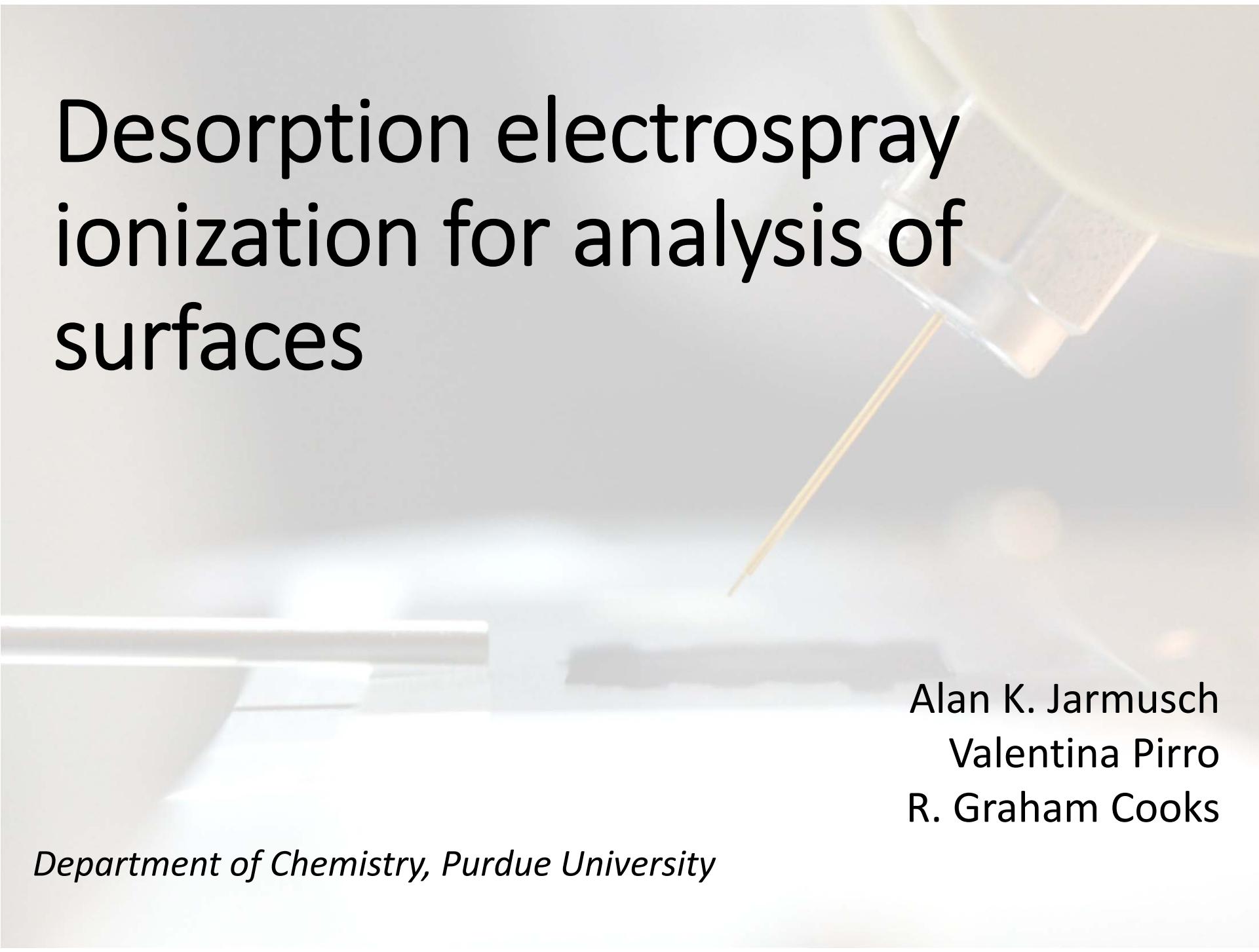


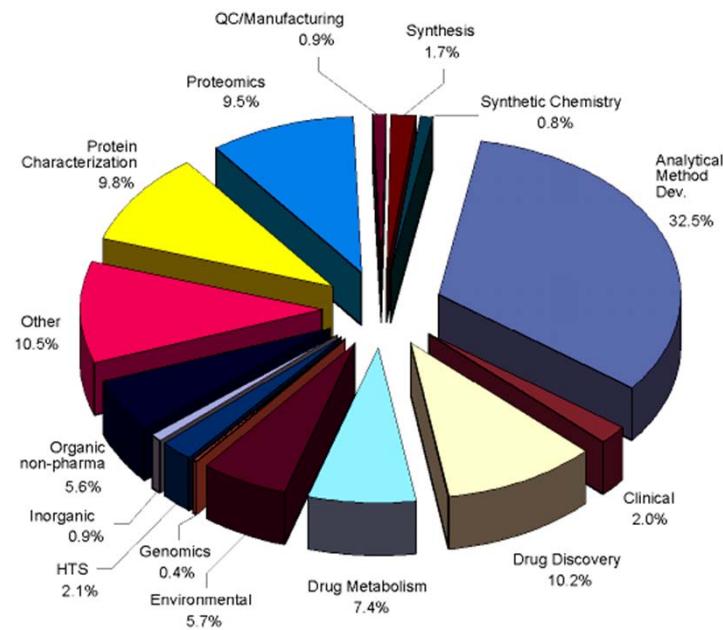
# Desorption electrospray ionization for analysis of surfaces



Alan K. Jarmusch  
Valentina Pirro  
R. Graham Cooks

*Department of Chemistry, Purdue University*

## ❖ Mass spectrometry moves across disciplines



*Medicine & Life Sciences*

*Biology and Pharmaceutical  
Science (1990)*

*Earth & Atmospheric Sciences  
and Material Science (1955)*

*Chemistry (1945)*

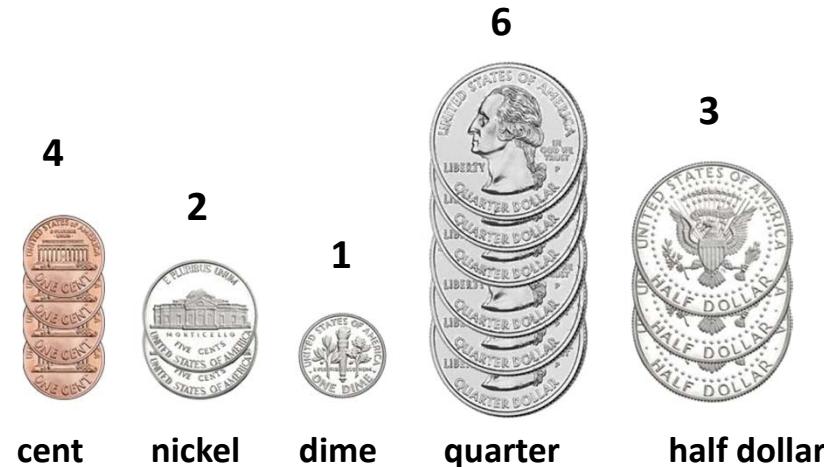
*Physics (1910)*

# ❖ What is mass spectrometry?

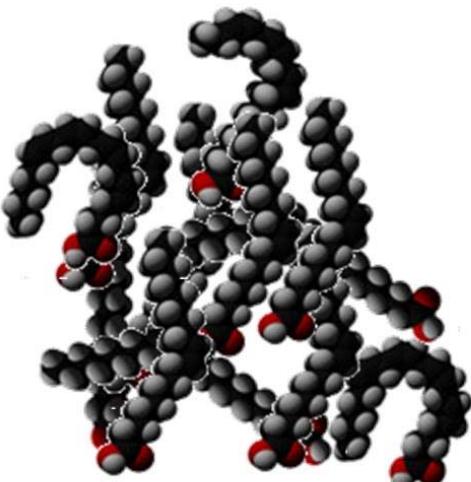
*Technique that measures the mass-to-charge ratio and abundance of gas-phase ions.*



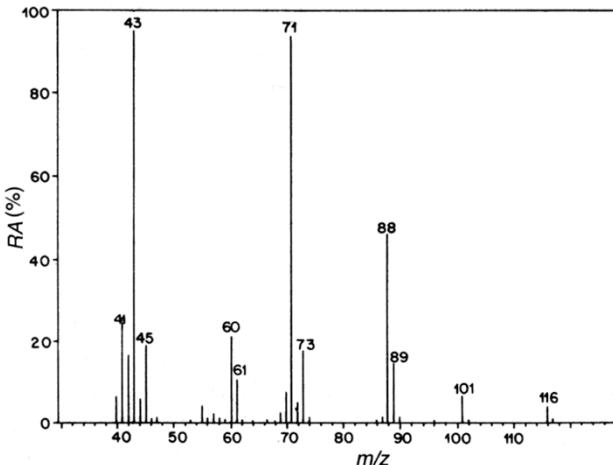
Quantity



Value



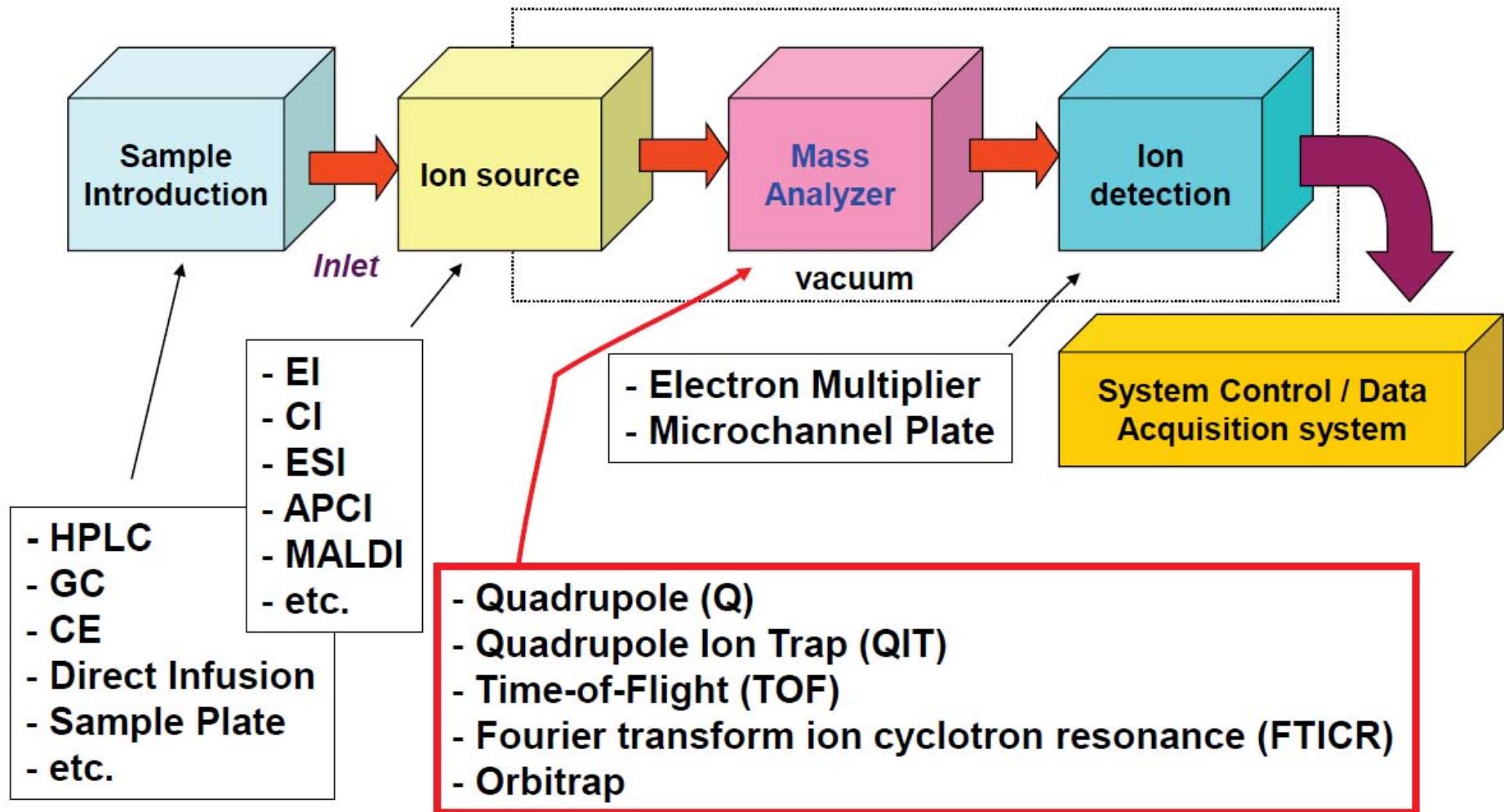
Ion intensity



$m/z$

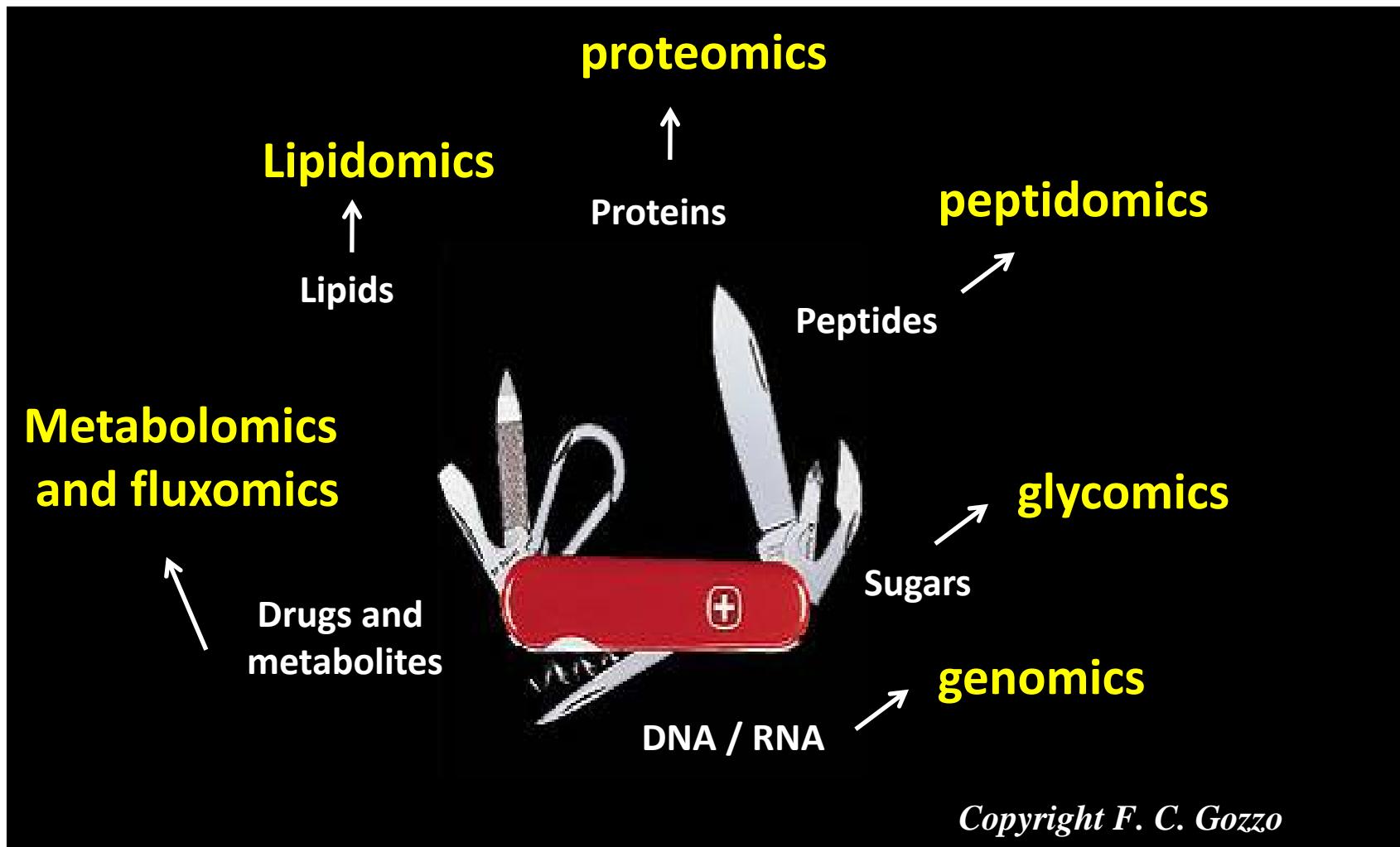
Molecules

## ❖ Components of a mass spectrometer



- ❖ Versatile
- ❖ Direct analysis or coupling
- ❖ High selectivity and specificity

- ❖ Hightthroughput
- ❖ Quantitative and qualitative analysis
- ❖ Imaging





# DESI: the *first* ambient MS technique

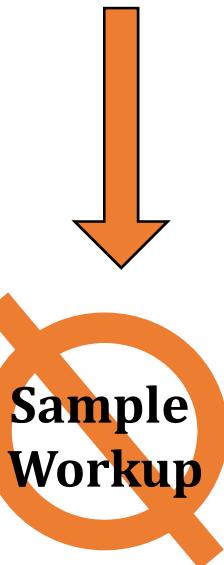
- ❖ Direct analysis of ordinary objects in their native environments

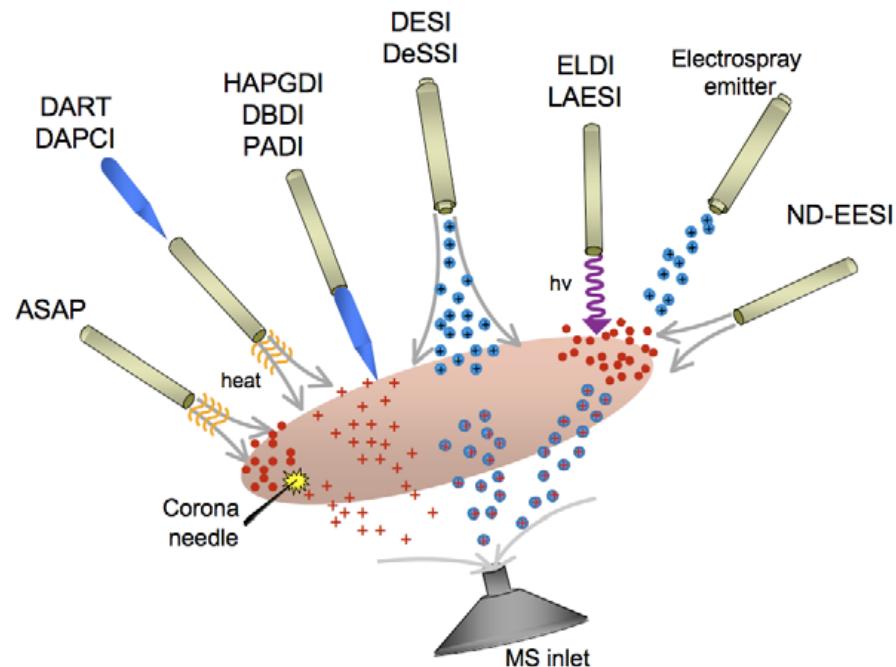
Main types of ionization methods

EI (Electron Ionization)	Energetic electrons	Vapors	EI
CI (Chemical Ionization)	Gas phase ions	Vapors	APCI
SI (Spray Ionization)	Electric field, nebulizing gas	Solutions	ESI
DI (Desorption Ionization)	Energetic particles, photons	Solids	MALDI SIMS



