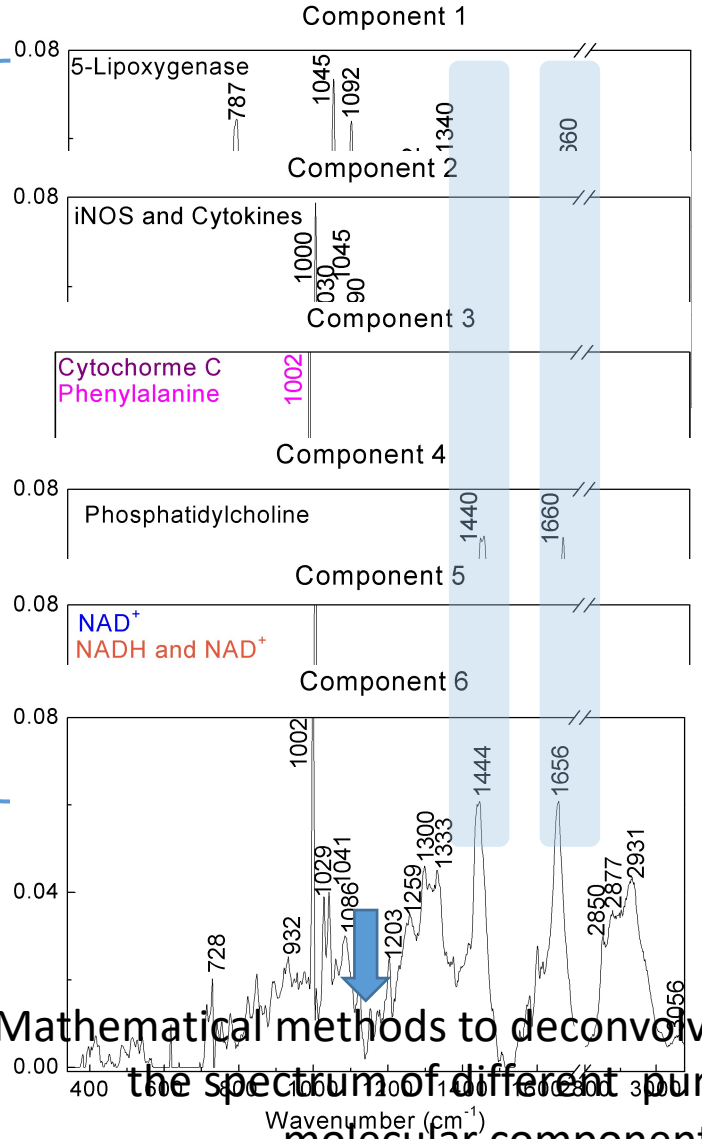
- understand disease initiation and progression
- Identify disease states
- Disentangle new therapeutic solutions

Raman spectroscopy can extract this powerful and other-wise inaccessible information:
add a **new molecular dimension**

Raman spectra of biological contains high amounts of entangled molecular information: need of data science

Mixed biological Raman spectra





Spectral decomposition: PCA, MCR-ALS
Classification: PLS-DA

Mathematical methods to deconvolve the spectrum of different pure molecular components

Raman spectroscopy

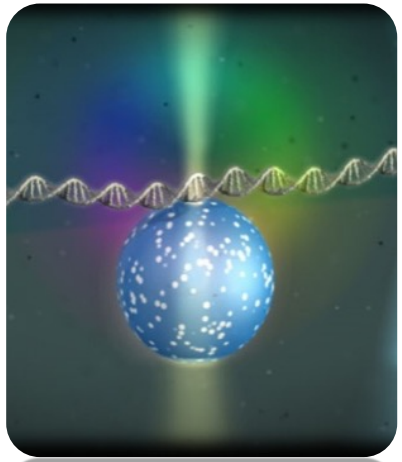
- Label-free
- Non-invasive
- High throughput
- High specificity

Data science

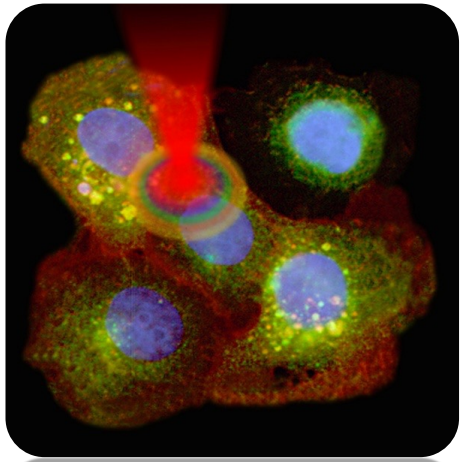
Extract novel and otherwise inaccessible molecular information

Better patient stratification: personalised medicine
New biomarkers
Improve histo-pathology
Fast In situ diagnosis

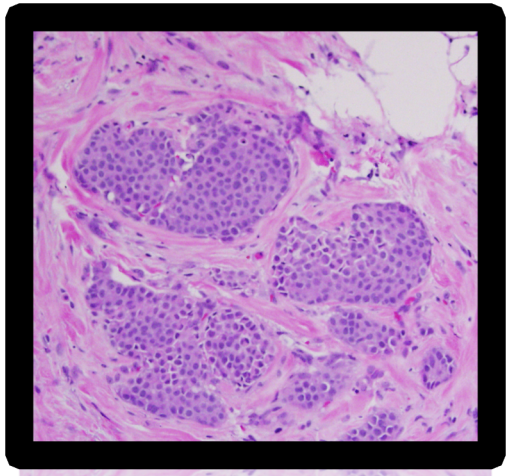
Subcellular



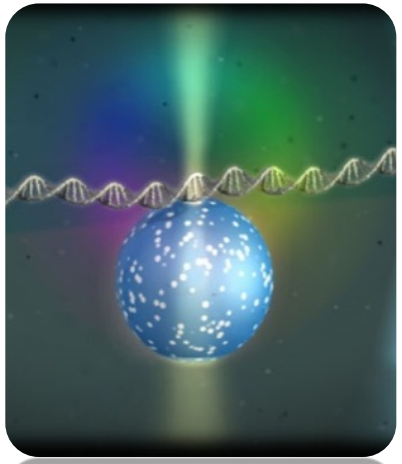
Cellular



Tissue



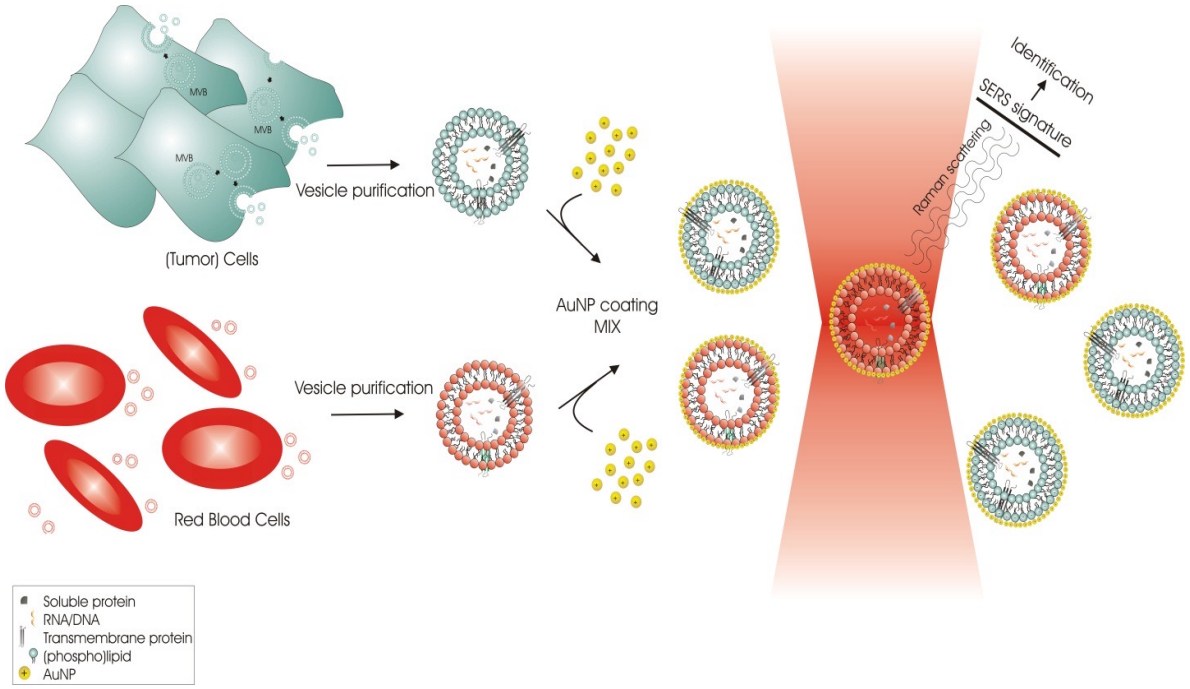
Subcellular level



Liquid biopsy:
Cancer exosomes identification

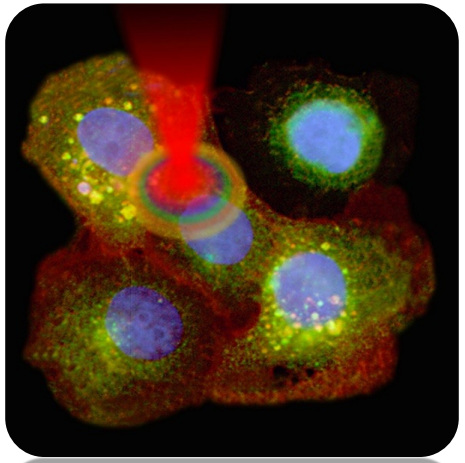
Identifcation of Individual Exosome-Like Vesicles (ELV) by Surface Enhanced Raman Spectroscopy (SERS)