Implication of Ambient Ionization



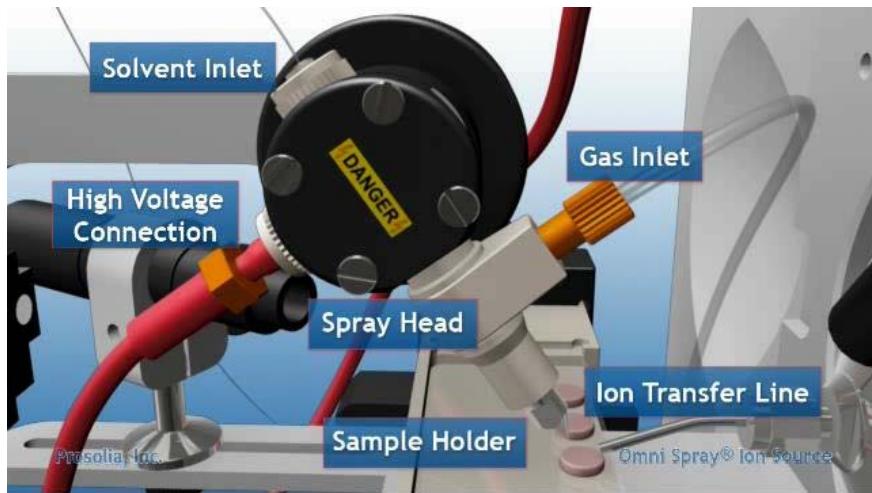


- ❖ Direct analysis
- ❖ No sample preparation
- ❖ Ionization in open environment (in-situ)
- ❖ Real time
- ❖ High throughput

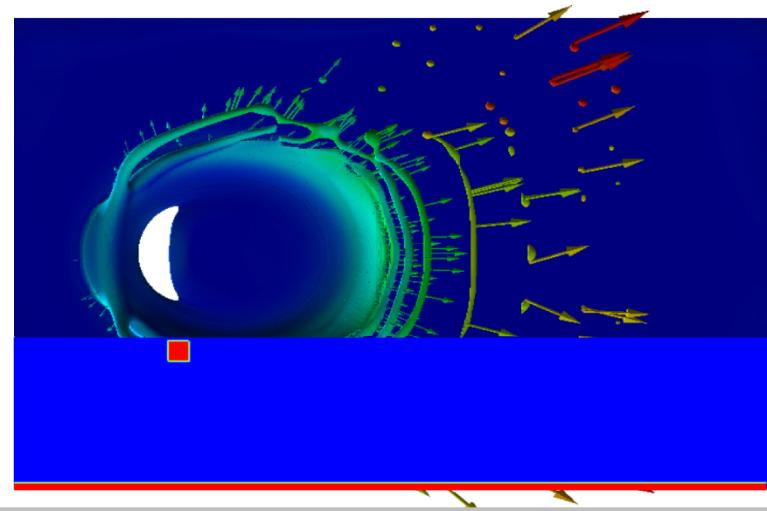
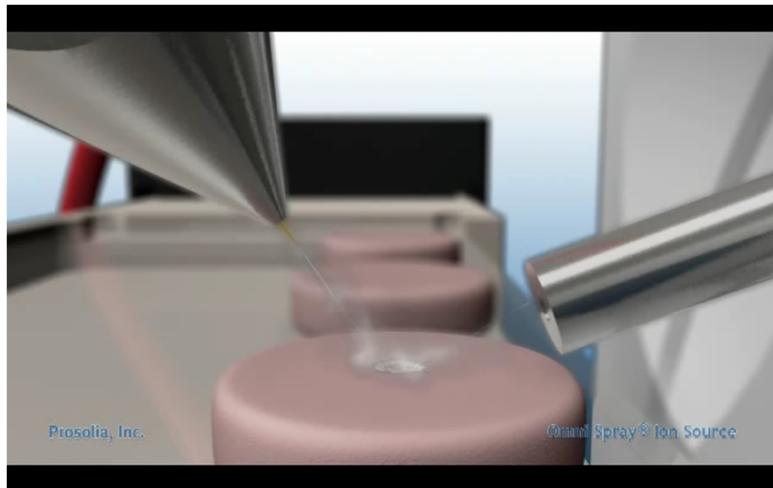
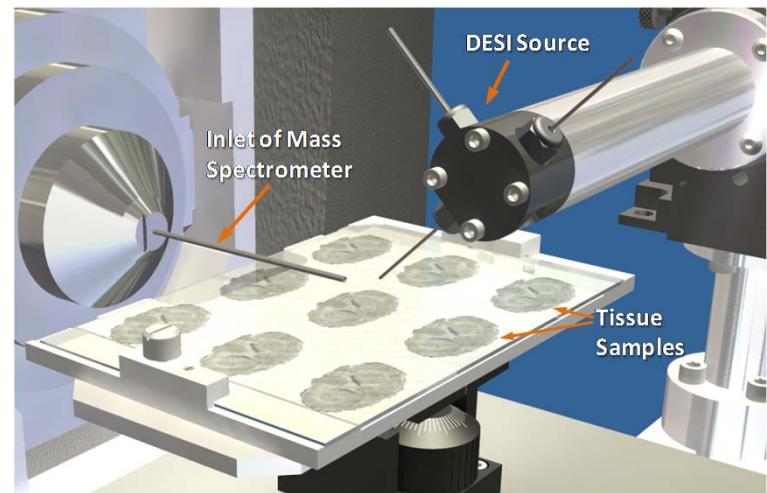
**DESI**, SSP, DART, ASAP, ELDI, FD-ESI, DAPCI, AP-IR-MALDI, MALDESI, JeDI, EESI, DeSSI, APTDI, LAFAPA, PADI, DBDI, ND-ESSI, LTDI, LAESI, IR-LAESI, DAPPI, APGDDI, EASI, RASTIR, PESI, FA-APGD, LTP, DEMI, LMJ-SSP/ESI, SACI, SPAMS, LTP, DICE, LAMICI, EASI, PESI, Paper Spray, touch spray....

❖ Direct analysis of ordinary objects in their native environments

### *DESI-MS PROFILING*

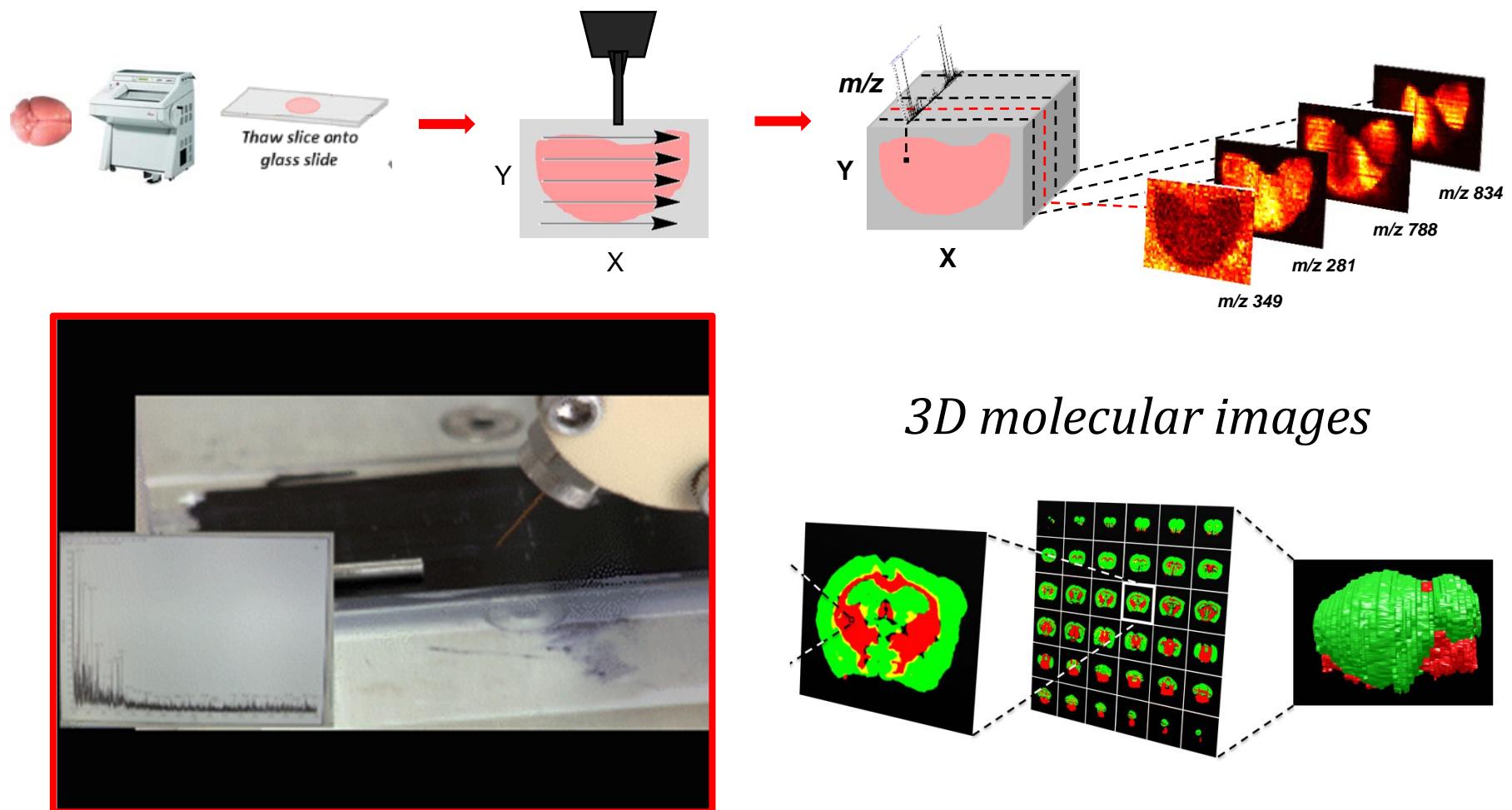


### *DESI-MS IMAGING*



# DESI imaging

- ❖ Mass Spectra linked Spatial Coordinates (X,Y)

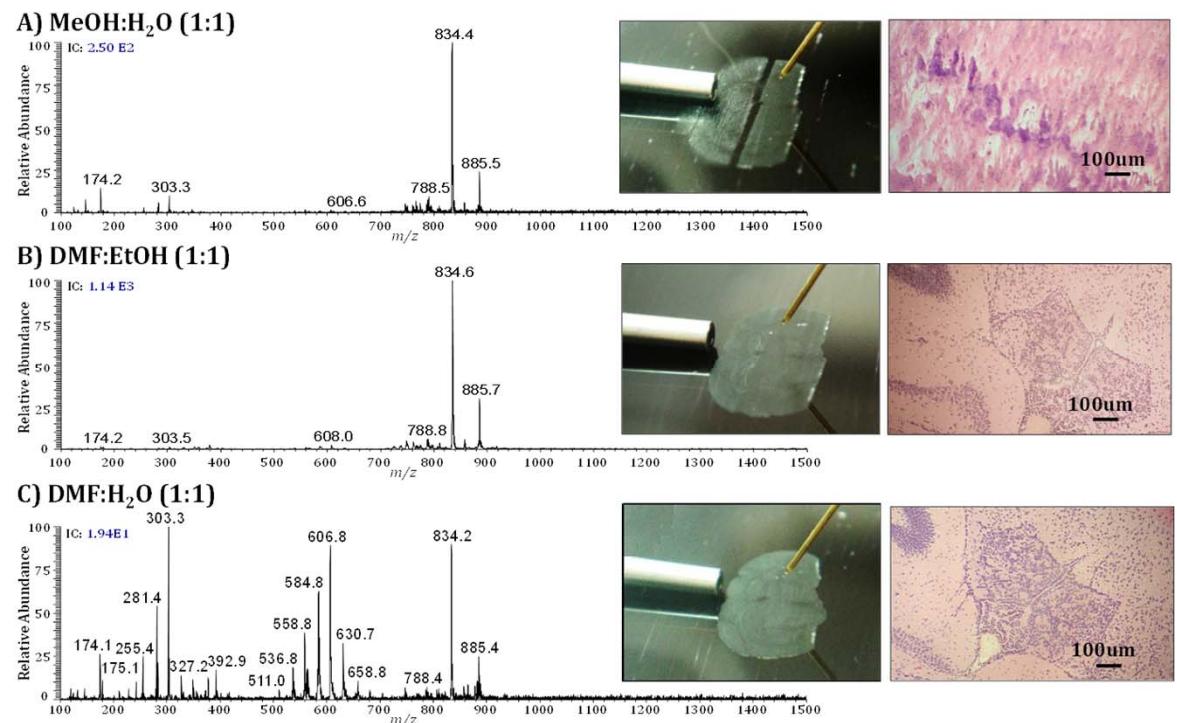
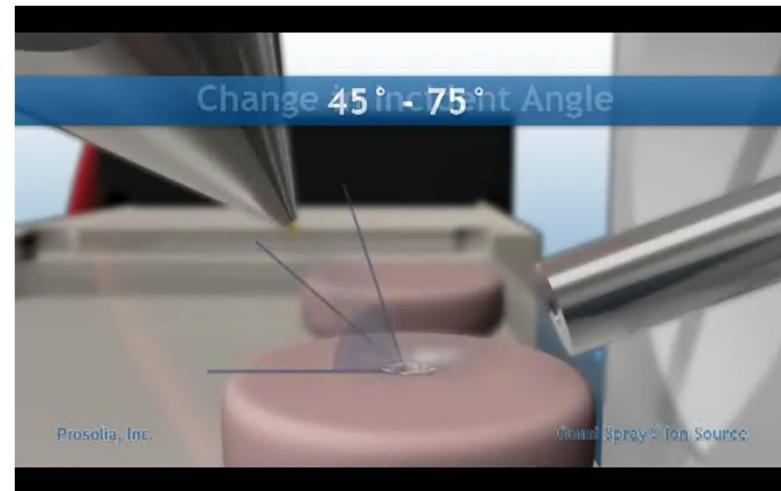
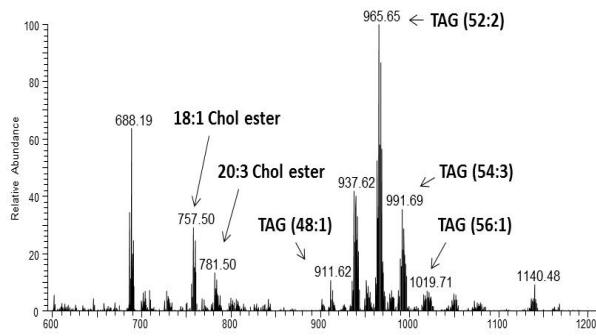


# DESI methodology

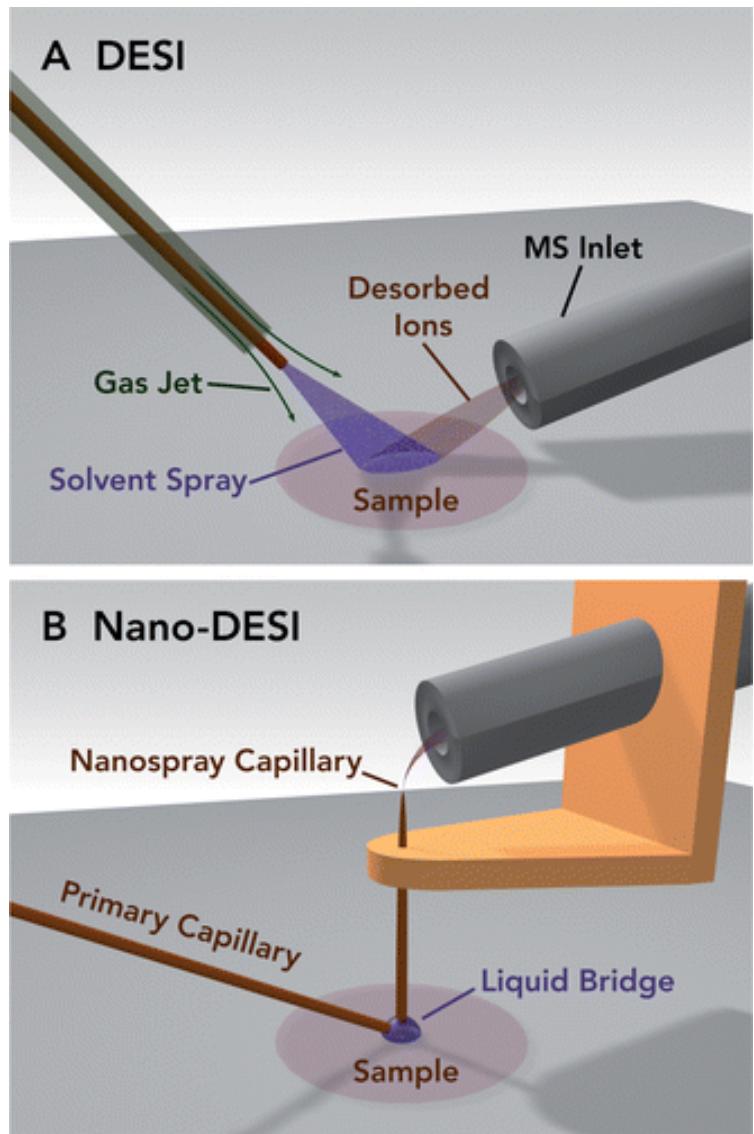
- ❖ Geometry
- ❖ Solvent system
- ❖ Solvent flow rate
- ❖ Gas pressure
- ❖ High voltage
- ❖ Reactive DESI