UNIVERSITEIT GENT
A. Skirtach
K. Braeckmans



Sample	Sensitivity (%)	Specificity (%)
AuNP	95.8	95.5
B16F10 + AuNP	88.0	95.4
RBC + AuNP	95.1	98.0

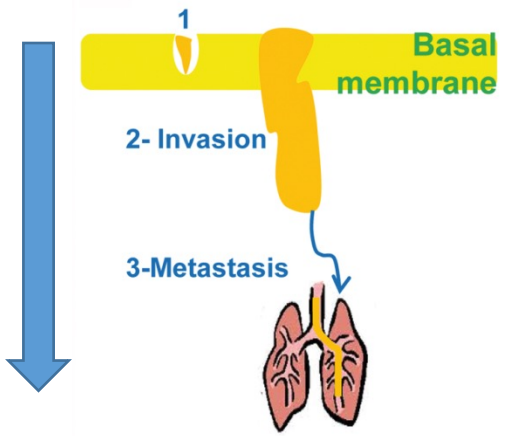
S. Stremersch , M. Marro, et al **Small**, DOI: 10.1002/smll.201600393 , 2016



Cancer diagnosis at the cellular level

Monitoring metabolic changes in breast cancer cells during malignant transformation

Lipogenic phenotype: Low TUFA/TFA

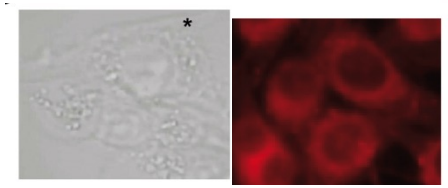


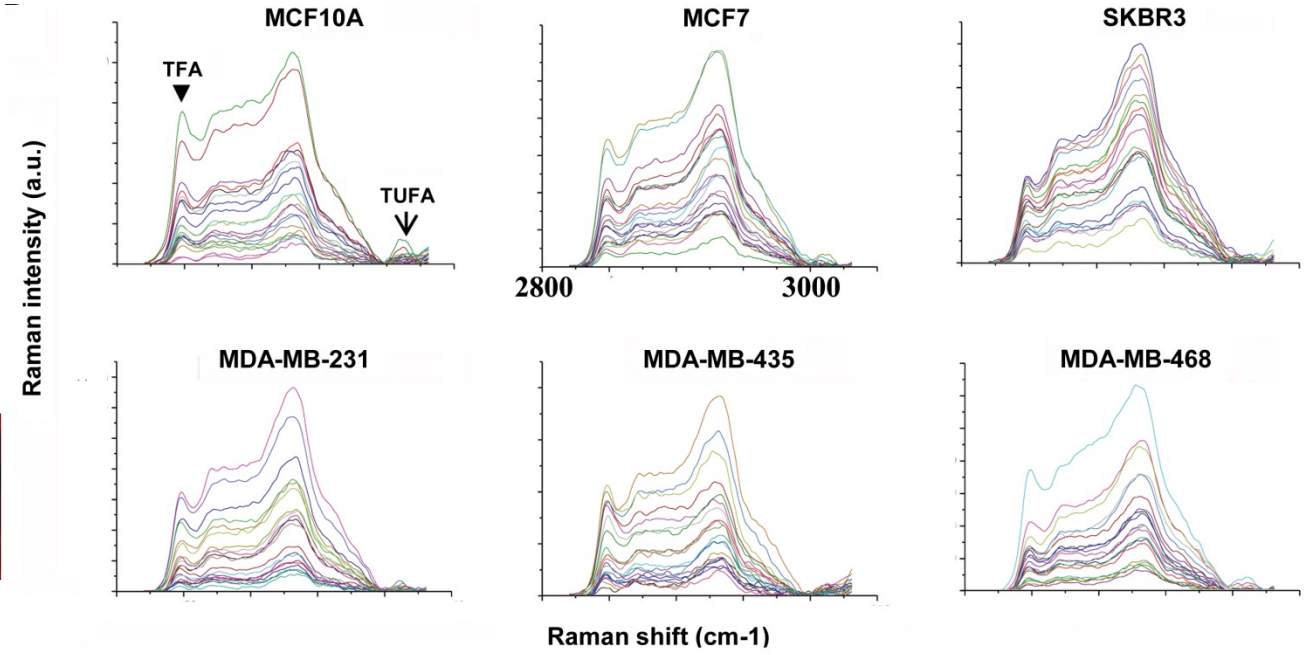
MCF10A

MCF7, SKBR3, MDA-MB-468

MDA-MB-231, MDA-MB-435

Raman spectra in the CH stretching region in the cell cytoplasm





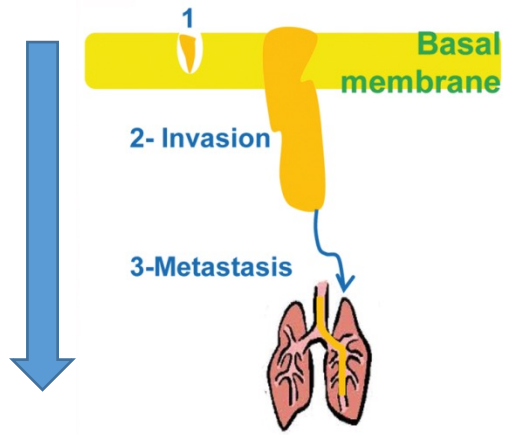
C. Nieva, M. Marro, et al ***PLoS ONE*** 7, e46456, 2012

Epithelial to mesenchymal transition (EMT) involve metabolic changes that are revealed with RS and MCR

IDIBELL
Institut d'Investigació Biomèdica de Bellvitge

Lipogenic phenotype: Low TUFA/TFA

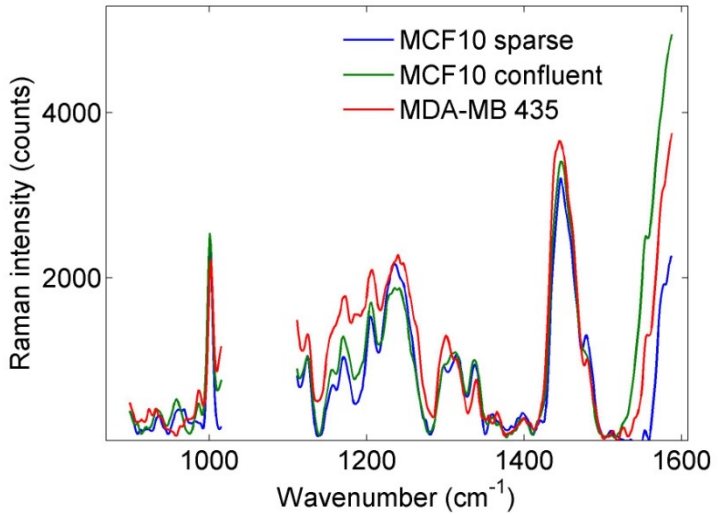
And other unknown metabolites?



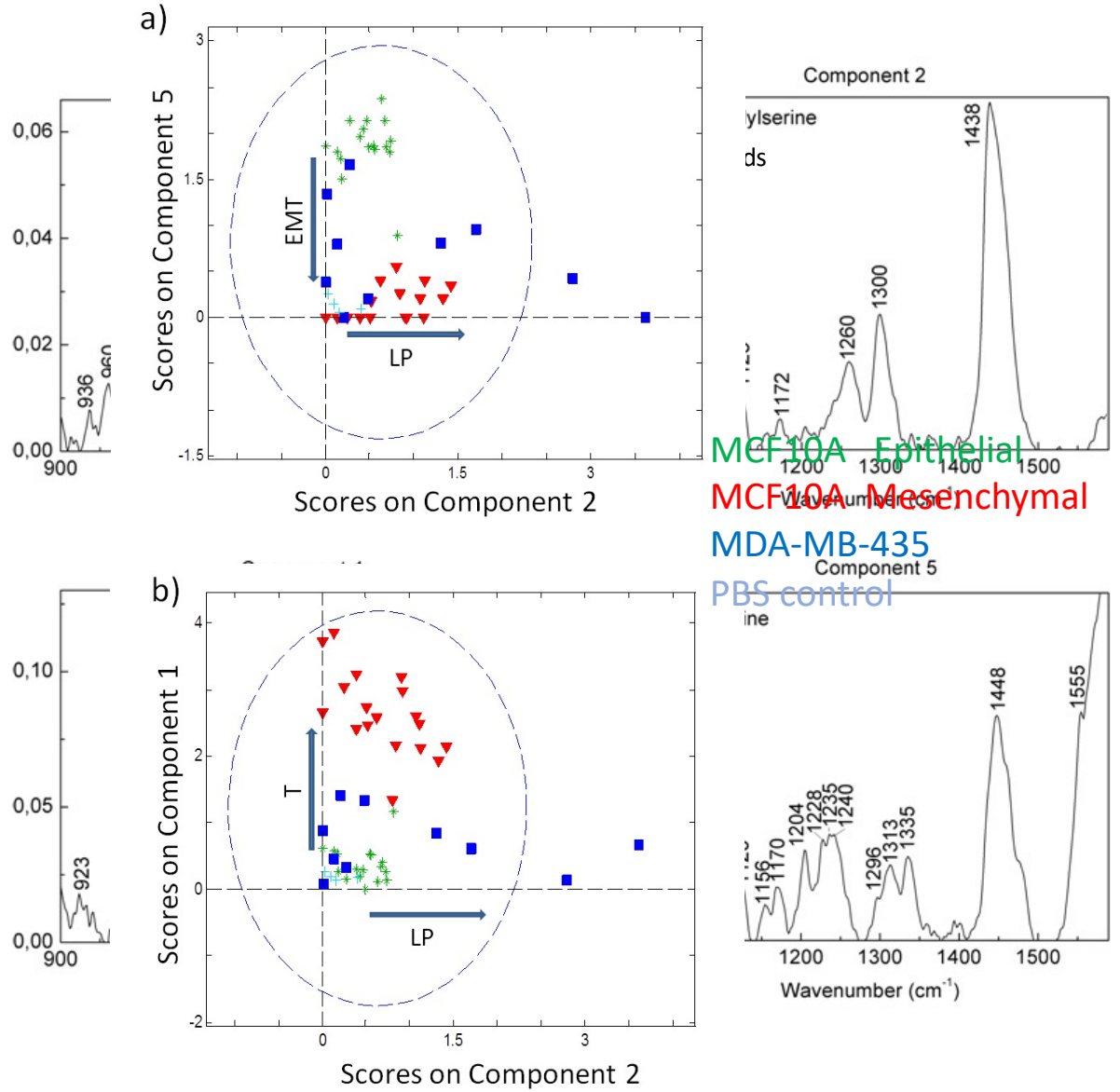
MCF10A

MCF7, SKBR3, MDA-MB-468

MDA-MB-231, MDA-MB-435



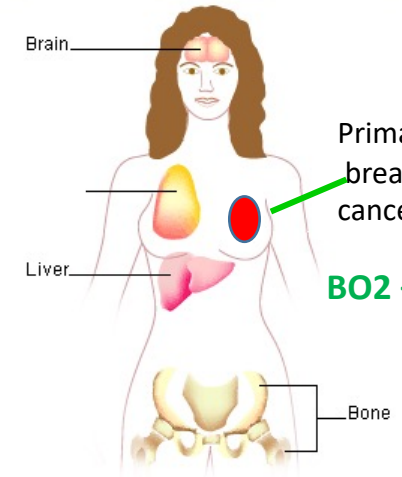
Multivariate Curve Resolution (MCR) give meaningful components



MCF10A Epithelial
MCF10A Mesenchymal
MDA-MB-435
PBS control

M. Marro, et al **BBA-MOL CELL RES** *1843(9)*, 1785-1795, 2014
C. Nieva, M. Marro, et al. **PLoS ONE** 7, e46456, 2012.
V. Stresing, et al. **Oncogene**, 32(6):724-35, 2012

Raman spectroscopy identify biomarkers to give cancer prognosis

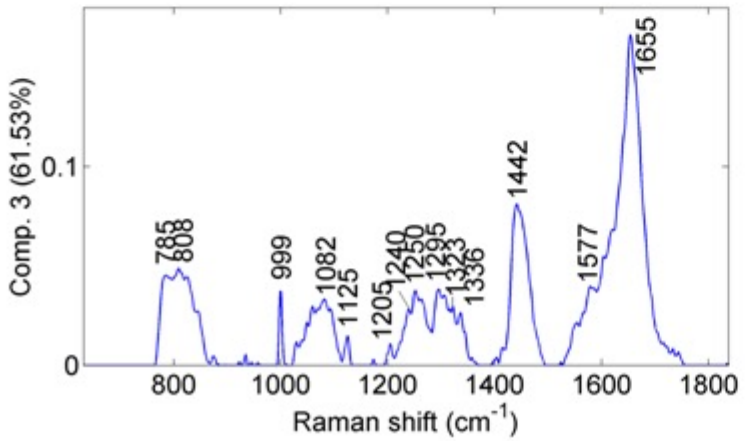


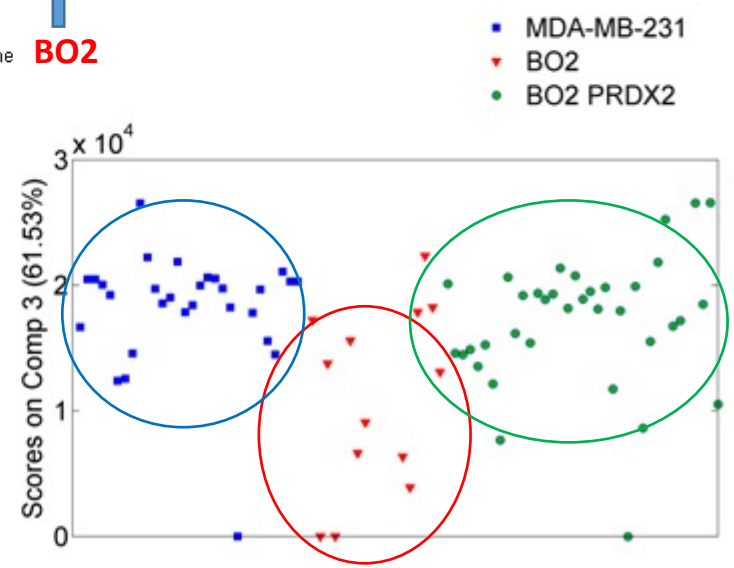
Primary breast cancer

MDA-MB-231

BO2 + PRDX2 NO bone metastasis

BO2

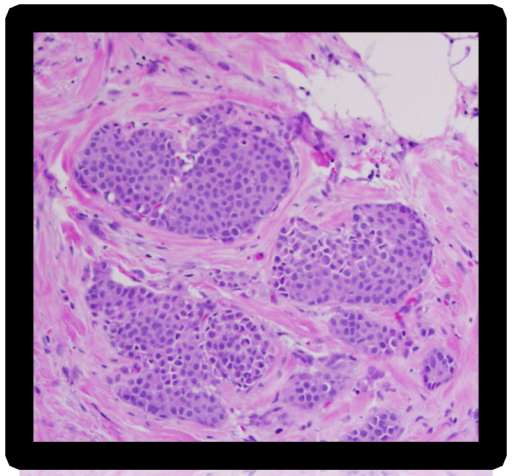




Metastatic cells treated with PRDX2 return to the primary tumor phenotype

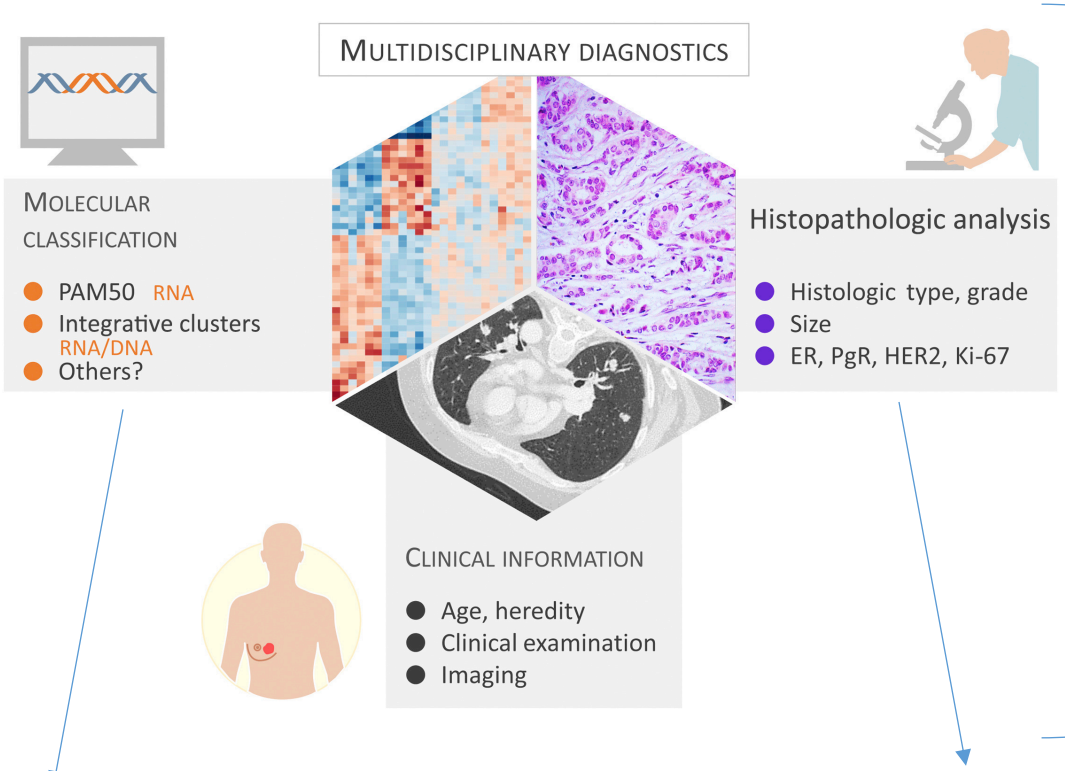
M. Marro, et al, **Anal Chem**, 2018

Tissue level



Breast cancer diagnosis

Raman spectroscopy to improve histopathology and cancer stratification



Some groups of patients does not respond to therapy
They don't fit current classification

Better methods to improve patient stratification are necessary:
Personalised medicine

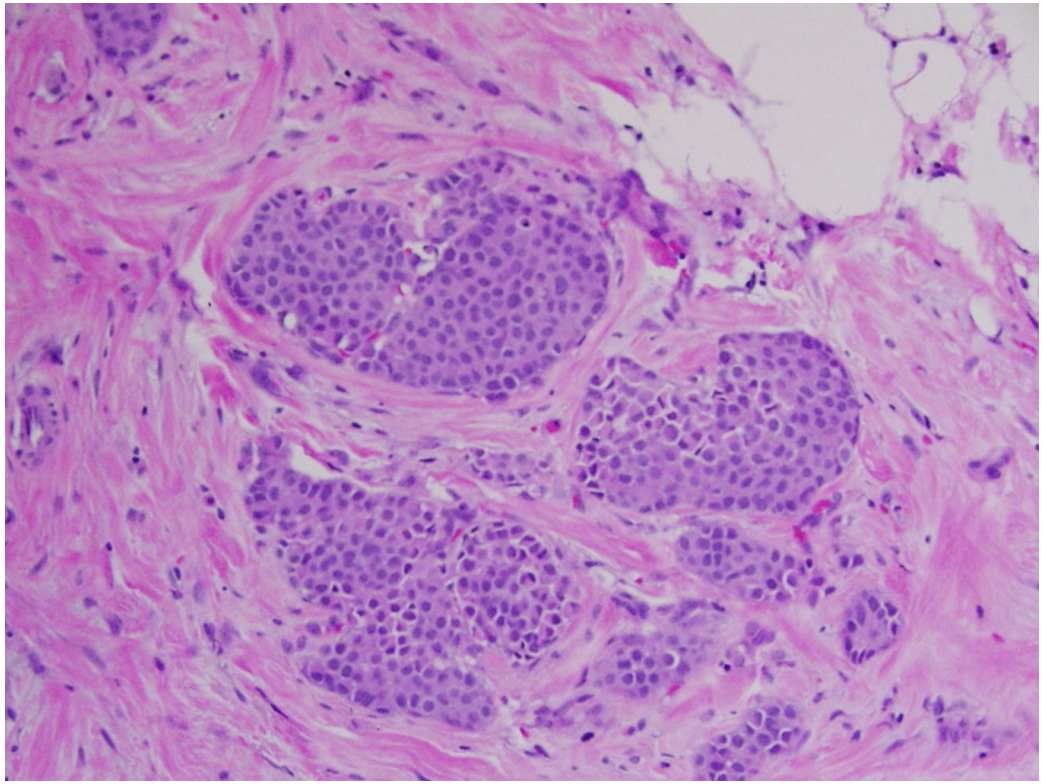
~~Expensive and time-consuming~~

Inmunohistochemistry (IHC):