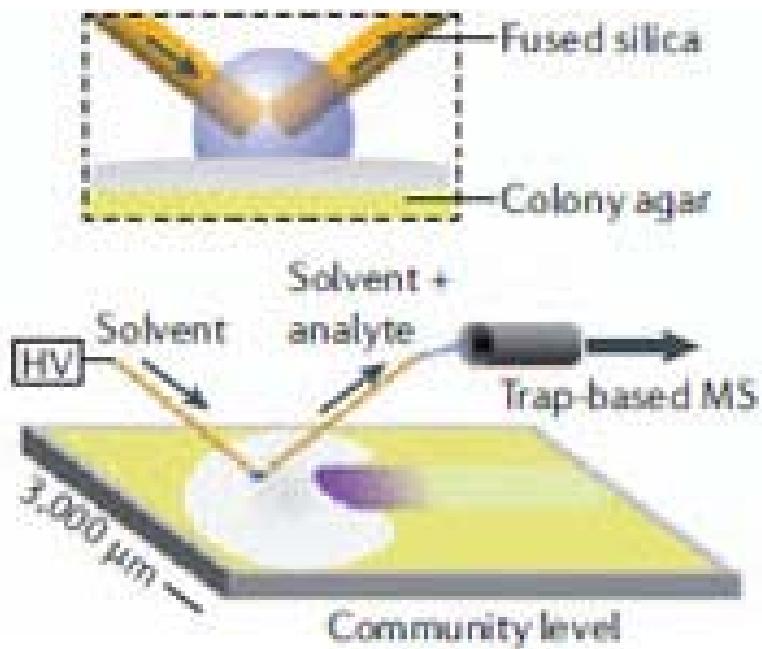
**Double-bond  
derivatization with  
silver cations**



## ❖ Nano-DESI



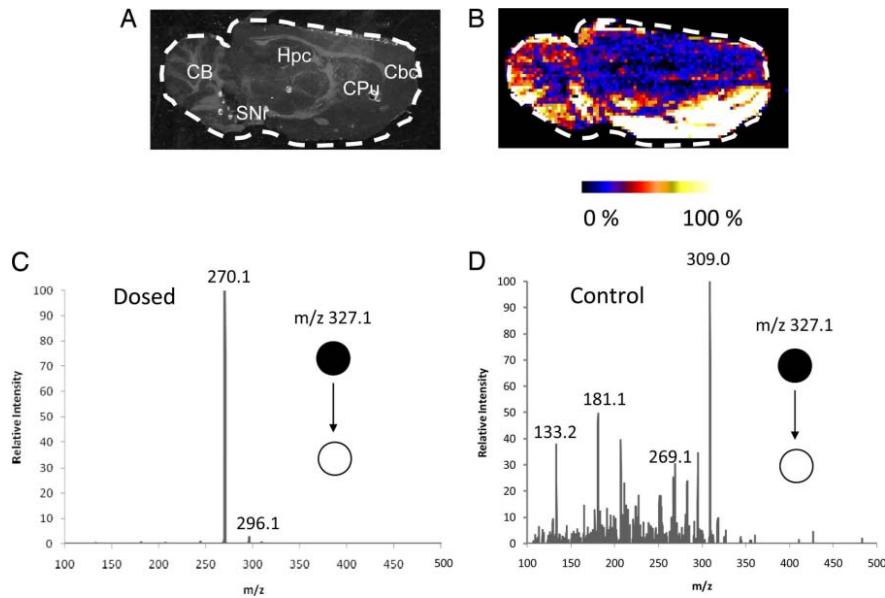
- ❖ Higher spatial resolution
- ❖ Imaging



# DESI-MS applications: surface analysis

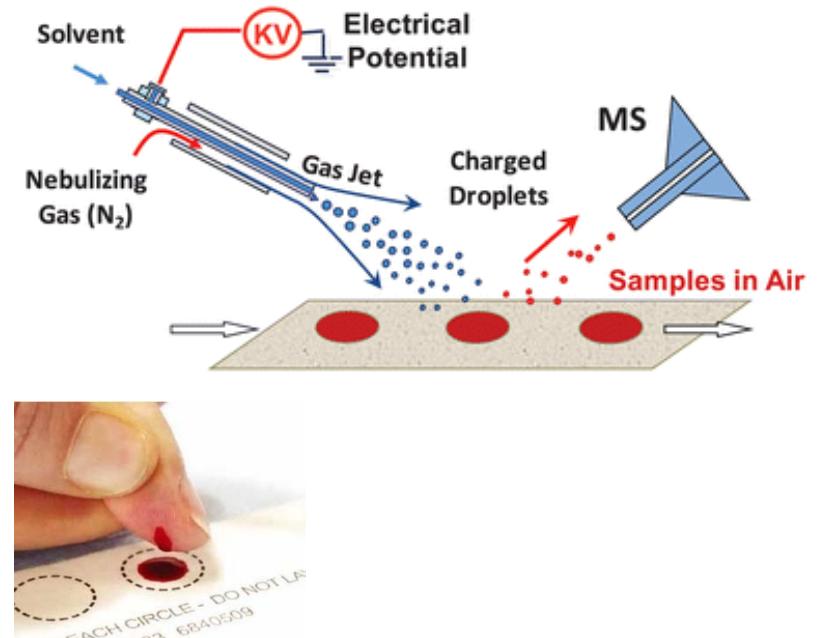
## *Drug mapping and screening*

### *Clozapine tissue distribution*



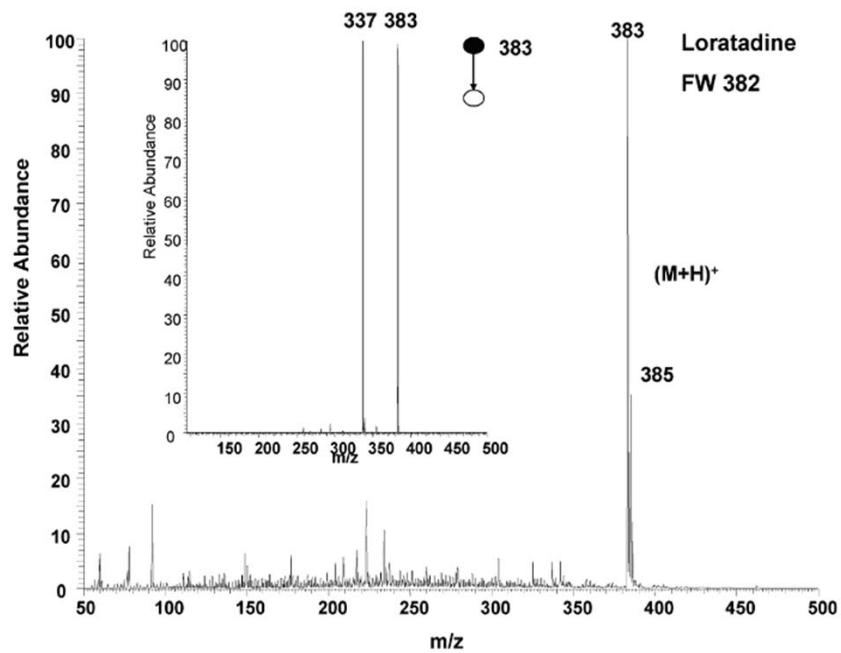
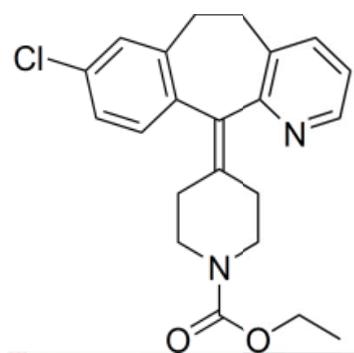
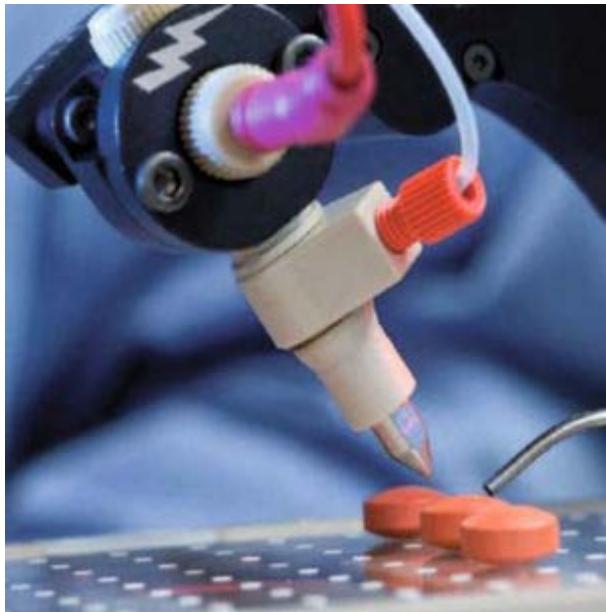
Wiseman JM et al. Proc Natl Acad Sci U S A. (2008)

### *Dried blood spot drug screening*

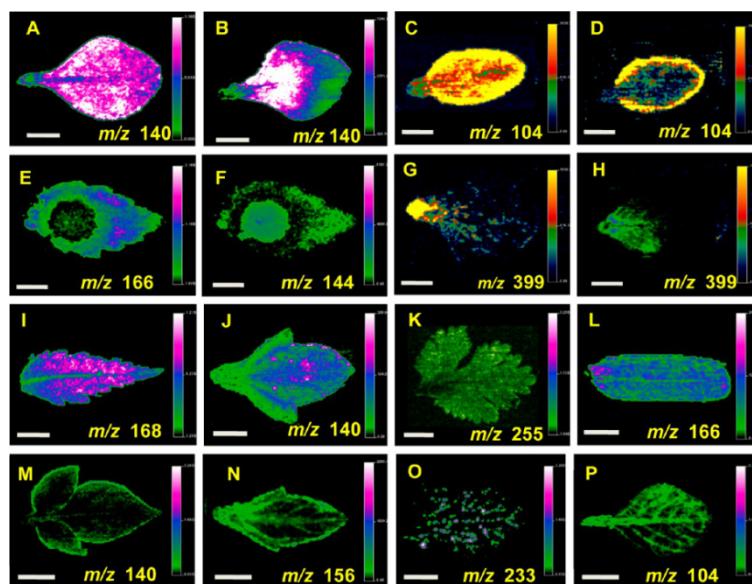
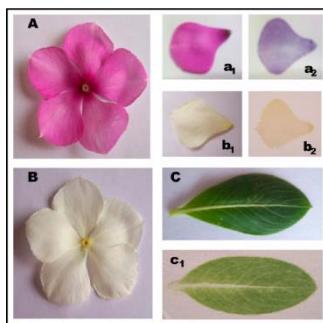


Wiseman et al. Methods Mol Biol. (2014) 1198:291-7.

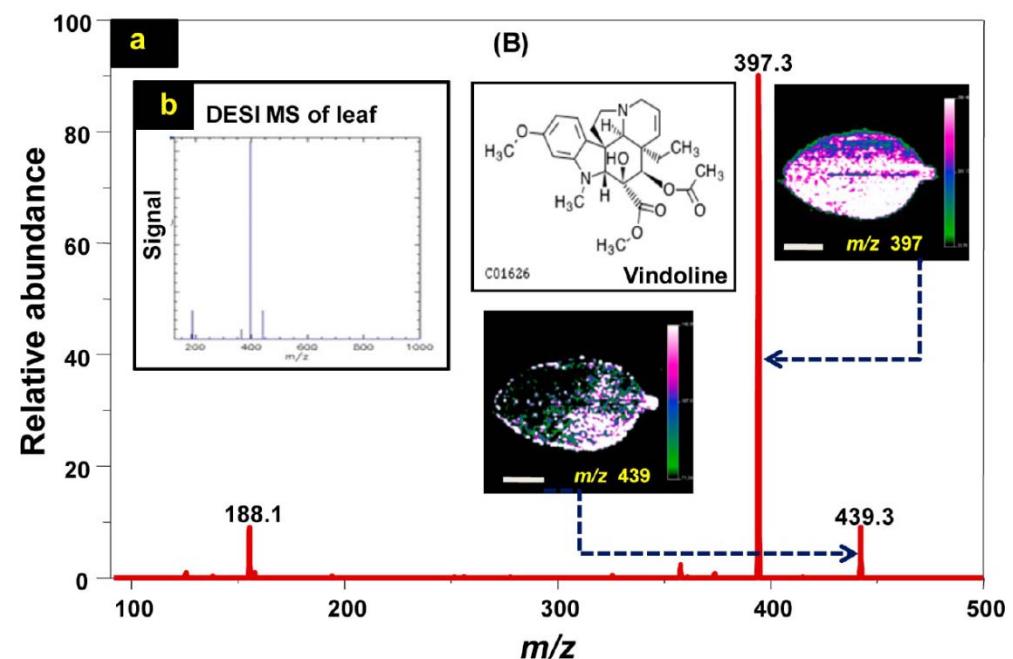
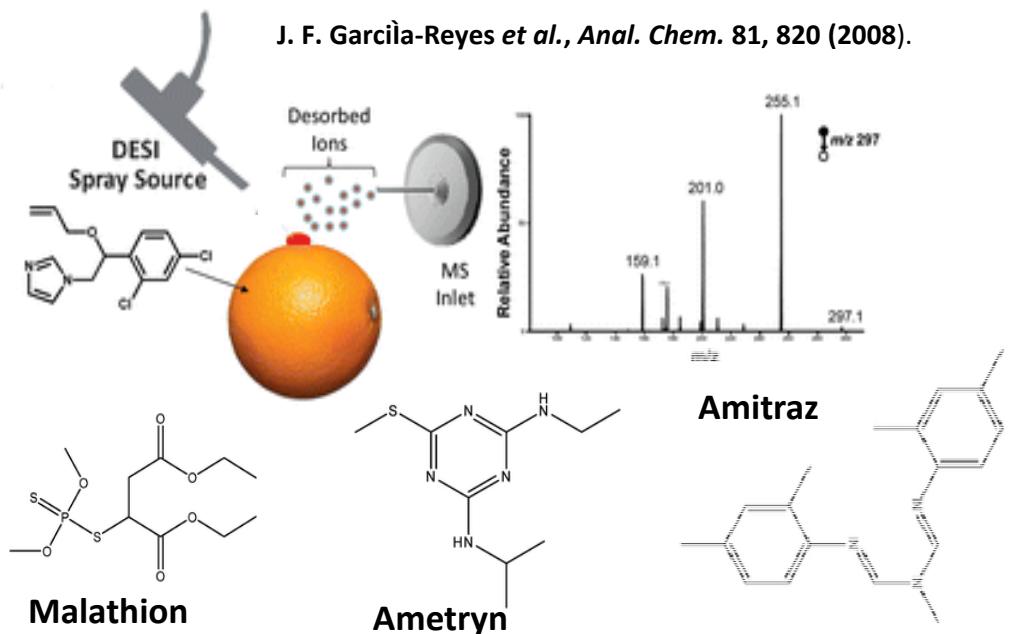
# *Pharmaceutical tablet analysis*



# *Food and leaves analysis*

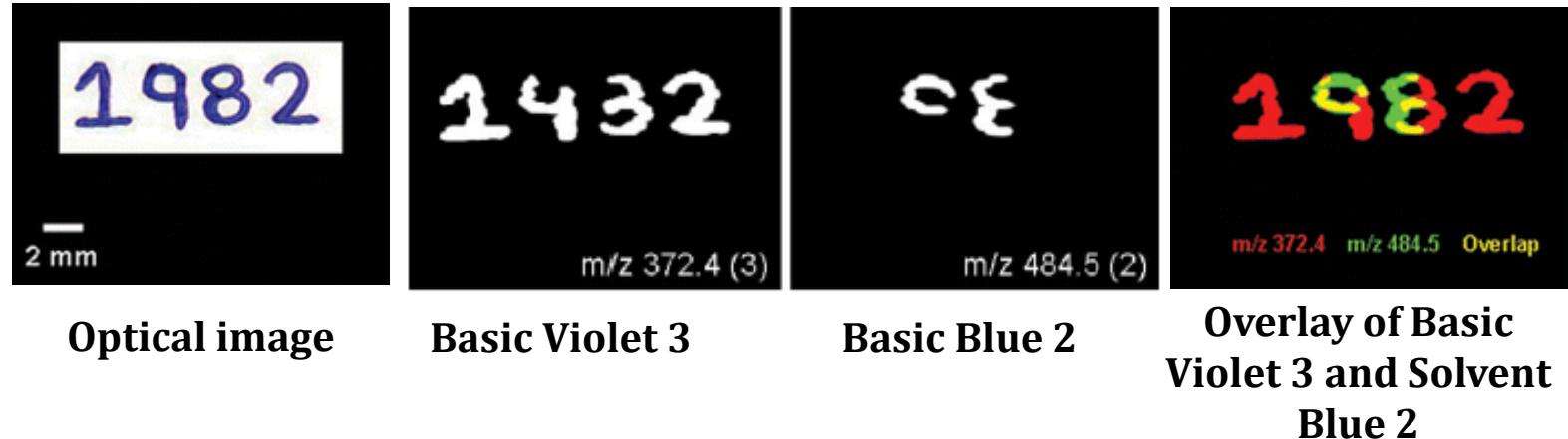


Bjarnholt et al., Nat. Prod. Rep., 2014, 31, 818



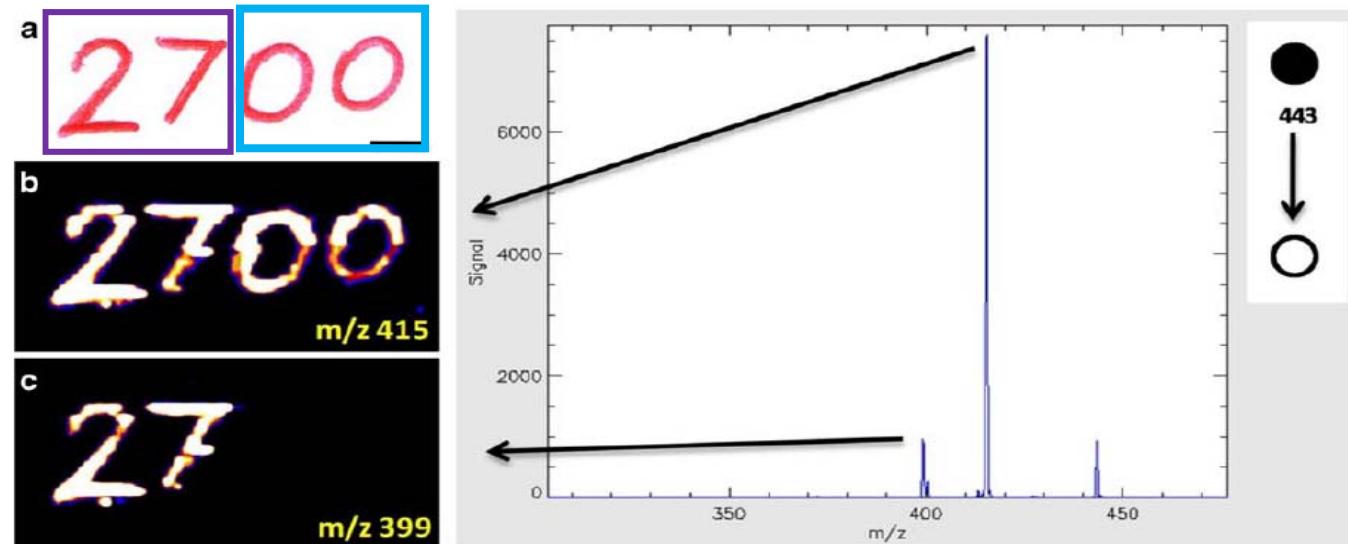
# Ink analysis

DR. Ifa, LM. Gumaelius, LS. Eberlin, NE. Manicke and RG. Cooks, Analyst, 2007, 132, 461



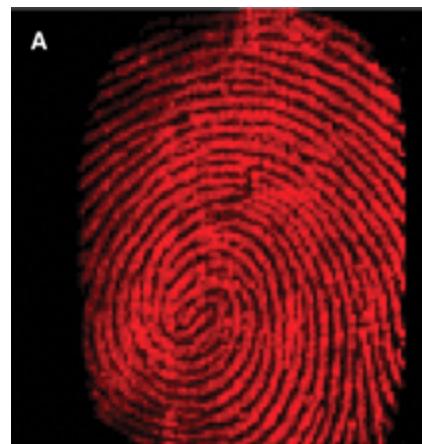
Mixture of rhodamine B  
and rhodamine 6G.