- Lack of sensitivity and specificity,
- Interlaboratory differences: Differences in antibodies, detection systems and protocols

Hege G. Russnes, ***Am. J. Pathol***., 187 (10) 2017

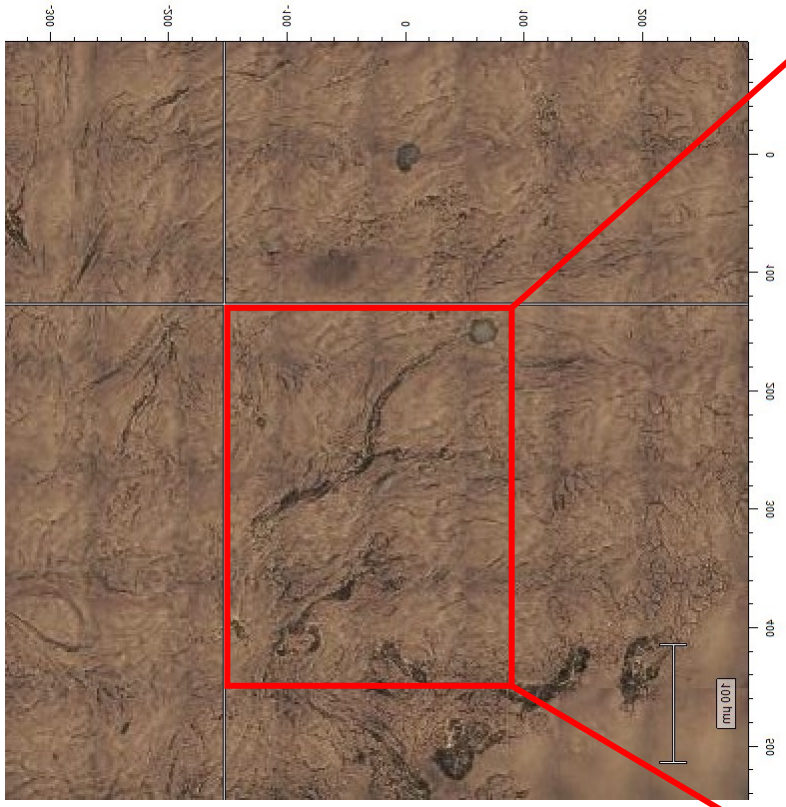
Raman spectroscopy to improve histopathology and cancer stratification



Current histopathology:
Only morphological features, no molecular information

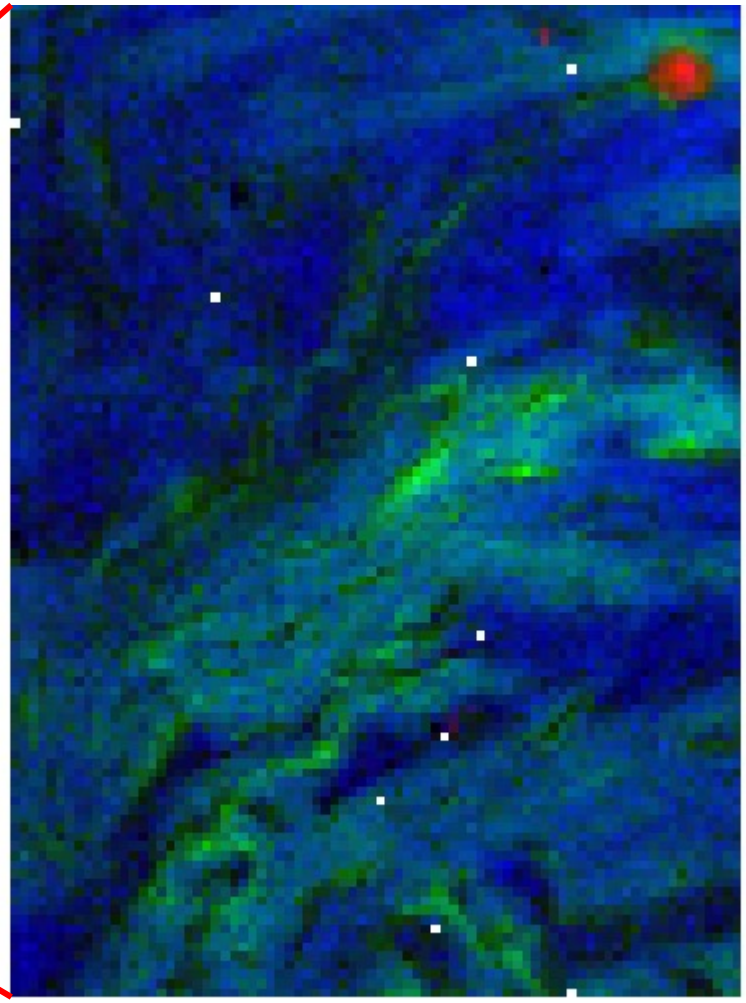
Raman spectroscopy to improve histopathology and cancer stratification

Optical image



Bright field un-stained tissue section

Molecular image



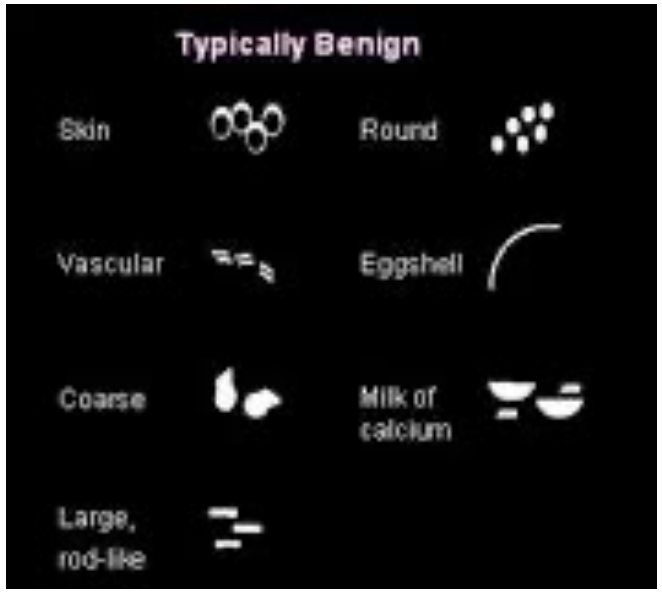
Raman imaging:
Label-free multiplexed molecular information

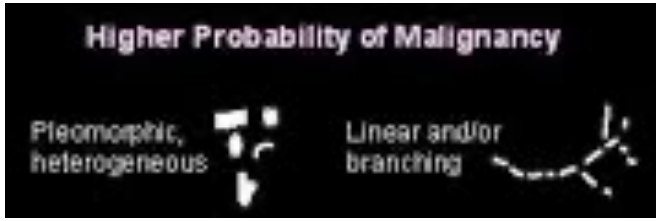
Understanding the origin of breast tissue calcifications and its relationship with cancer

Germans Trias i Pujol Hospital

Tissue calcifications are the first indicators to detect and diagnose breast cancer

Cancer aggressiveness





How are calcifications formed?

How are they related to metastasis?

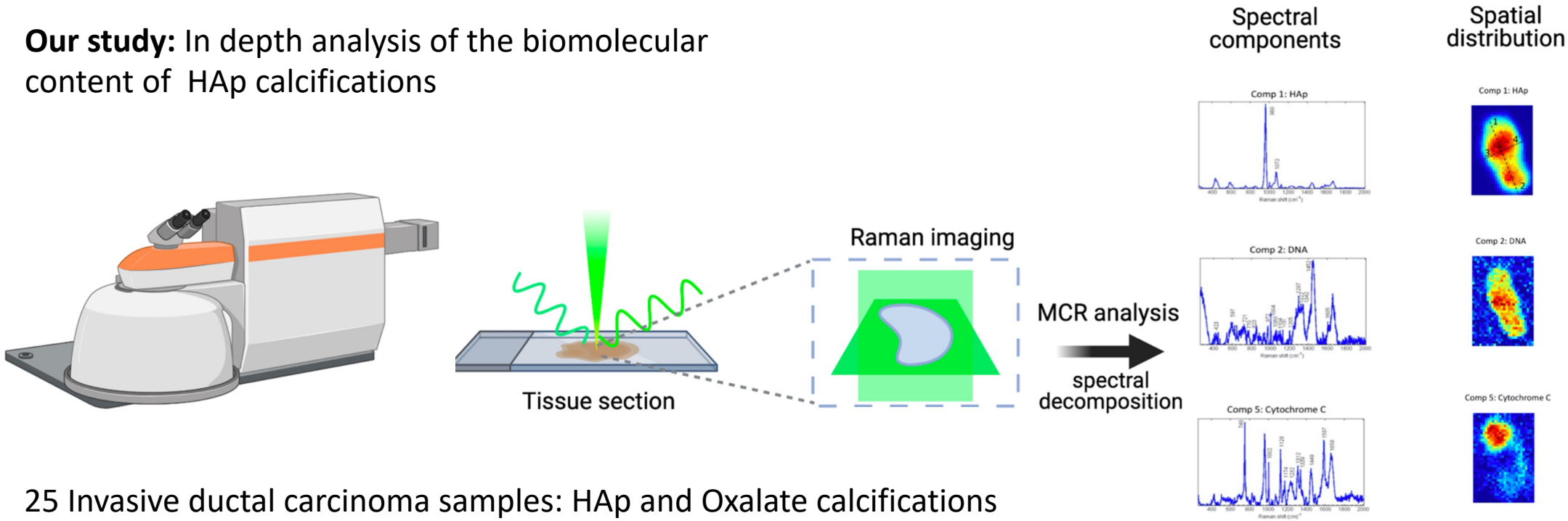
Raman spectroscopy to study the biomolecular content of breast tissue calcifications

Preliminary Raman results:
Vanna et al. RS of calcifications correlates with histopathology

How are calcifications formed?