Only rhodamine B



# *Latent fingerprint chemical imaging by mass spectrometry*

*DESI image of  
distribution of cocaine  
on a LFP blotted on glass*



*Ink fingerprint blotted on  
paper and optically  
scanned*



*Computer-  
generated  
fingerprint from  
DESI image*



*Computer-generated  
fingerprint from  
optical image*

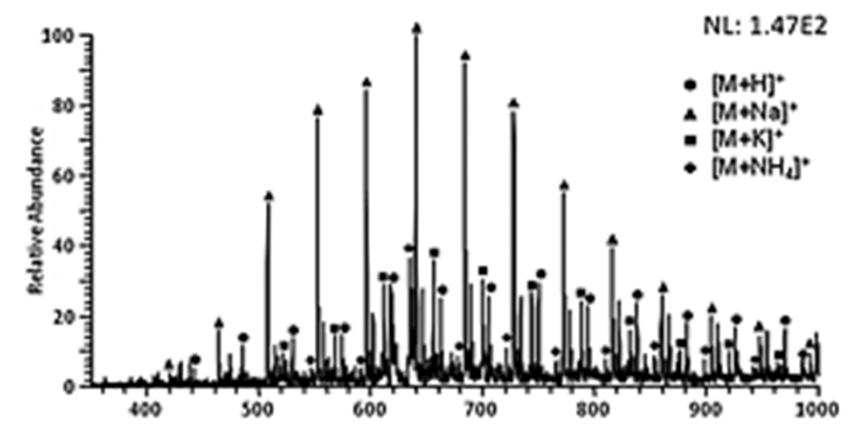
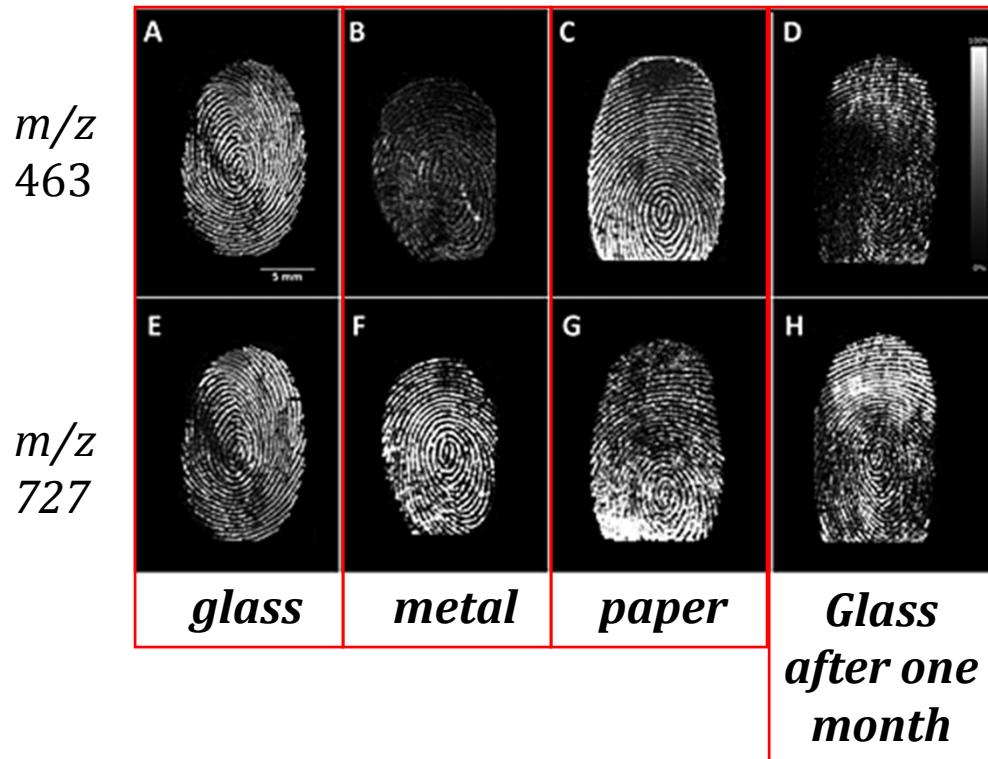


# CSI video on DESI-MS imaging of latent fingerprint



# *Analysis of sexual assault evidence by desorption electrospray ionization mass spectrometry*

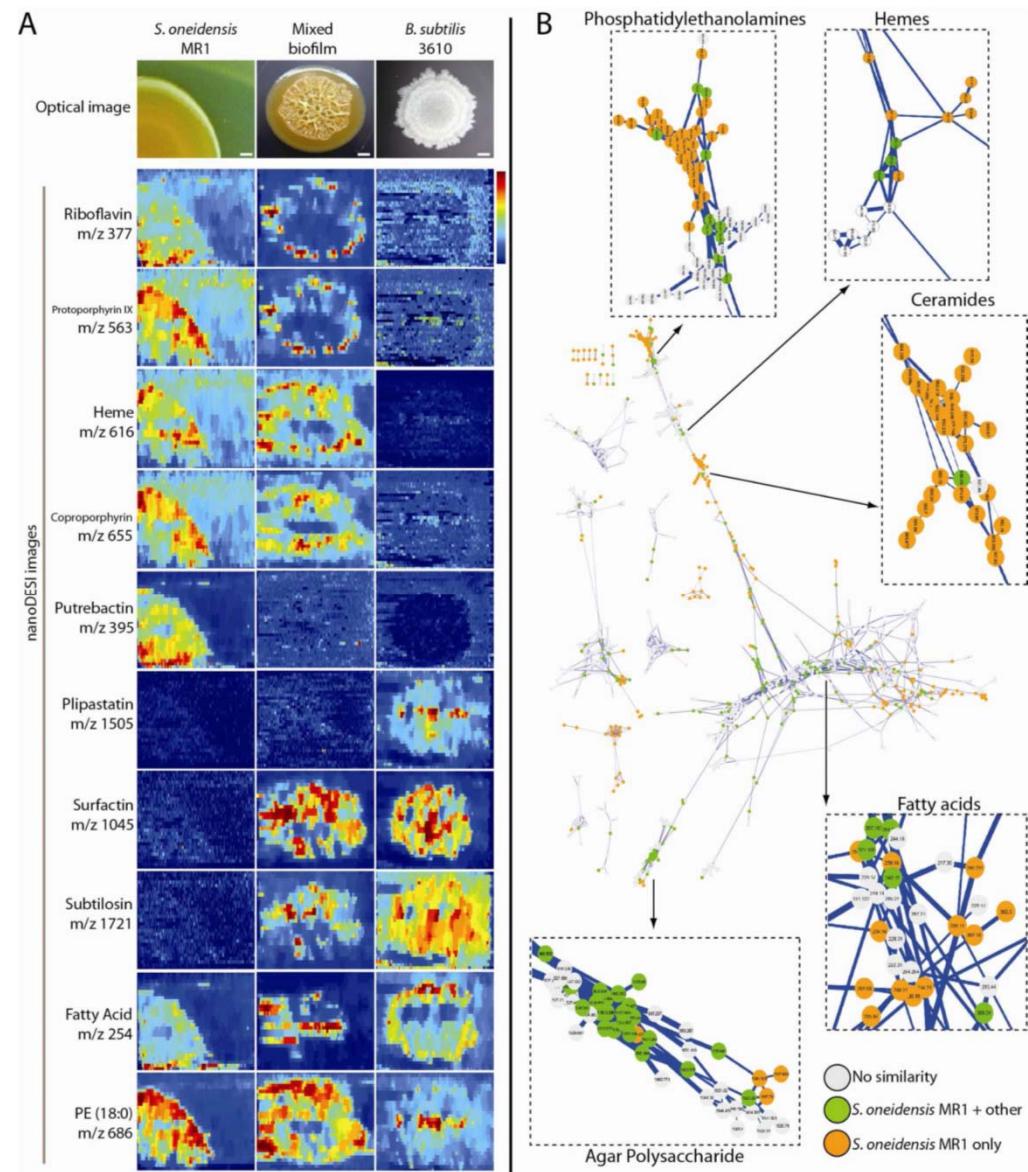
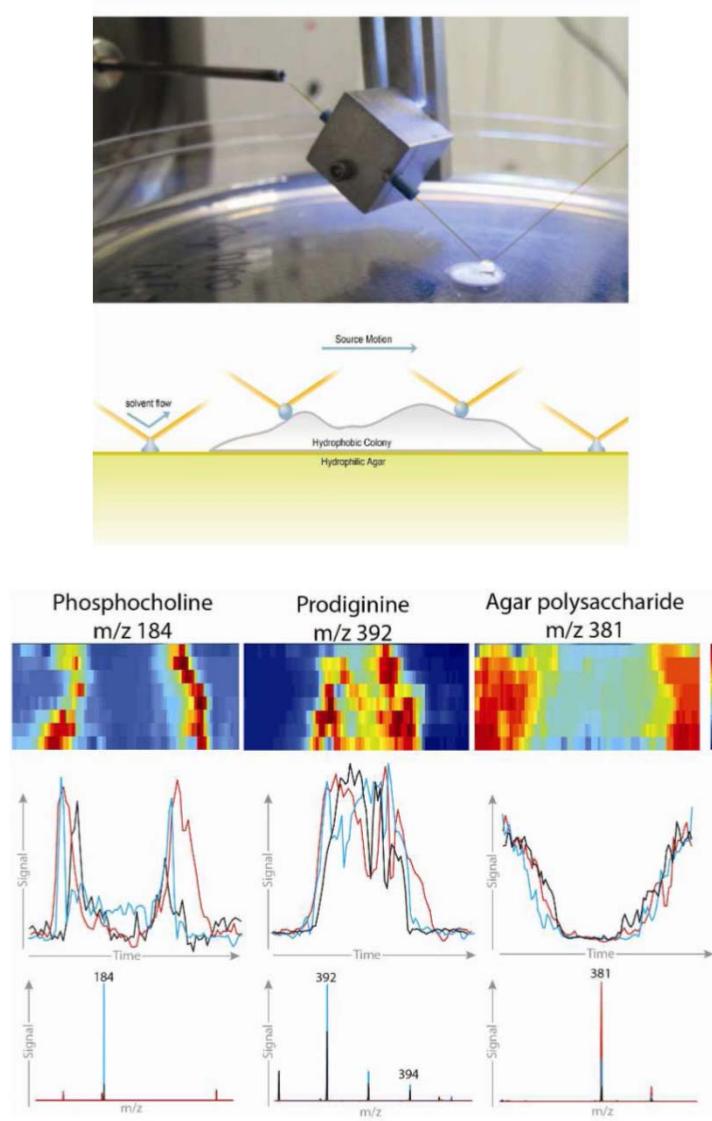
latent fingerprints blotted on different materials after touching a Trojan Enz® condom

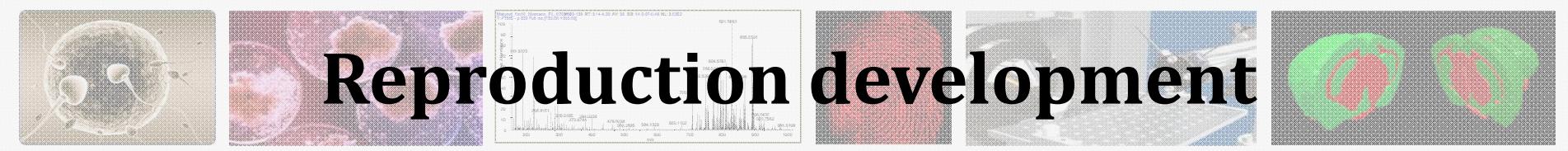


*Polymers: nonoxynol-9; polydimethylsiloxane; polyethylene glycol*

*J Mass Spectrom. 2013 Jul;48(7):774-8.*

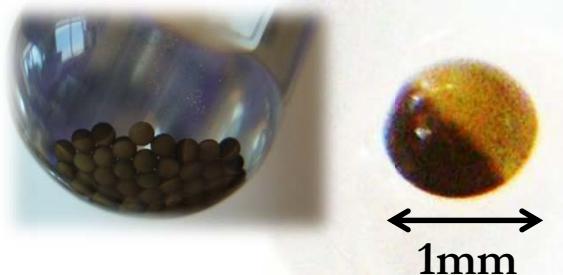
# Metabolic profiling directly from the Petri dish using nanoDESI imaging mass spectrometry





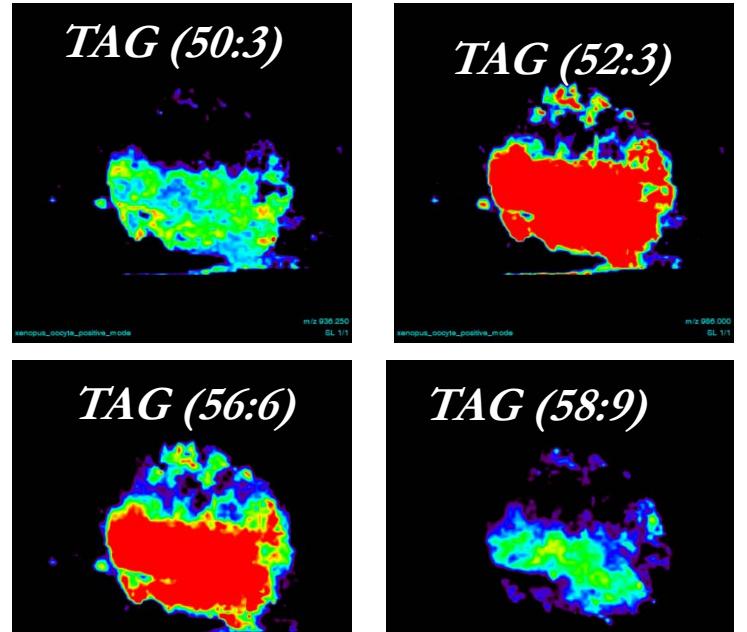
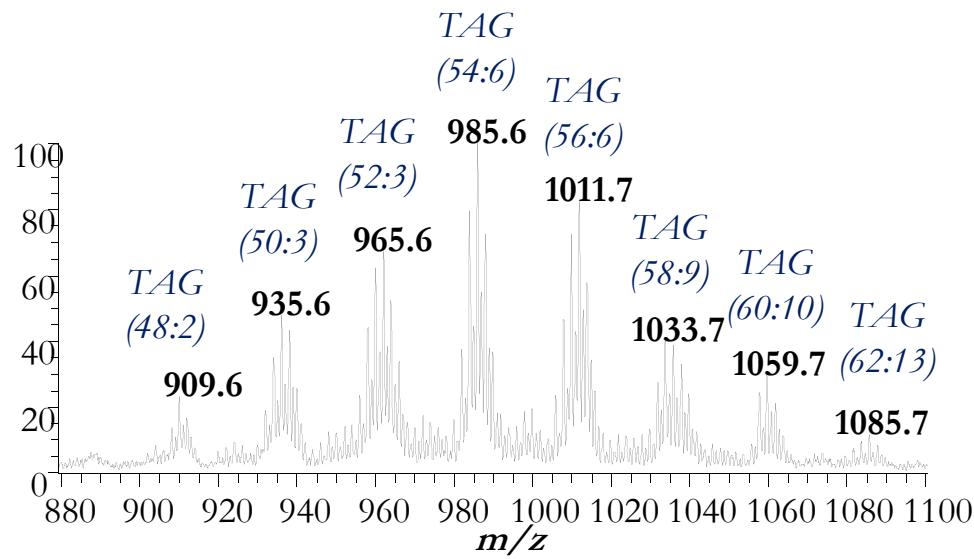
# Reproduction development

❖ African clawed frogs (*Xenopus laevis*) oocytes

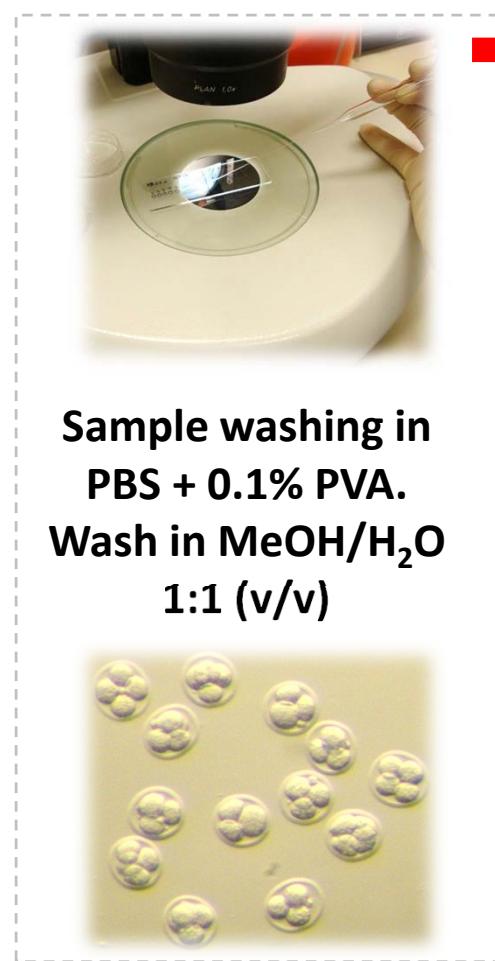
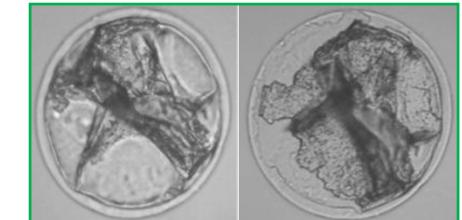
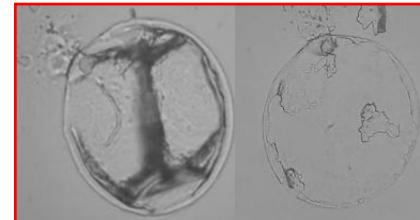


*pale vegetal pole: source of energy during early embryogenesis.*

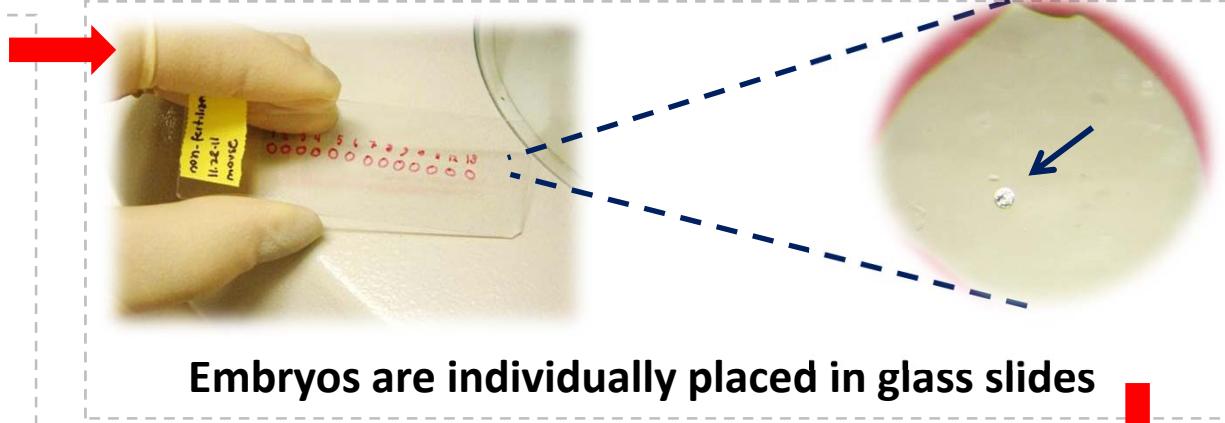
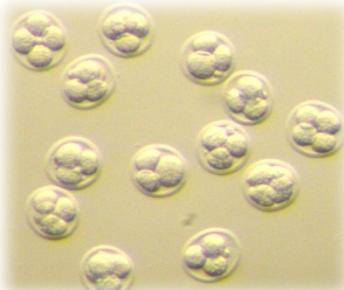
*pigmented animal pole: nucleus and cytoplasmic machinery for protein production*



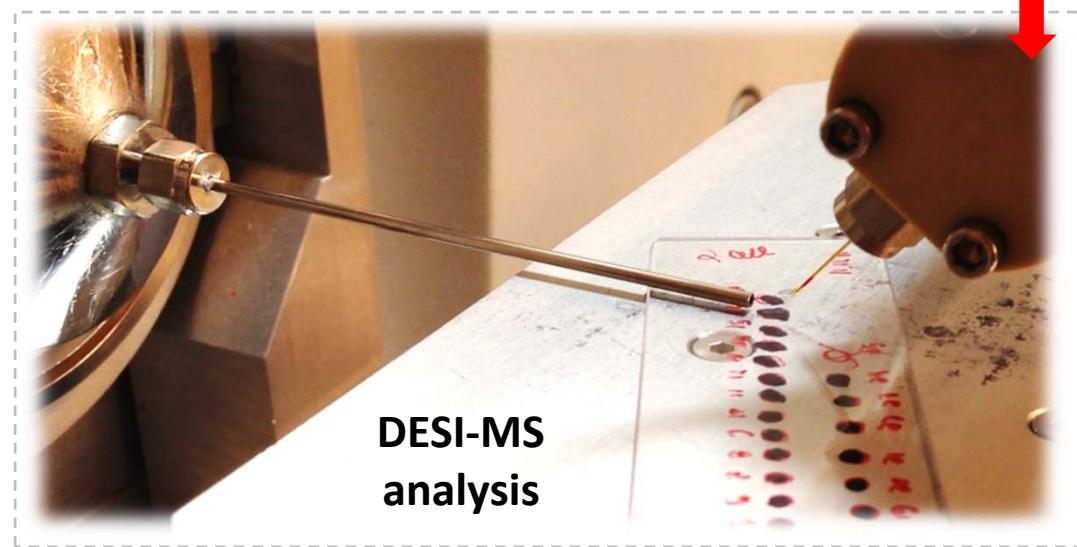
# Individual oocyte and embryo analysis by DESI - Workflow



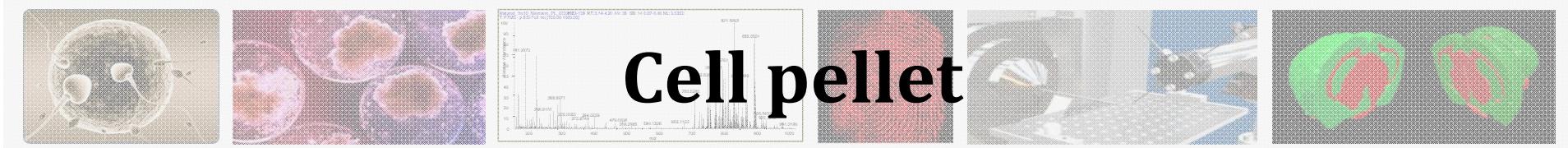
Sample washing in  
PBS + 0.1% PVA.  
Wash in MeOH/H<sub>2</sub>O  
1:1 (v/v)



Embryos are individually placed in glass slides



DESI-MS  
analysis



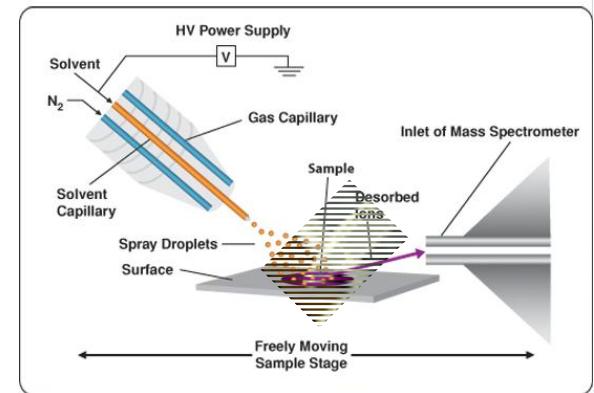
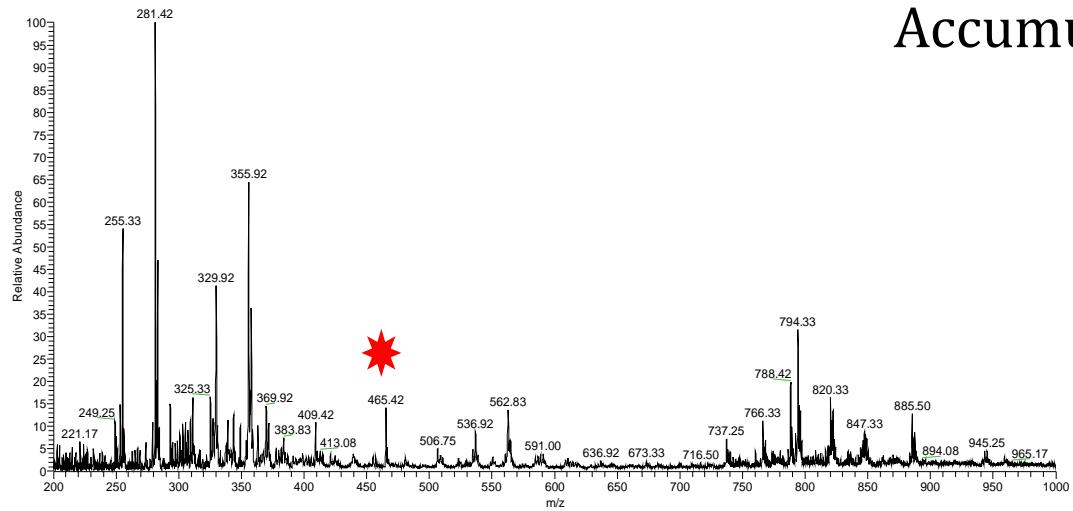
## Inhibition of Cholesterol Sulfotransferase (SULT) 2B1b Results in Impaired Prostate Cancer Cell Growth and Diminished Androgen Receptor Activity

❖ Cholesterol accumulated in prostate lesions

Cancer incidence and progression

❖ Accumulation of Cholesterol sulfotransferase (SULT2B1b) in intraepithelial neoplasia lesions

Accumulation of cholesterol sulphate

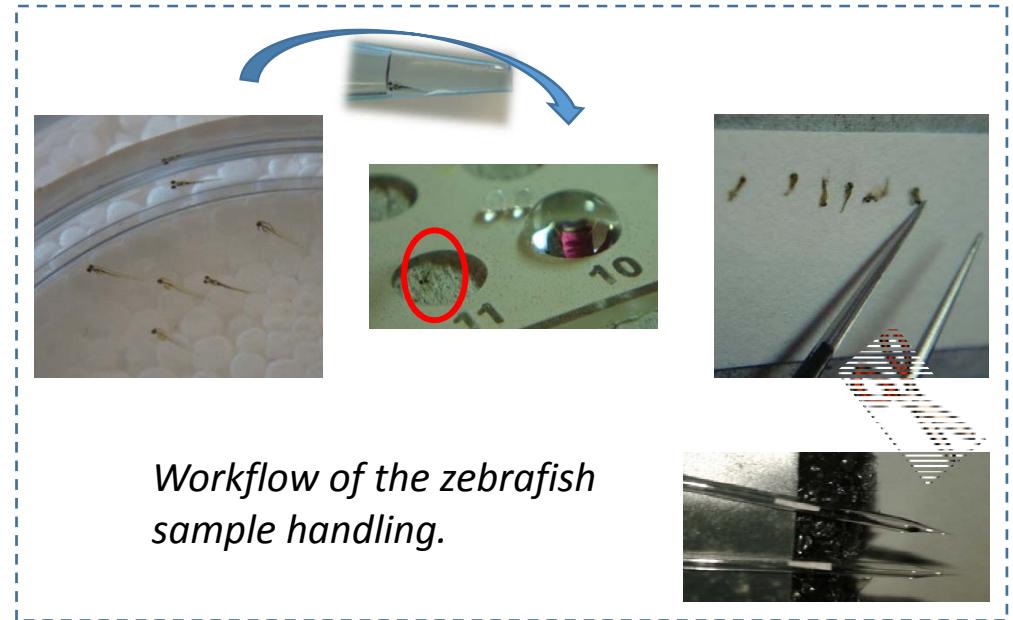


Unpublished data

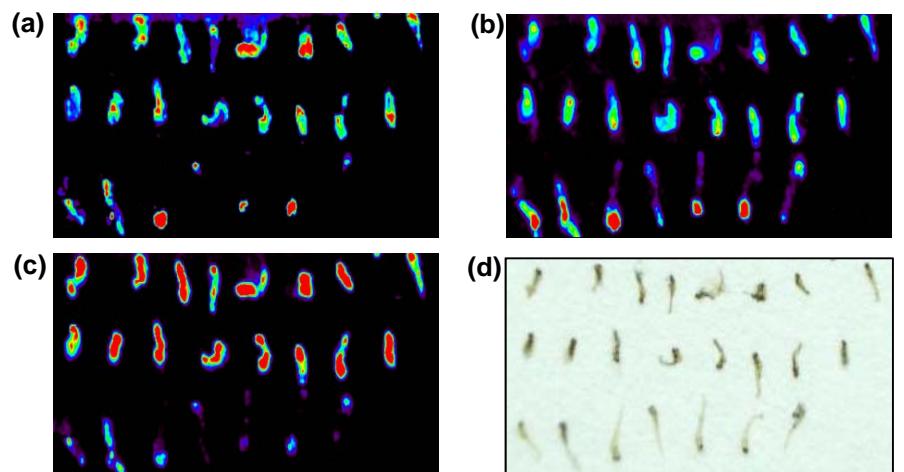
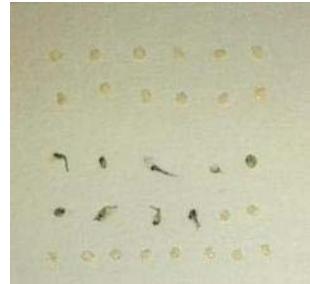
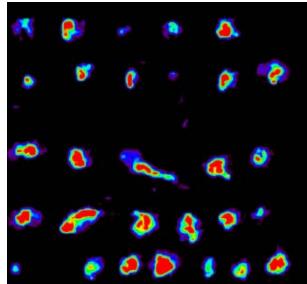
## ❖ Zebrafish. Lipid dynamics during development

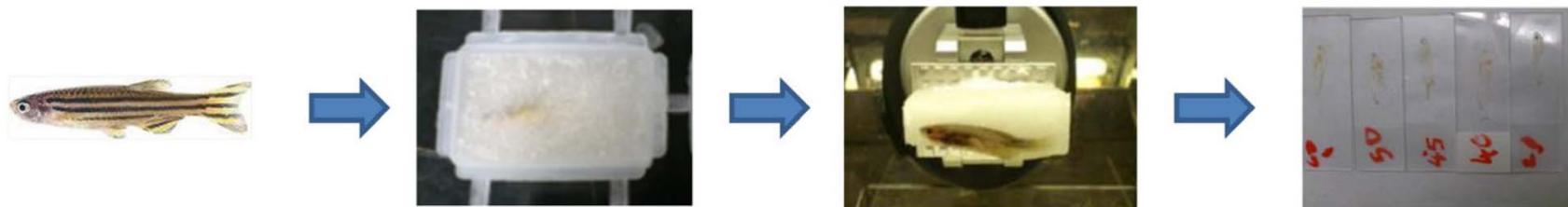
### *DESI-MS & nanoESI analysis*

<b>0 h</b> ( $N = 22$ )	<b>48 h</b> ( $N = 19$ )
<b>24 h</b> ( $N = 22$ )	<b>72 h</b> ( $N = 16$ )
	<b>96 h</b> ( $N = 13$ )