How are they related to metastasis?

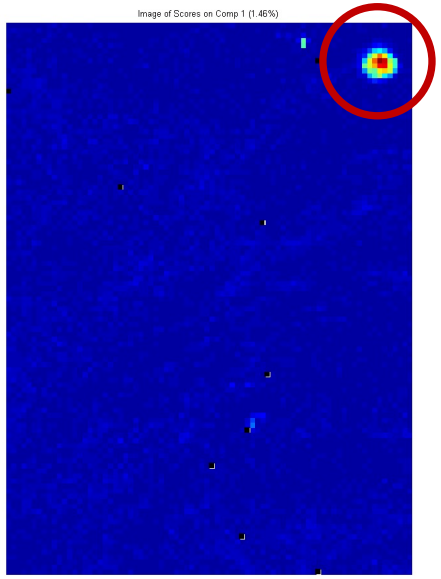
Our study: In depth analysis of the biomolecular content of HAp calcifications



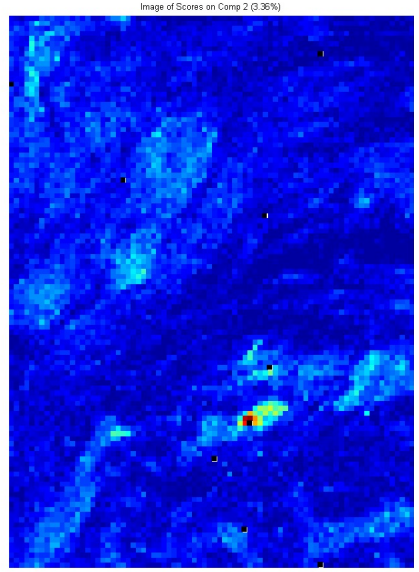
25 Invasive ductal carcinoma samples: HAp and Oxalate calcifications

M. Marro, et al. ***Cancers***, accepted

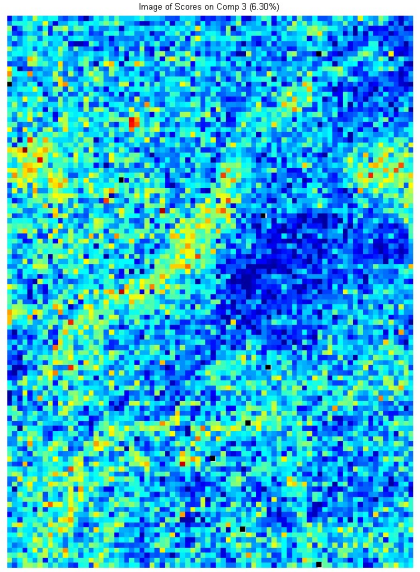
INVASIVE DUCTAL CARCINOMA



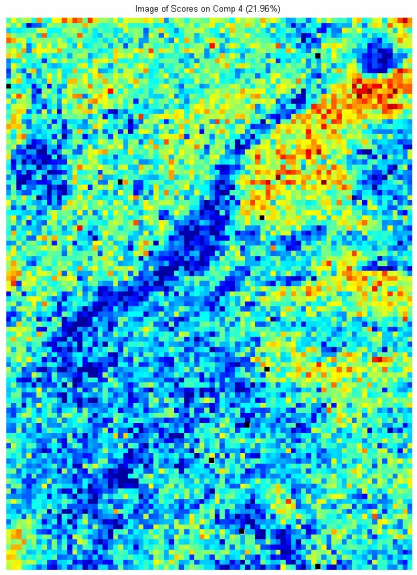
HAp



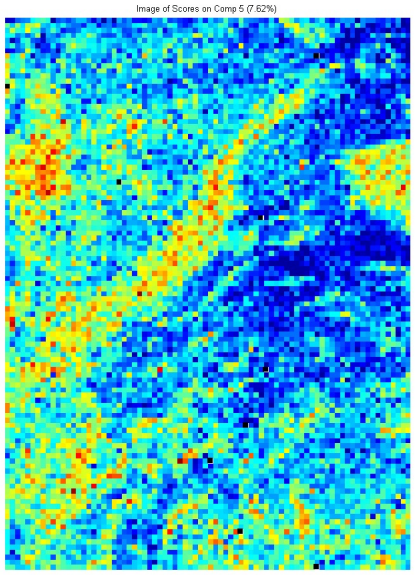
Cytochrome C



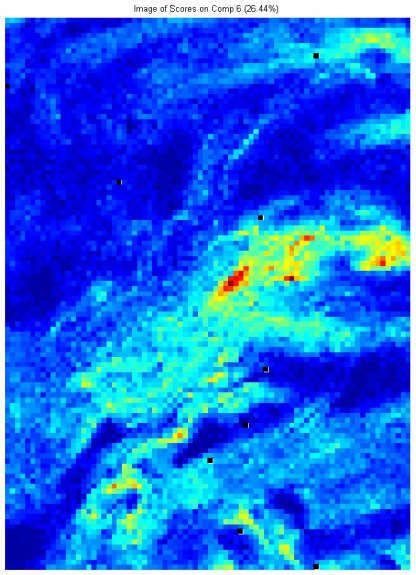
Collagen



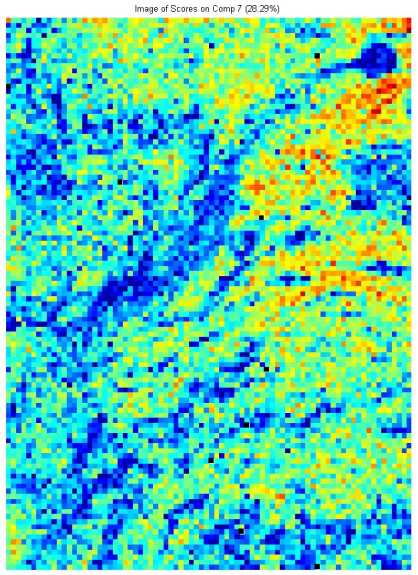
Glycogen



DNA

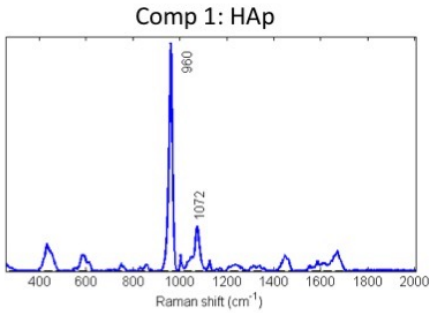


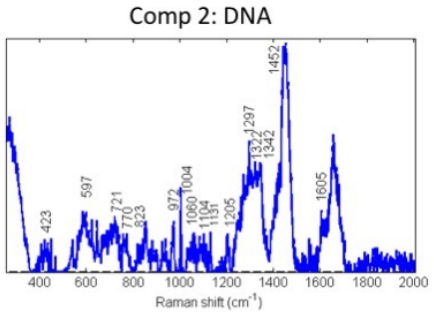
Phosphates

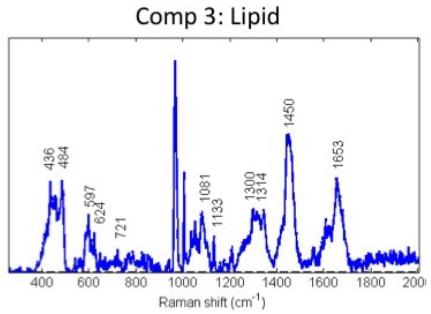


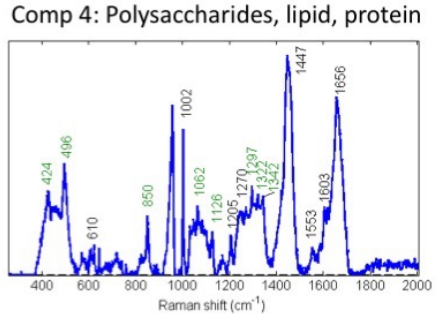
Proteins

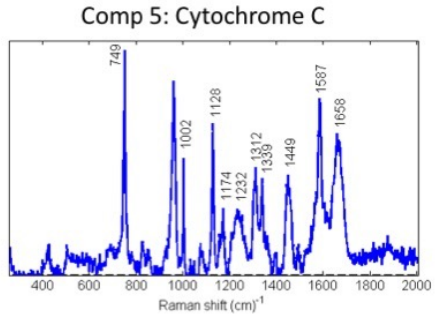
Raman imaging reveals biomolecules encapsulated in breast cancer calcifications