### *negative ion mode*



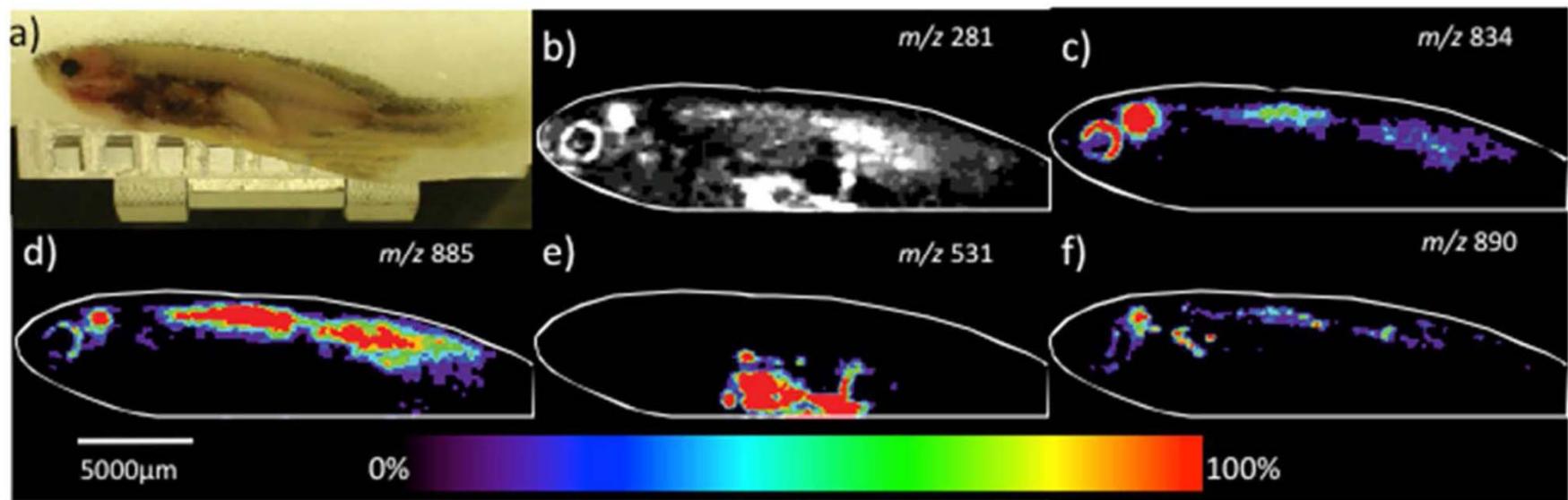


**Whole Zebra fish**

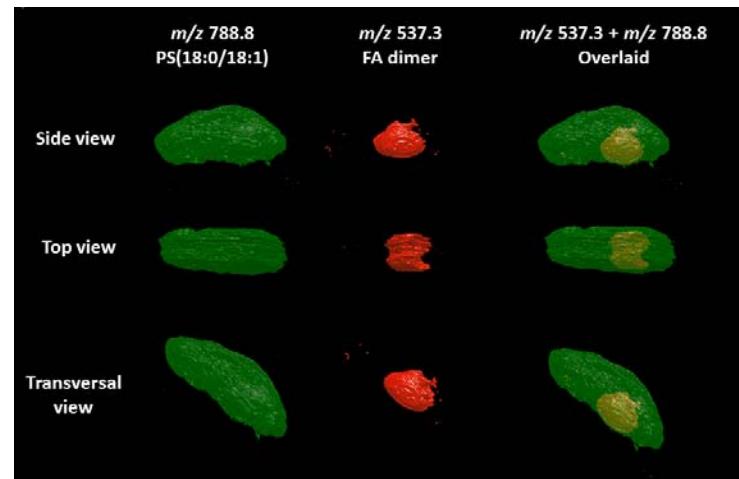
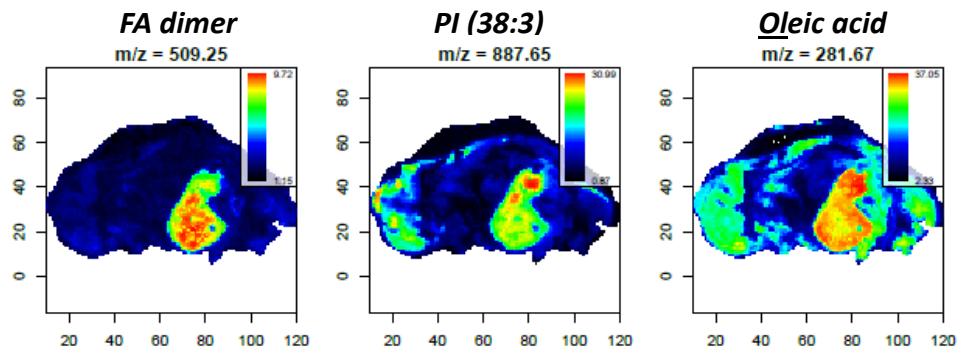
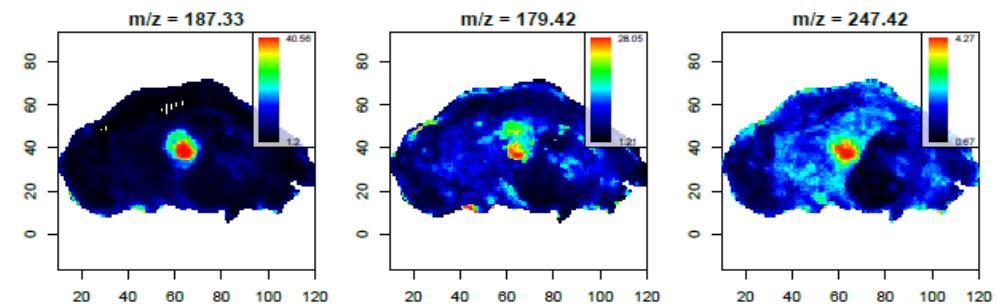
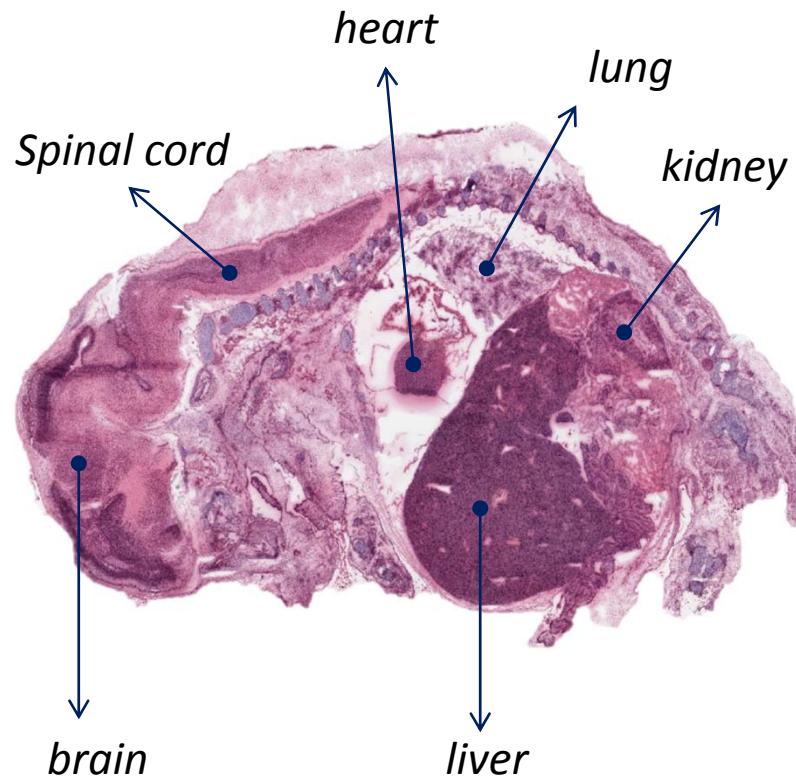
**Frozen moulds of carboxymethyl cellulose**

**Mount mould onto cryomicrotome**

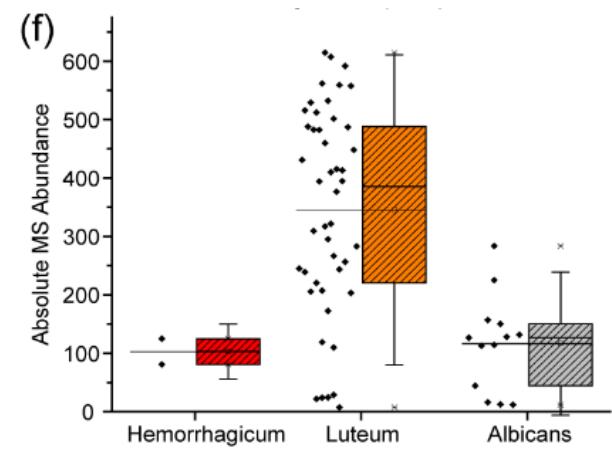
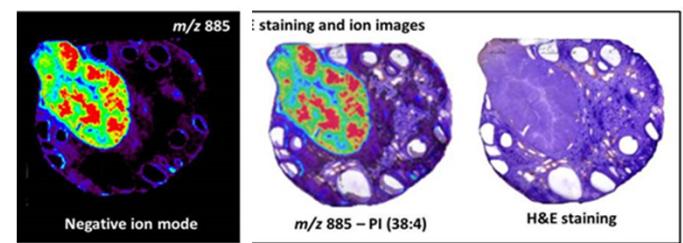
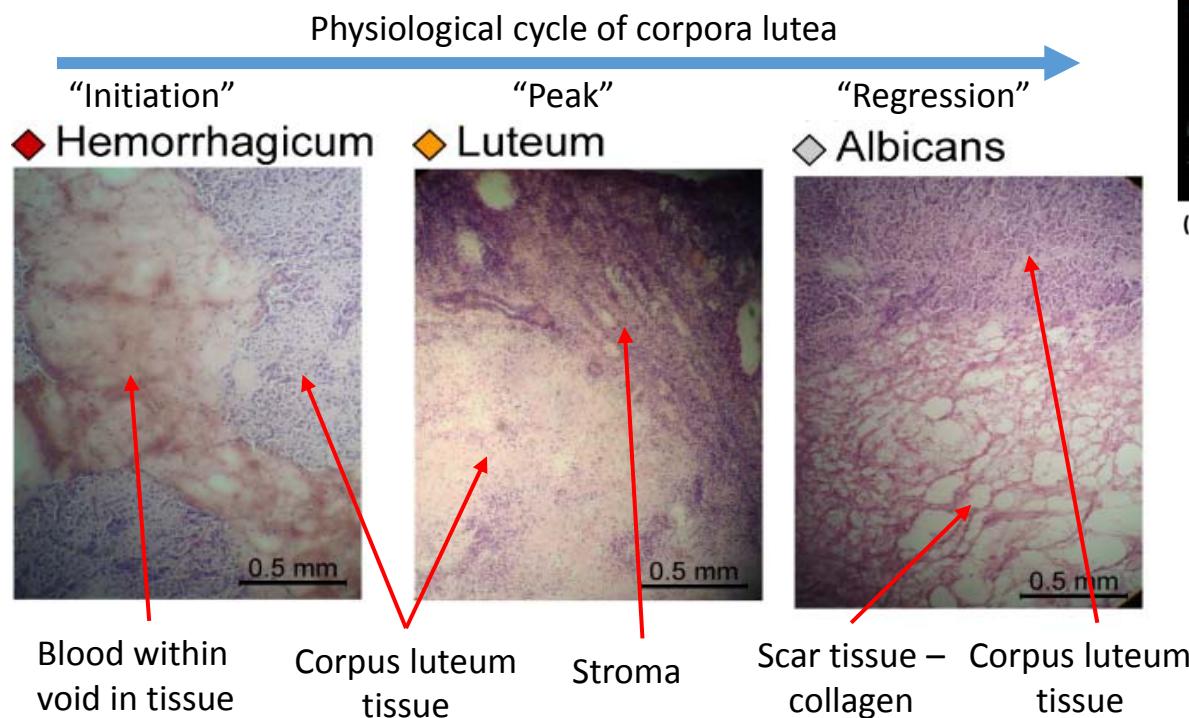
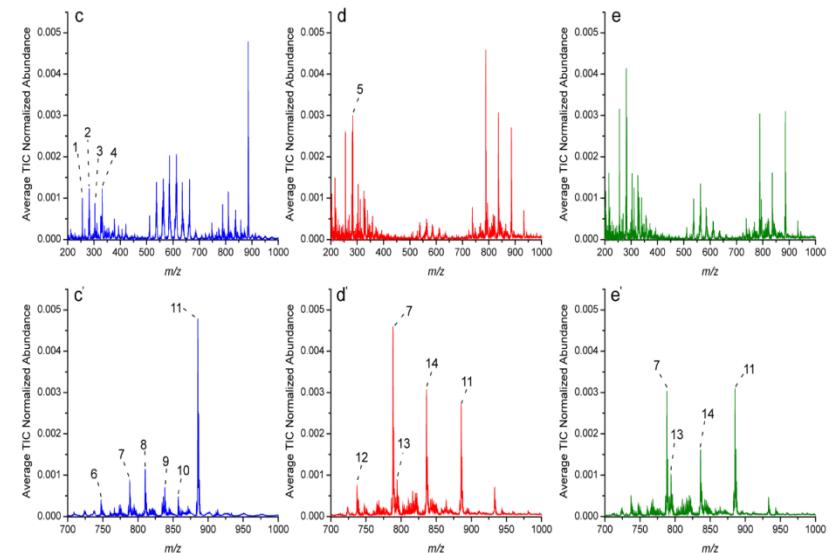
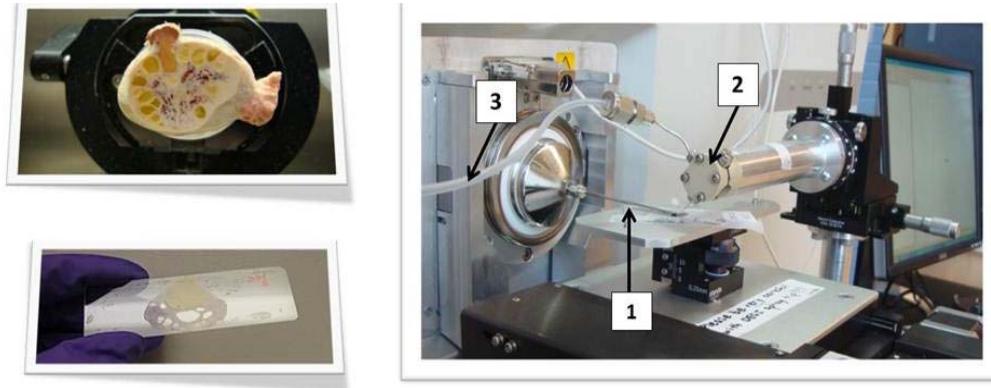
**Zebra fish tissue slices**



❖ Pig fetus, 35 days of gestation. Organogenesis

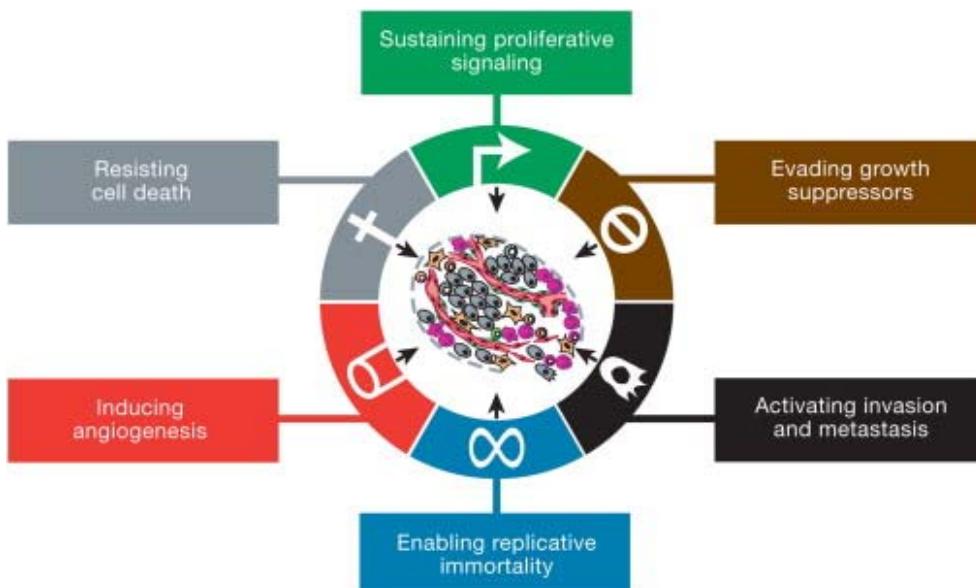
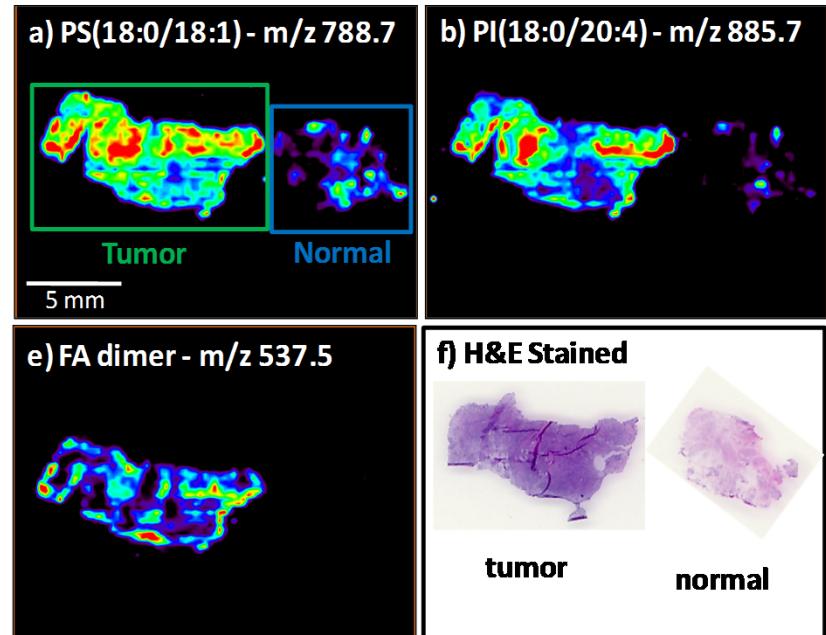
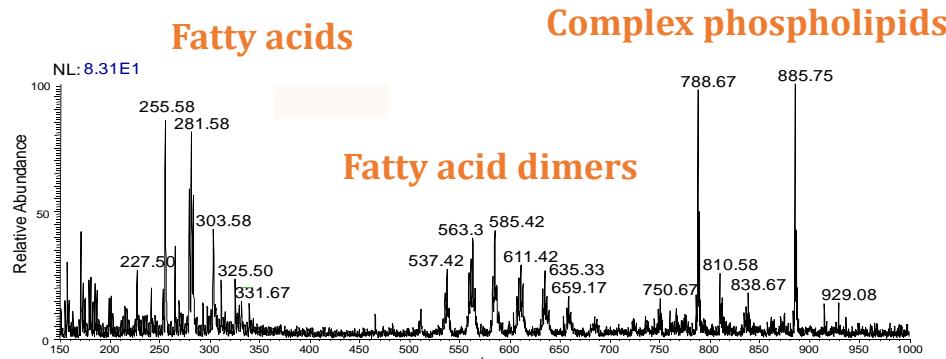


## ❖ Ovarian cycle lipid dynamics



Data in publication

# Cancer diagnostics



*Cell.* 2011 Mar 4;144(5):646-74.  
*Hallmarks of cancer: the next generation.*  
*Hanahan D, Weinberg RA.*