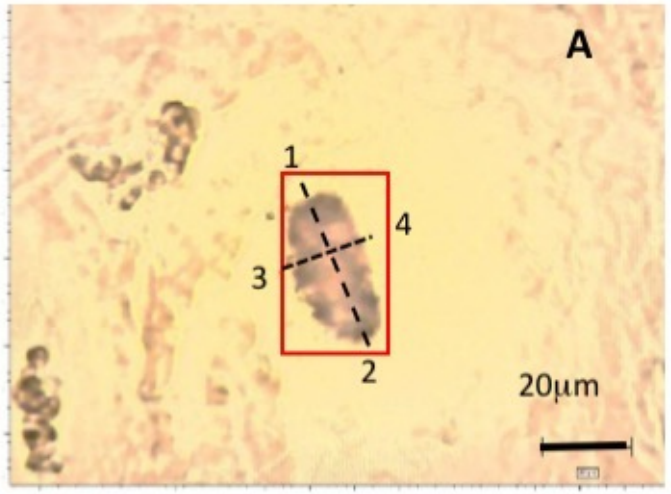


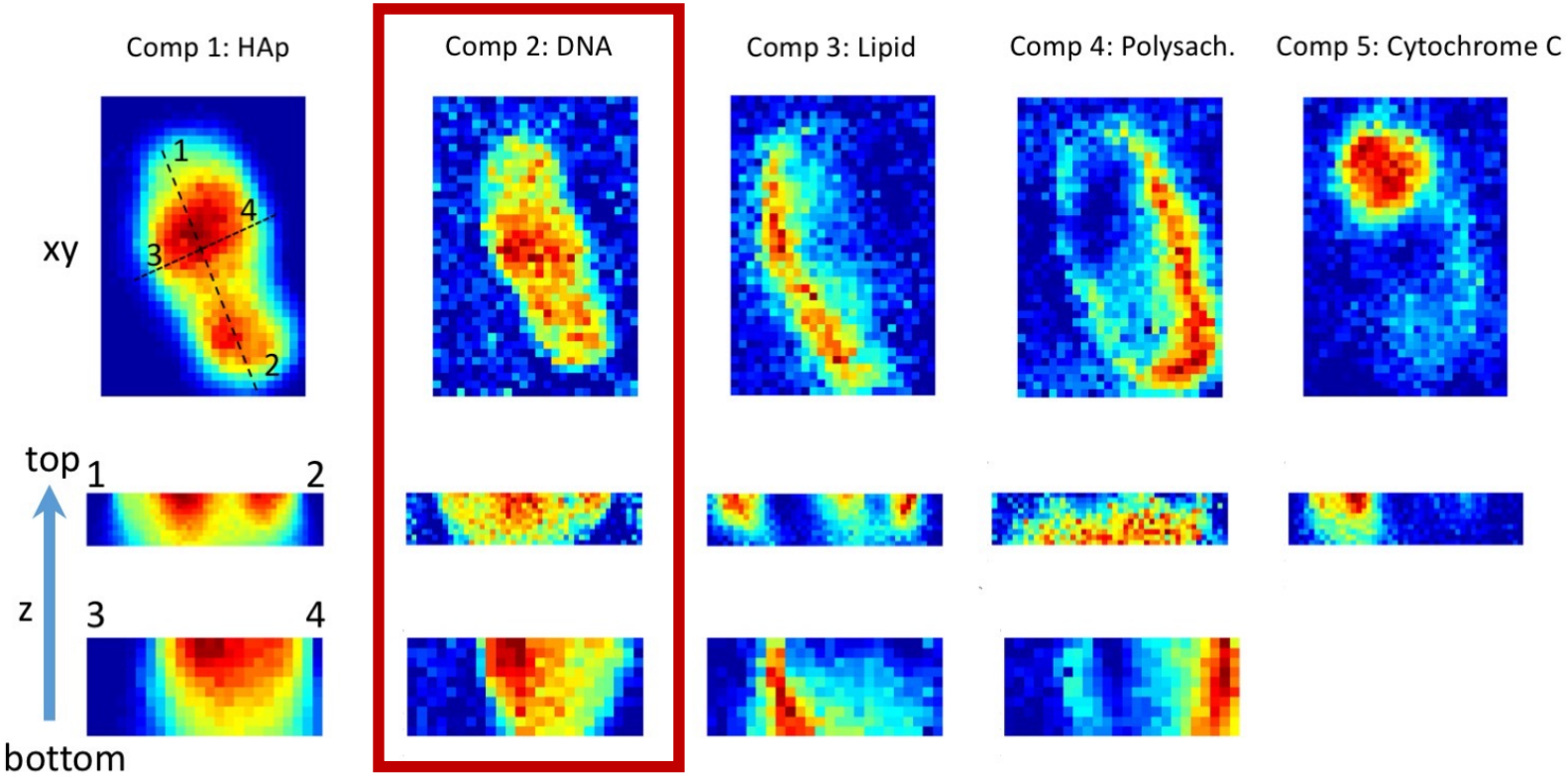








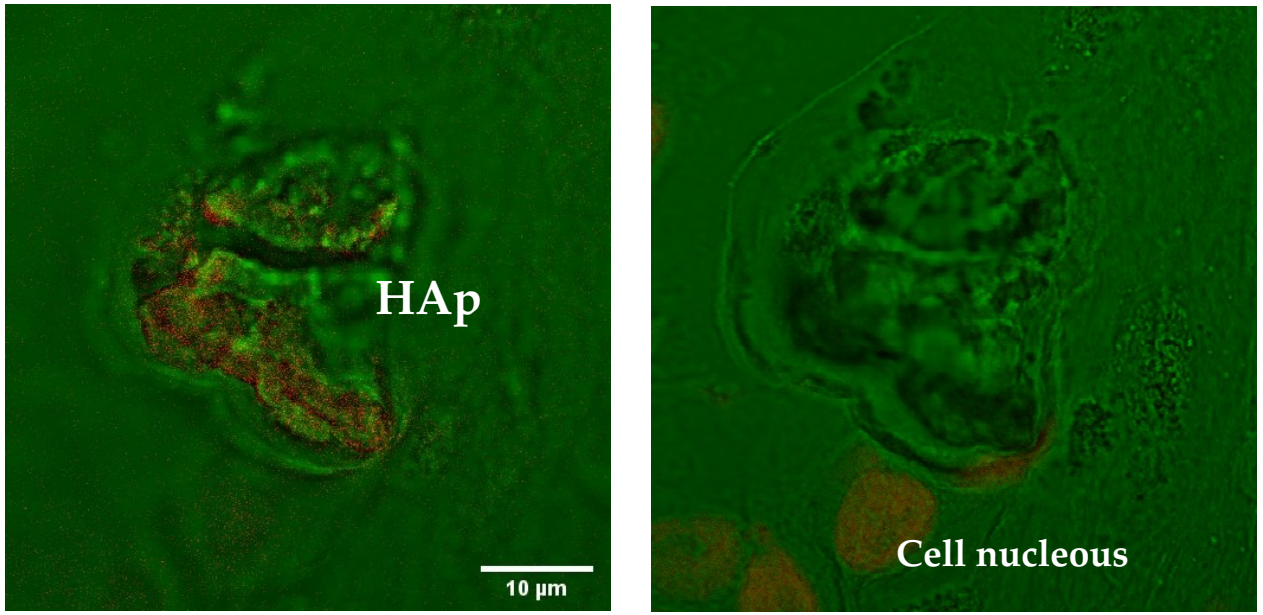




M. Marro, et al. ***Cancers***, accepted

DNA presence in HAp tissue calcifications give hints on its association to worse prognosis

DAPI staining corroborated the presence of DNA in HAp calcifications



Conclusions:

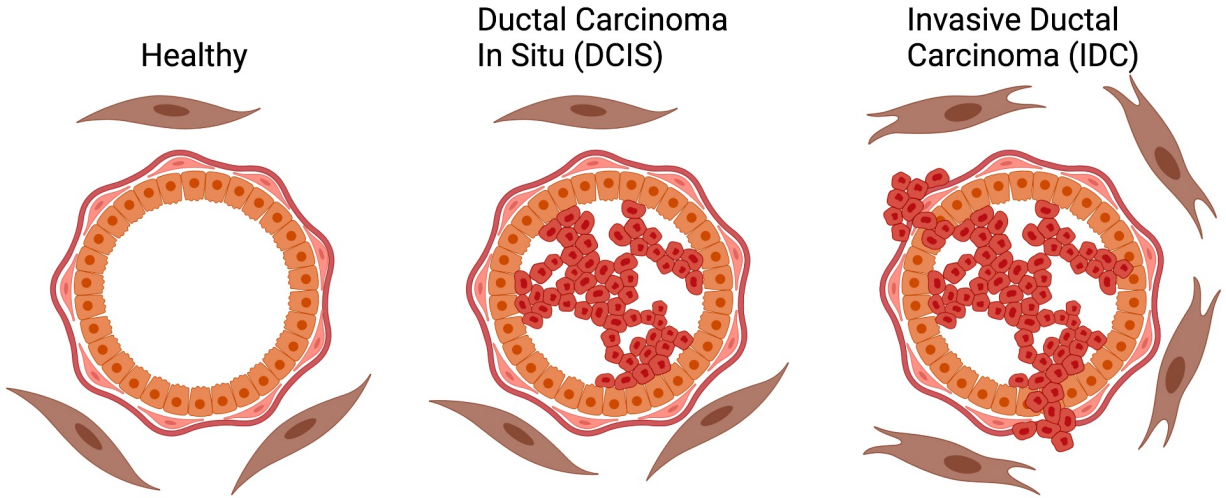
- DNA is present in more than 90% of the HAp calcifications

- These results could explain the correlation with worse prognosis:

- Cancerous DNA can be preserved in tissues biomineralized
- DNA could transfect healthy cells after some time

M. Marro, et al. ***Cancers***, accepted

Comprehensive molecular and microspectroscopic profiling of breast carcinomas and their resistance to neoadjuvant treatment



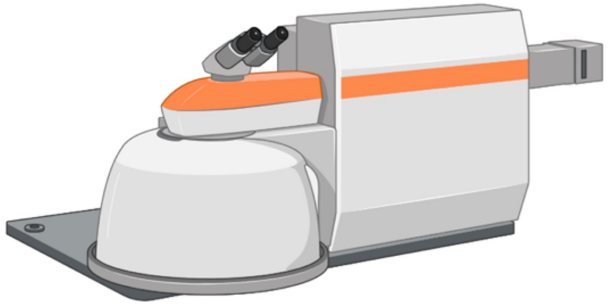
Molecular stratification :
Luminal A
Luminal B,
HER2-enriched
Basal-like

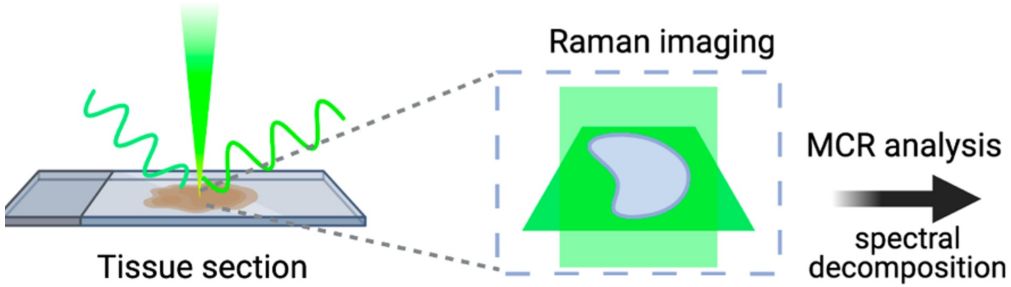
Fundació La Marató de TV3

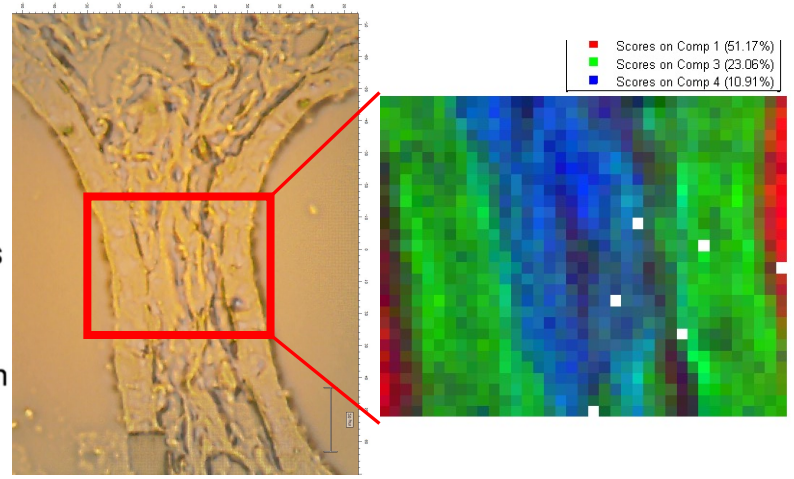
Germans Trias i Pujol Hospital

IGTP Germans Trias i Pujol Research Institute

Pedro L. Fernandez
Gemma Fuster



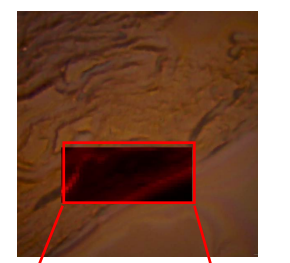


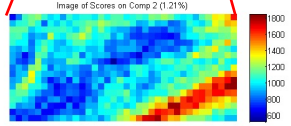


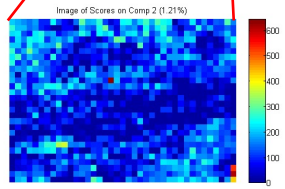
Fundació La Marató de TV3

Healthy

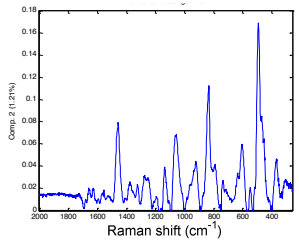
Invasive ductal carcinoma



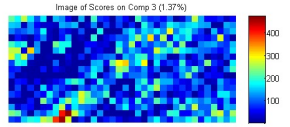


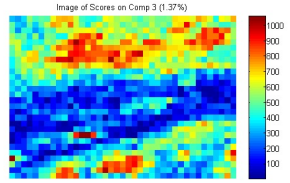


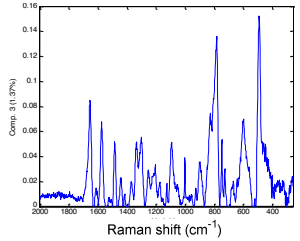
Raman fingerprints



Component 1







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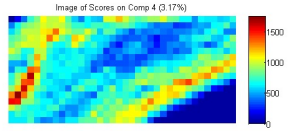
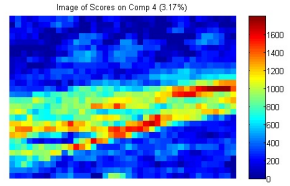
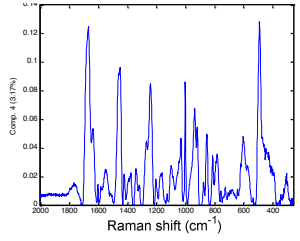
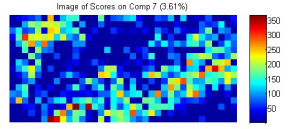
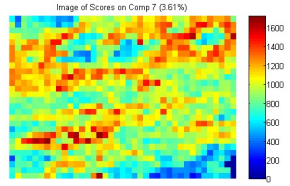


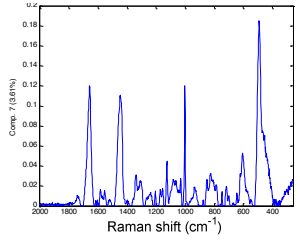




Component 3





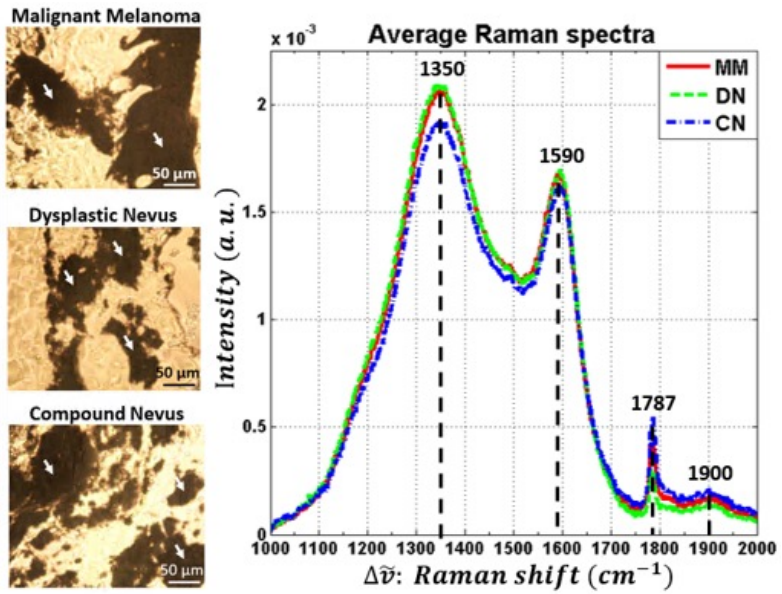


Component 4

M. Marro, et al. in preparation

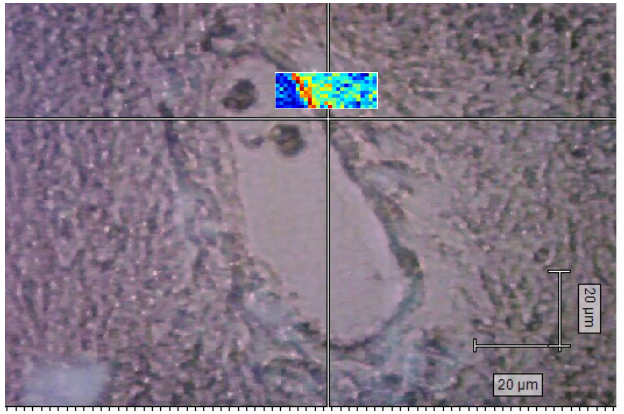
Other ongoing projects on Cancer

Dermatology:
rapid discrimination of skin lesions



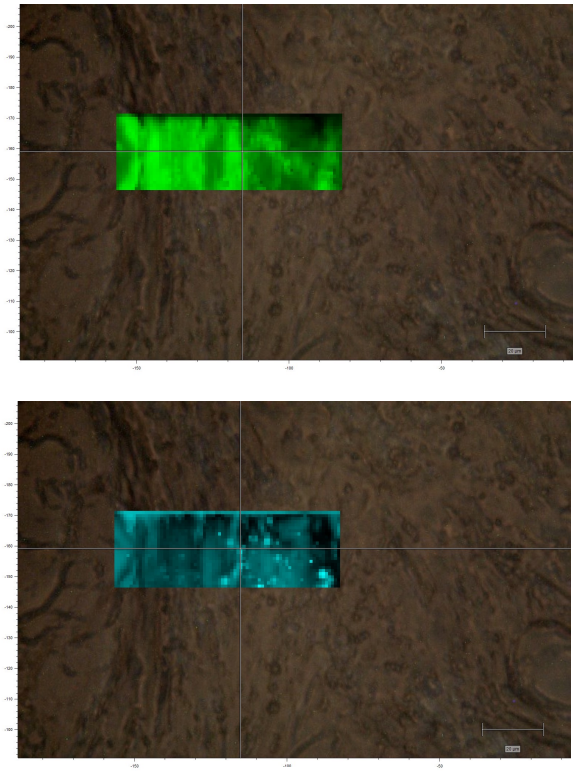
CSIC

Pediatric Retinoblastoma:
Non-invasive detection



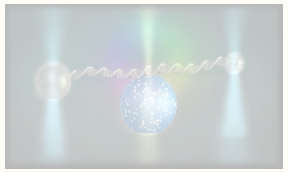
SJD
Sant Joan de Déu
Barcelona · Hospital