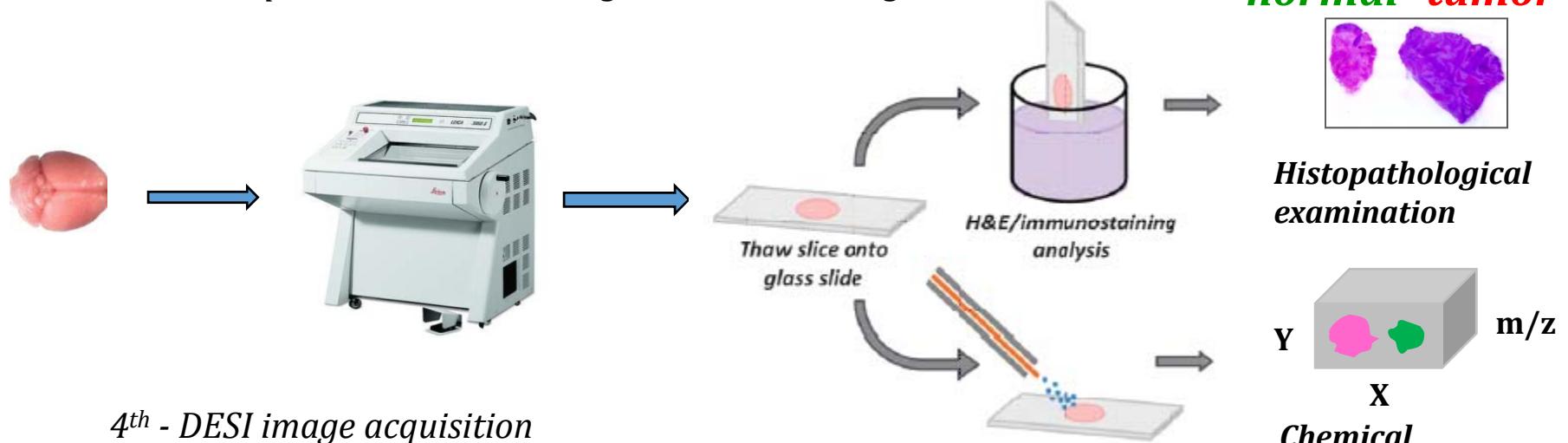


*1<sup>st</sup> - Tissue sample*

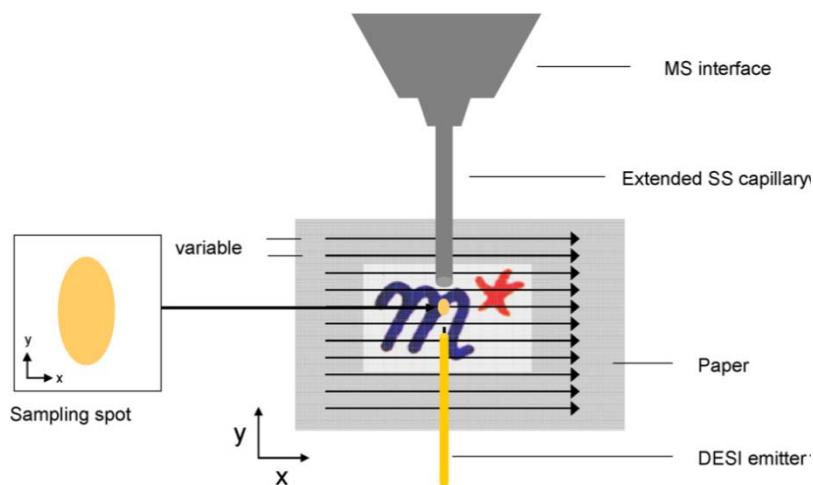
*2<sup>nd</sup> - Sectioning*

*3<sup>rd</sup> - Staining*

**normal tumor**

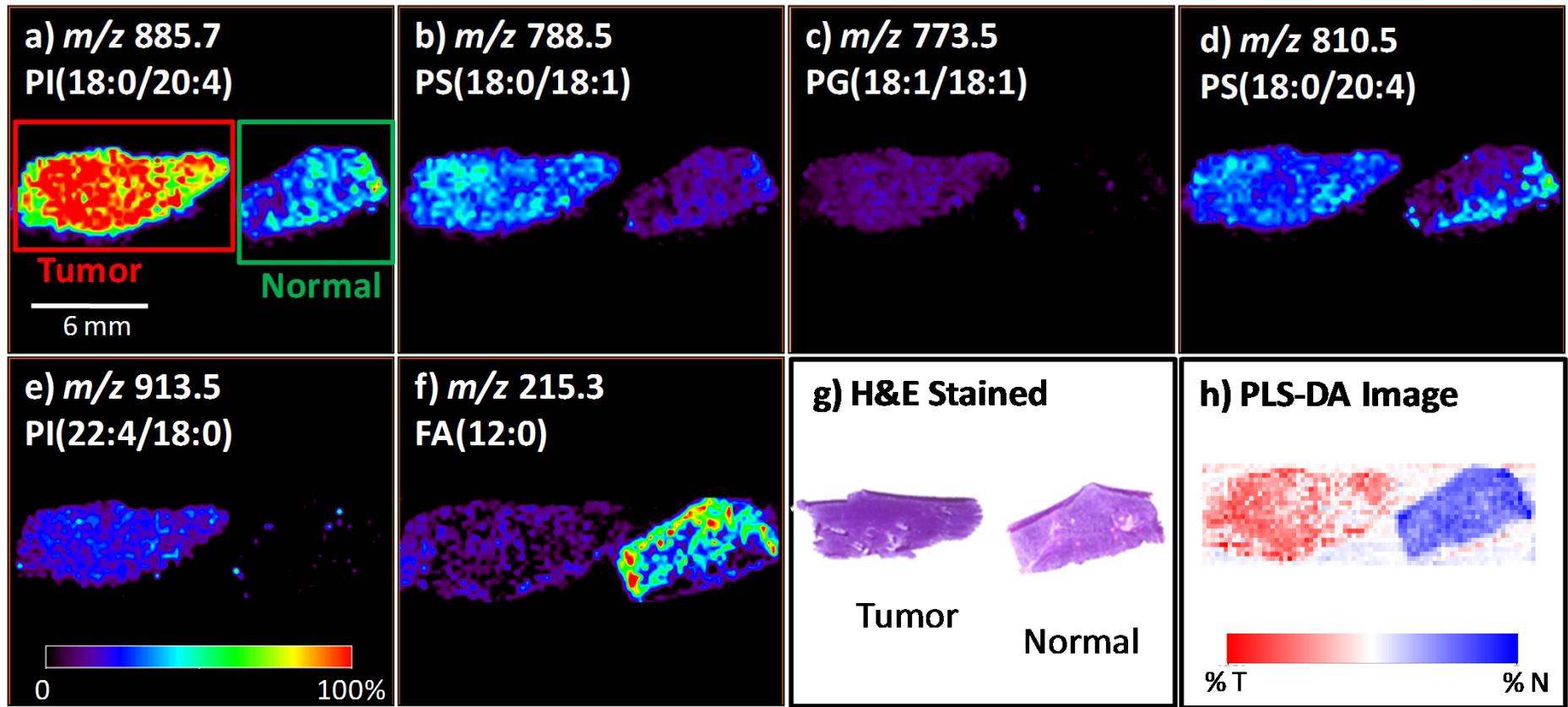
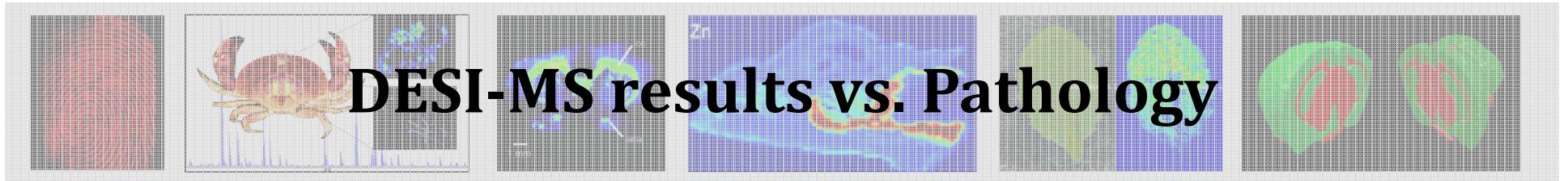


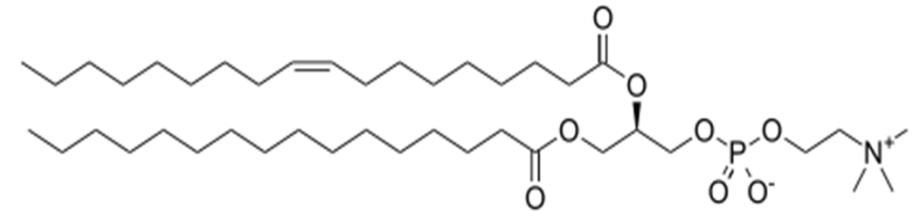
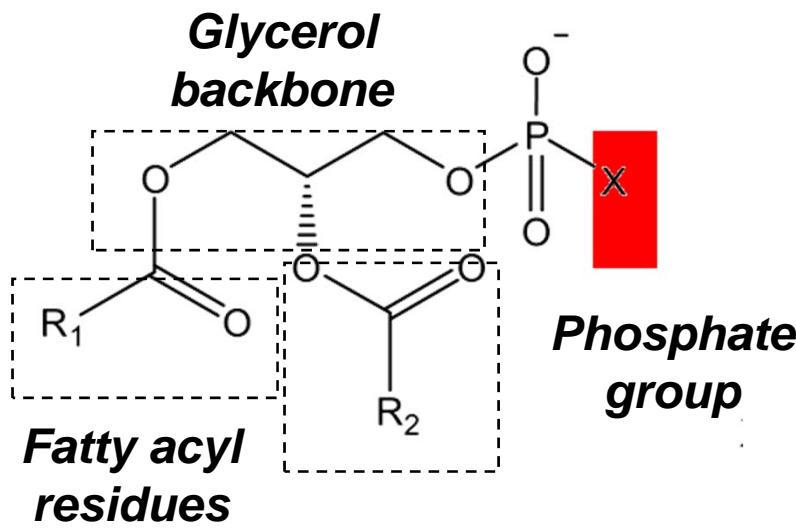
*4<sup>th</sup> - DESI image acquisition*



- sample measurement
- DESI spot size ~250  $\mu\text{m}$  » Pixel dimension
- Y : number of rows (steps of the motion system)
- X dimension : sampling rate of MS \* surface velocity
- MS: negative ion mode, mass range  $m/z$  150-1000
- DESI spray solvent acetonitrile: water (50:50 v/v)

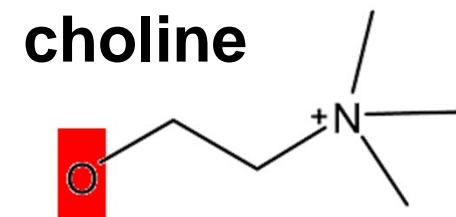
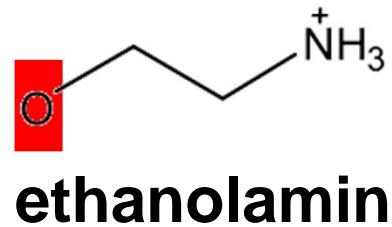
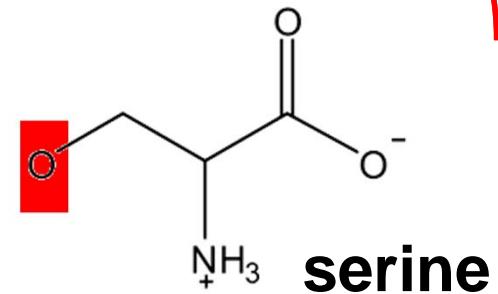
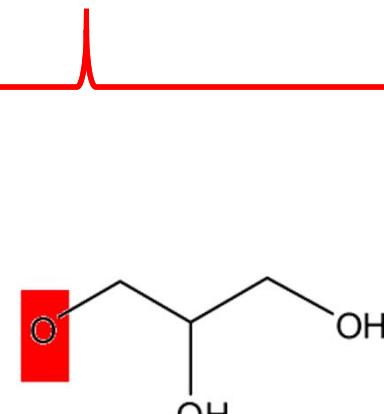
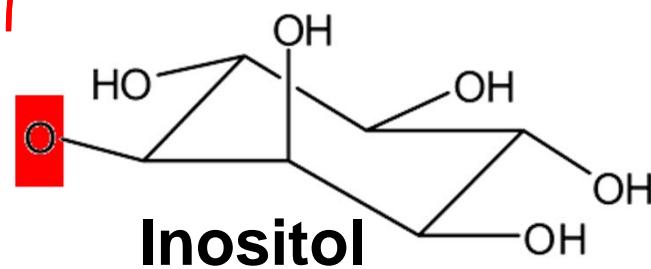




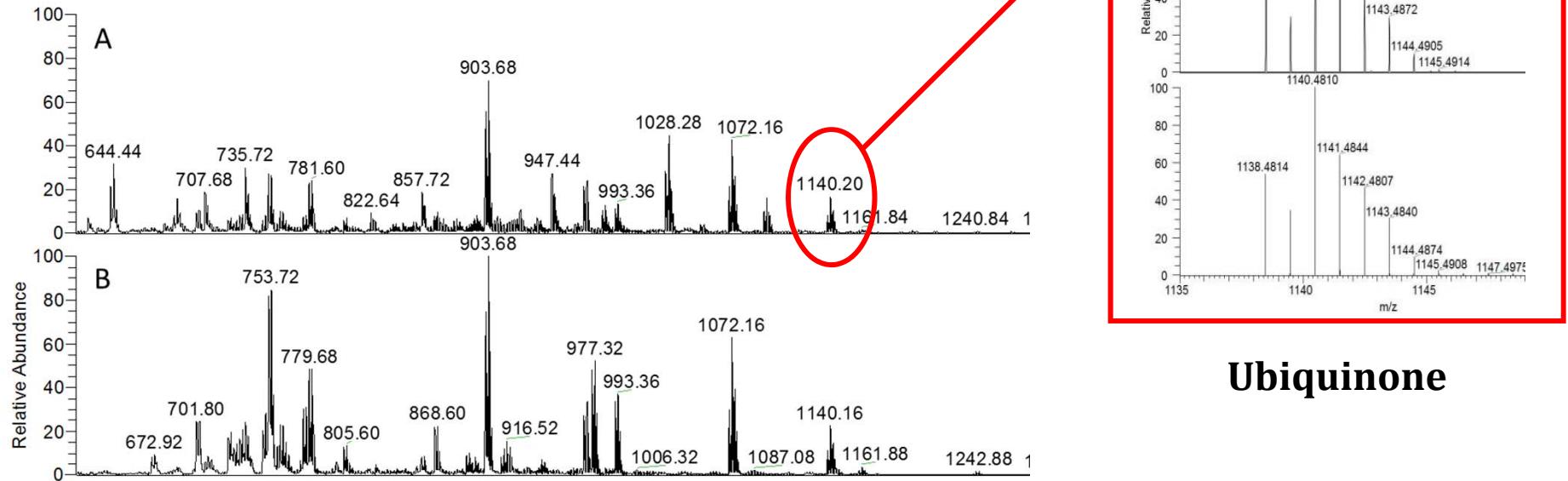


**Phosphatidylcholine: PC (16:0/18:1)**

## Glycerophospholipids



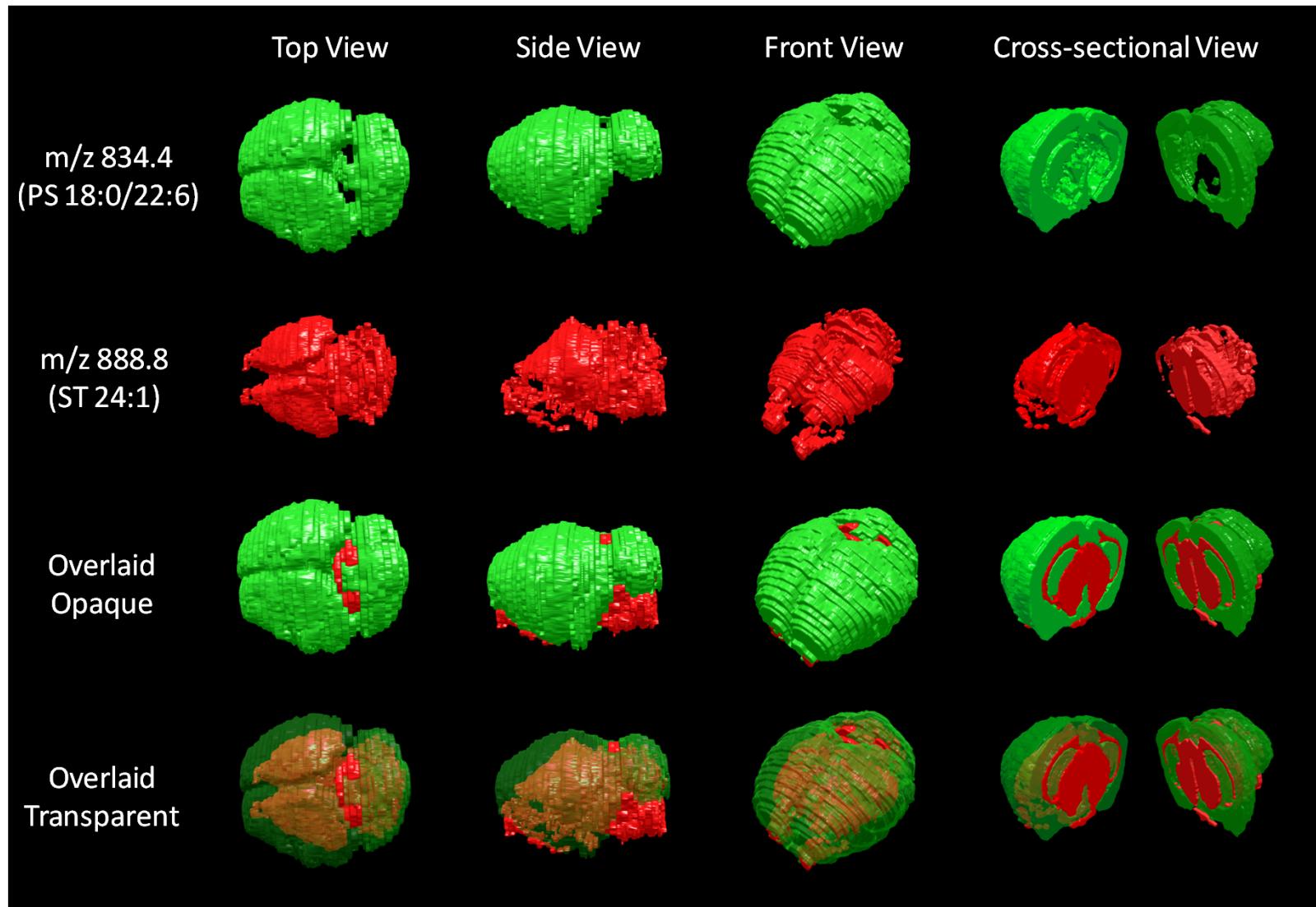
## *Metal cationization, Ag<sup>+</sup>*



**Ubiquinone**

Metal cationization is beneficial for ambient MS while avoiding extraction, clean-up, desalting process prior to MS analysis. Metal cationization (i) increases desorption and ionization efficiency, (ii) minimizes ion suppression, and (iii) adds chemical specificity leading to structural identification

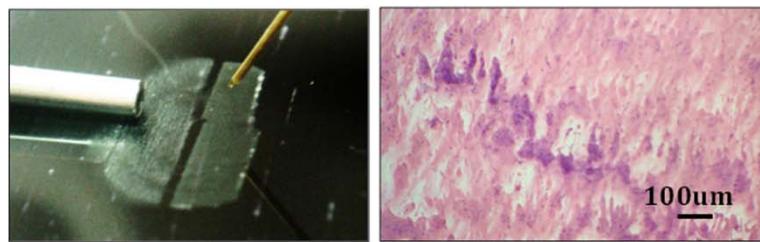
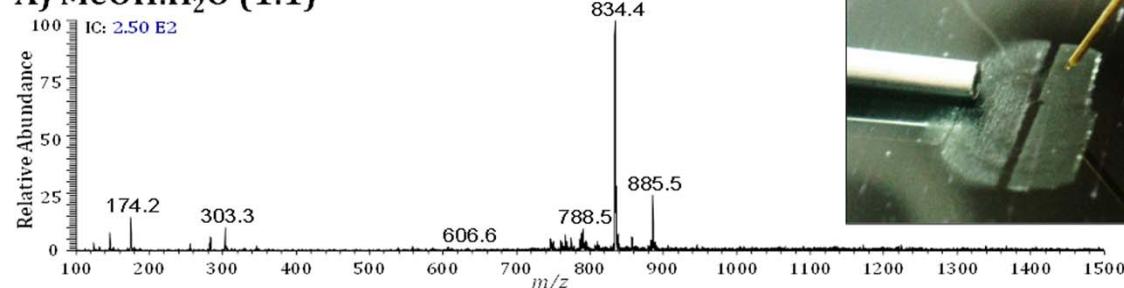
# 3D DESI-MS



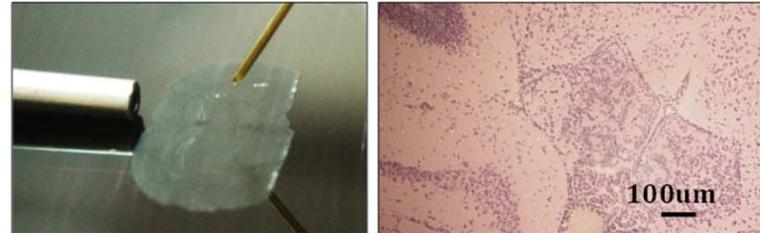
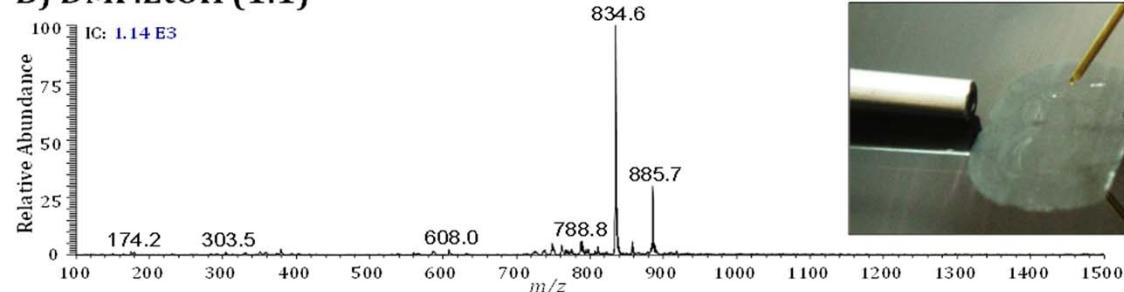