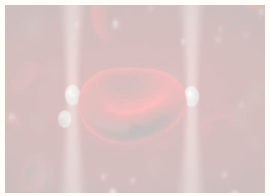
Thyroid cancer:
New molecular pathology



CLÍNIC
BARCELONA
Hospital Universitari

Mechano-biology





IBEC Institute for Bioengineering of Catalonia

A. Le Roux

ICFO

S. Wieser

D. Petrov

Cancer

CLÍNIC BARCELONA Hospital Universitari

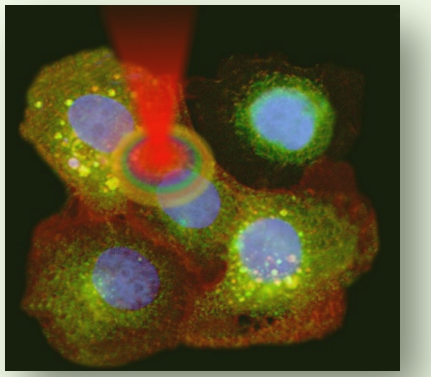
IDIBAPS

G. Fuster

NIH

KU MEDICAL CENTER The University of Kansas

F. Behbod



Germans Trias i Pujol Hospital

P. Fernández

UNIVERSITEIT GENT

K. Braeckmans

SJD Sant Joan de Déu Barcelona · Hospital

ICFO

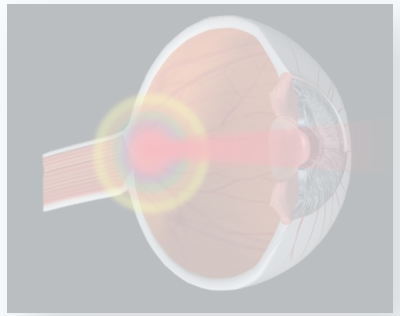
T. Durduran

R. Quidant

I. Galván

CSIC

Neurodegeneration



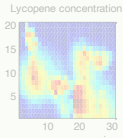
IDIBAPS

P. Villoslada

E. H. Martínez-Lapiscina

Fundació La Marató de TV3

Food



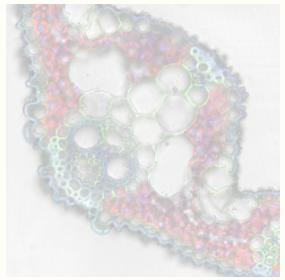
crag

M. Rodriguez

UCLM Universidad de Castilla-La Mancha

L. Gomez

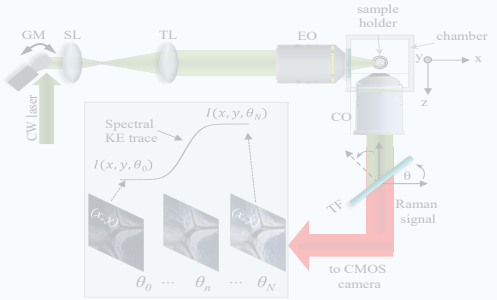
Data science



UNIVERSITAT DE BARCELONA

A. de Juan

Raman technology



Microbiology

A. Gomez-Zavaglia

CONICET

European Commission

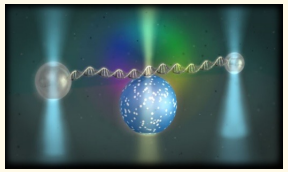
PREMIUM Preserving bacteria with oligosaccharides and eco-friendly processes

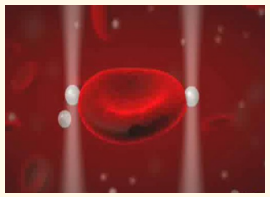
Raman4Clinics

cost EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY

Raman spectroscopy @ ICFO

Mechano-biology





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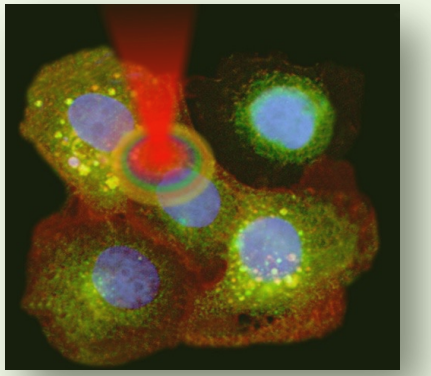

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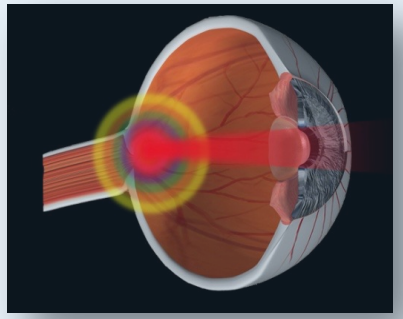

IDIBAPS

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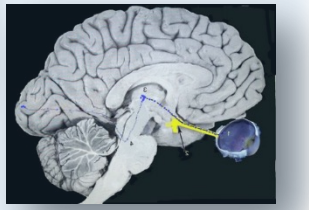
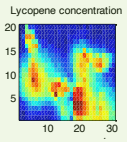


Fundació La Marató de TV3

Foodomics



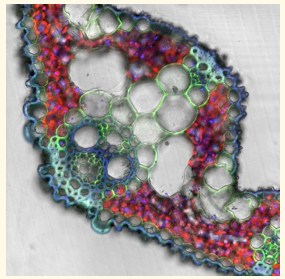
CRAG

M. Rodriguez

UCLM UNIVERSIDAD DE CASTILLA-LA MANCHA

L. Gomez

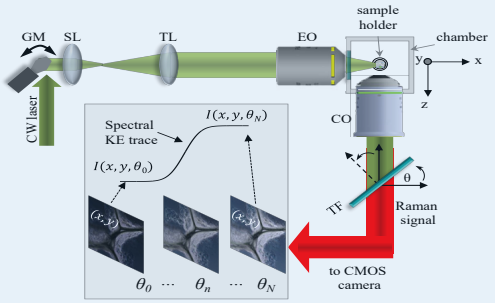
Data science



UNIVERSITAT DE BARCELONA

A. de Juan

Raman technology



Microbiology

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European Commission

PREMIUM Preserving bacteria with oligosaccharides and eco-friendly processes

Raman4Clinics

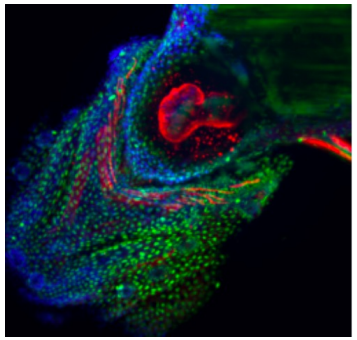
cost EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY

The Super-resolution Light microscopy and Nanoscopy Laboratory

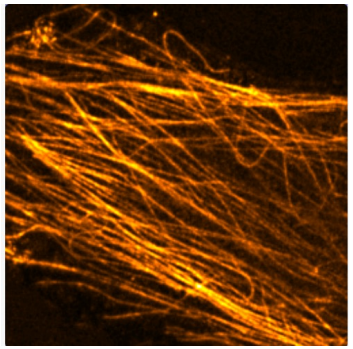
ICFO
Institut de Ciències Fotòniques

Dr. Pablo Loza-Álvarez (Head)

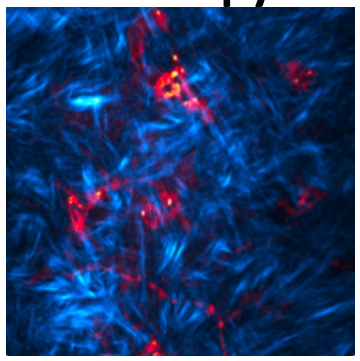
Light Sheet Fluorescence



Super-resolution Imaging

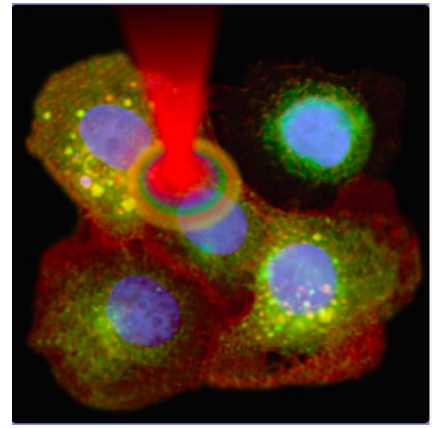


Multiphoton microscopy

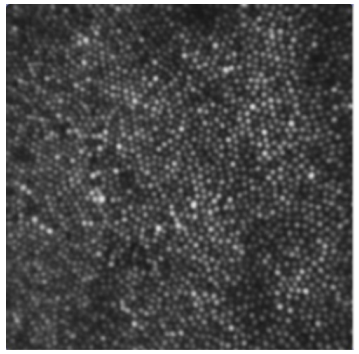


Raman Microspectroscopy

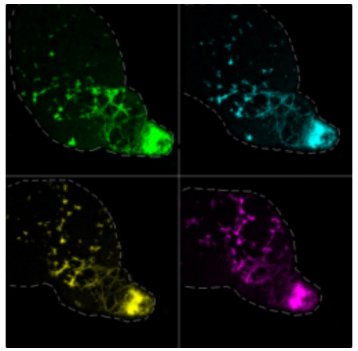
Dr. Monica Marro
monica.marro@icfo.eu



Ophthalmic microscopy



Structured Illumination Microscopy



Single particle tracking