## *“Morphologically friendly” solvent system*

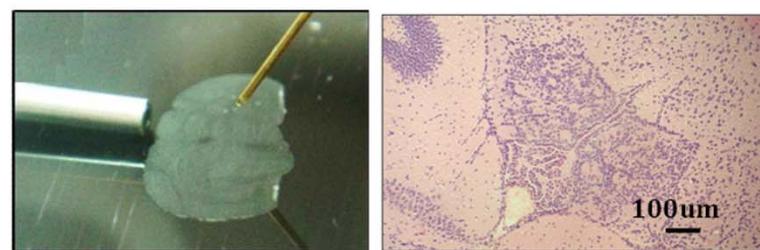
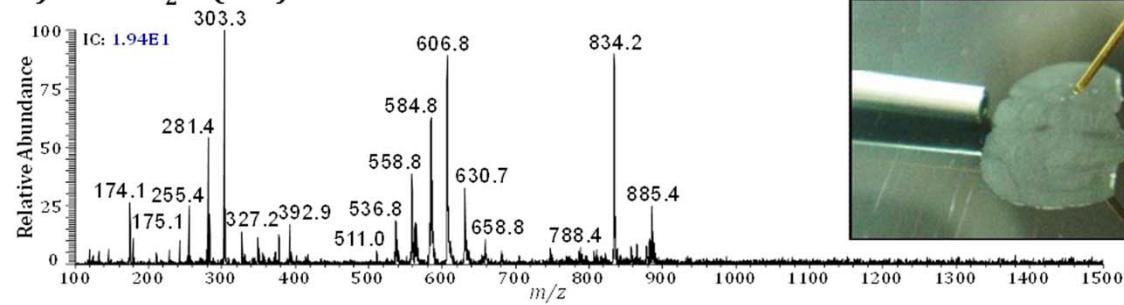
### A) MeOH:H<sub>2</sub>O (1:1)

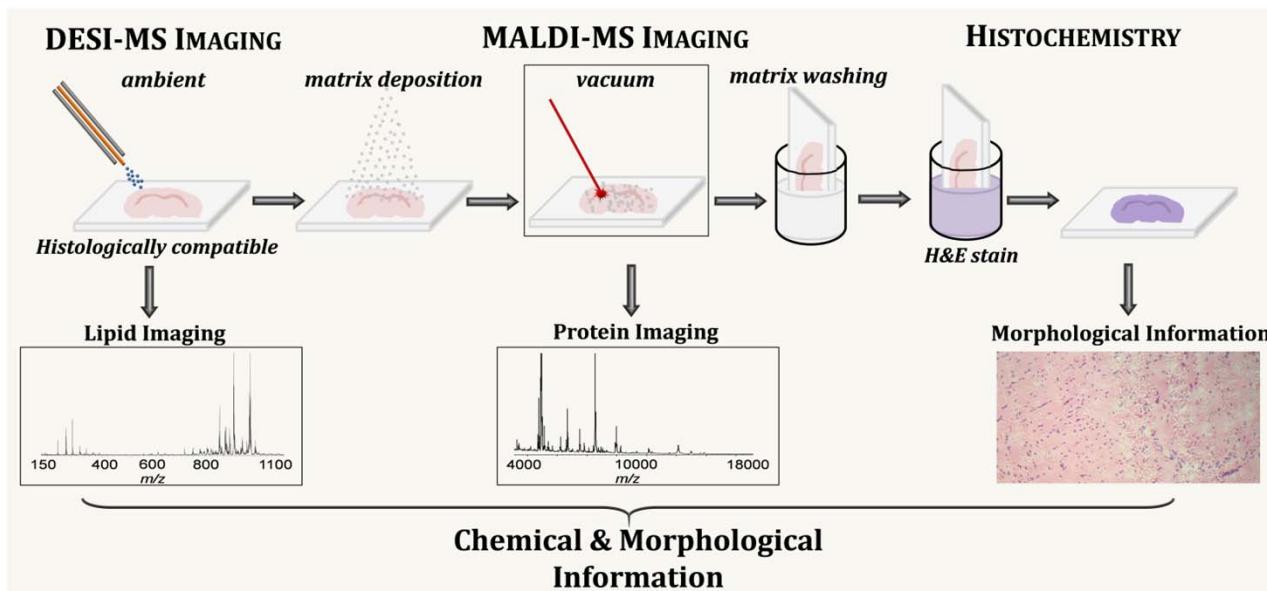


### B) DMF:EtOH (1:1)



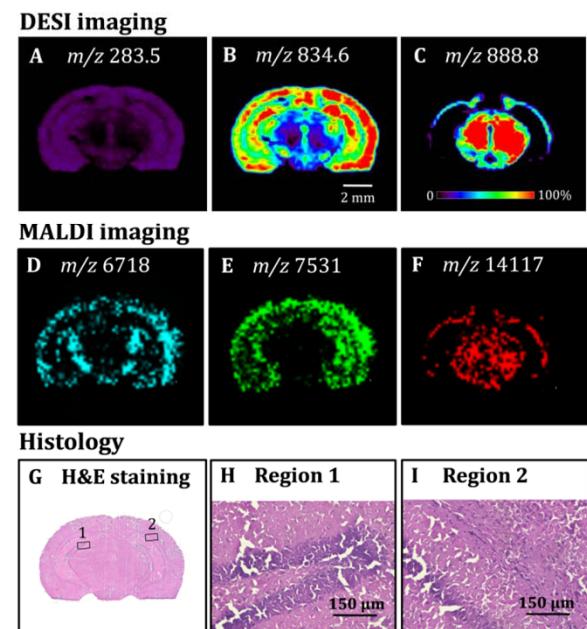
### C) DMF:H<sub>2</sub>O (1:1)





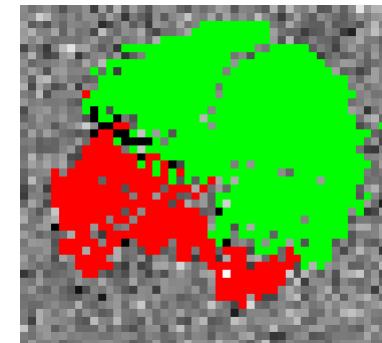
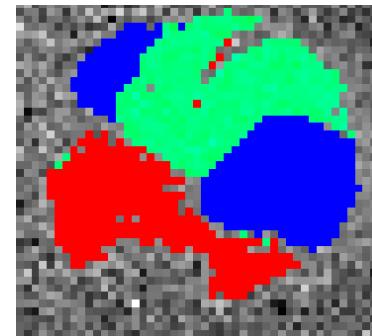
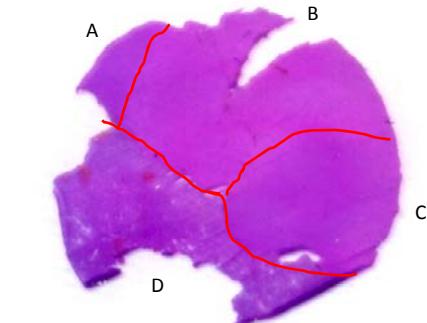
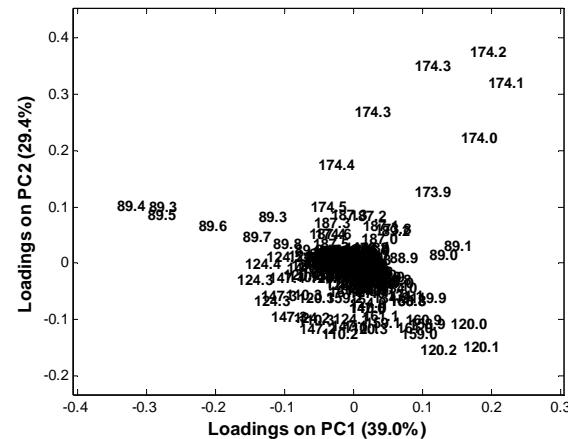
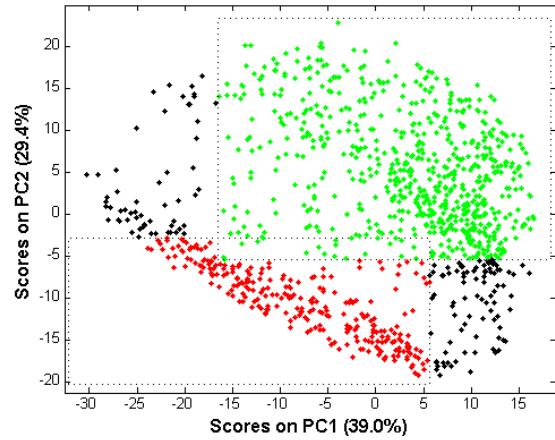
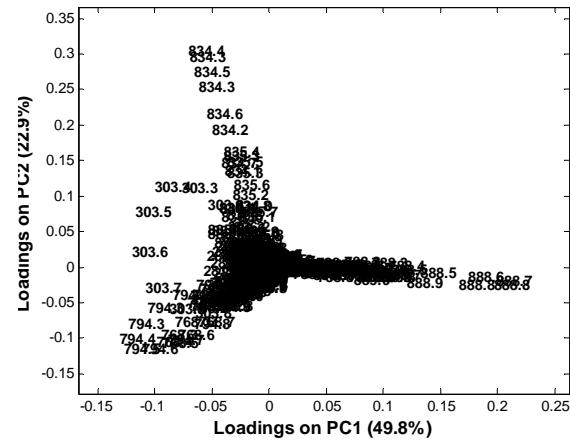
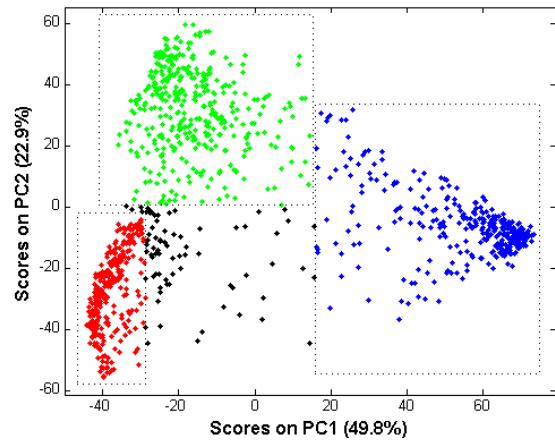
### Colocalization

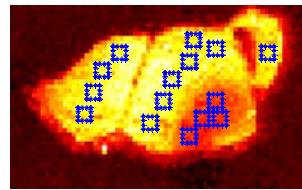
- (A)  $m/z$  283.5, FA(18:0)
- (B)  $m/z$  834.6, PS(18:0/22:6)
- (C)  $m/z$  888.8, ST(24:1)
- (D)  $m/z$  6718, PEP19
- (E)  $m/z$  7531, neurogranin
- (F)  $m/z$  14117, MBP isoform 8



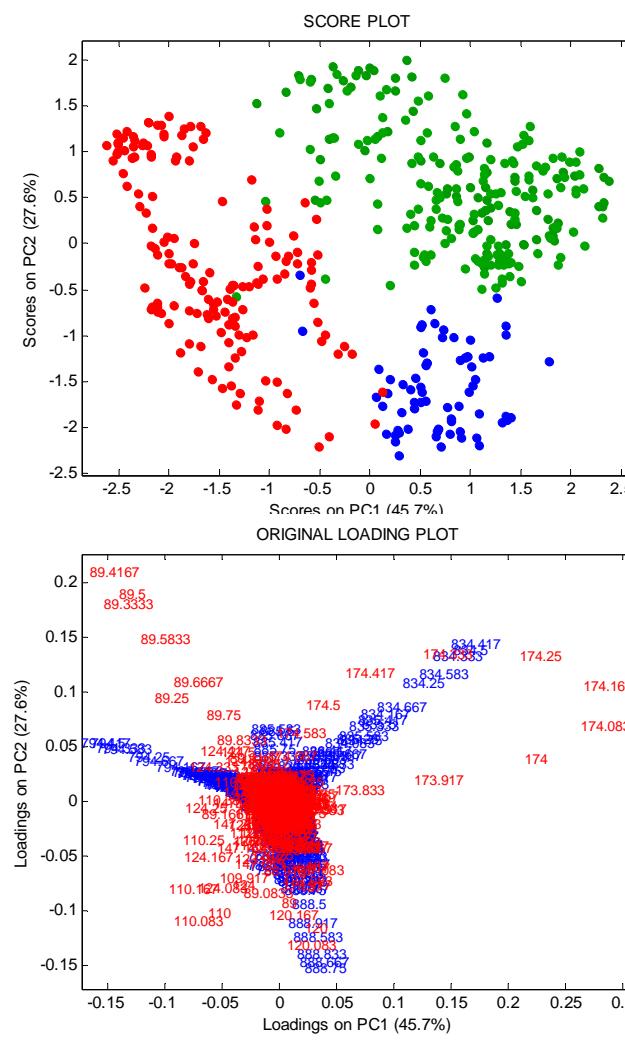
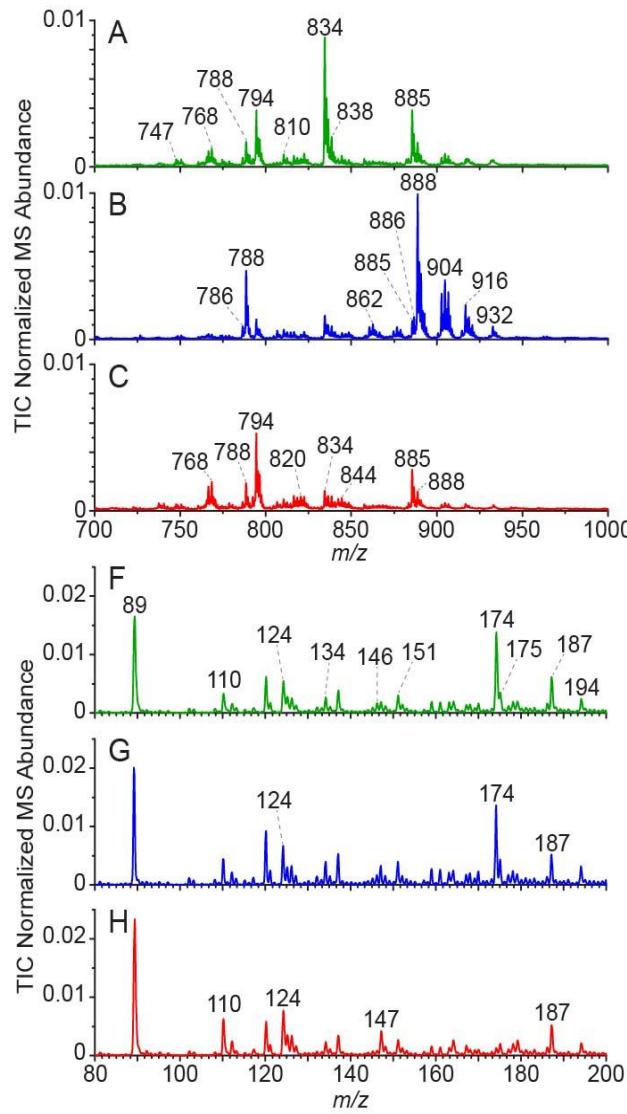
**Combination of lipid profile + protein profile + morphological information**

# Brain parenchima : glioma vs normal grey and white matter

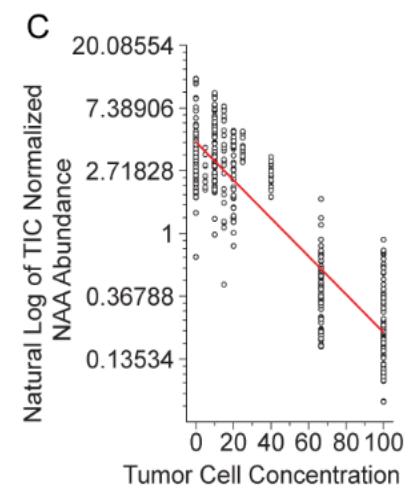
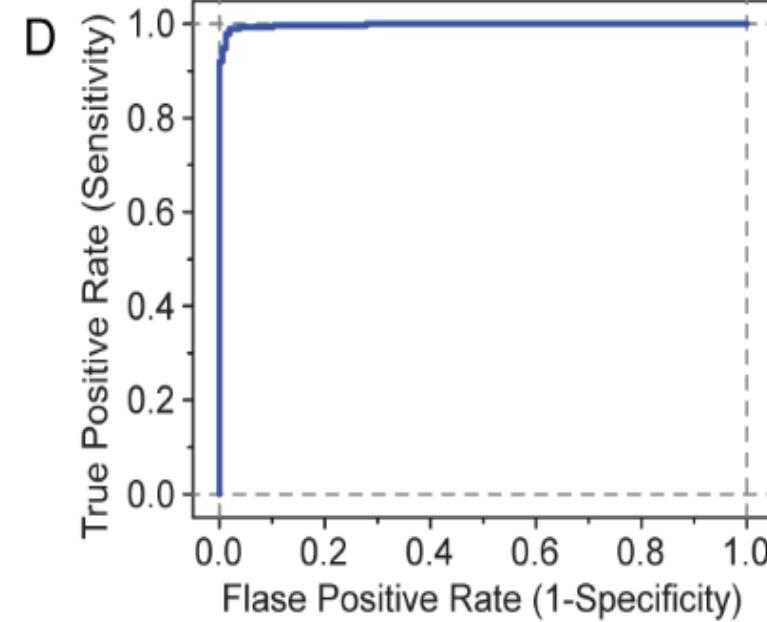
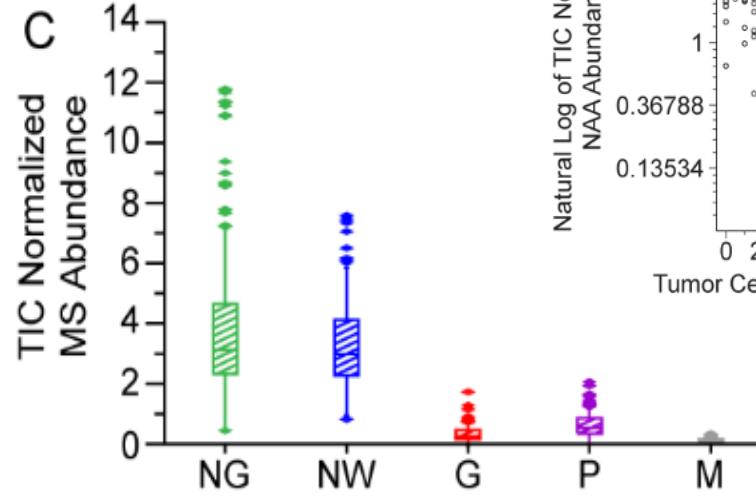
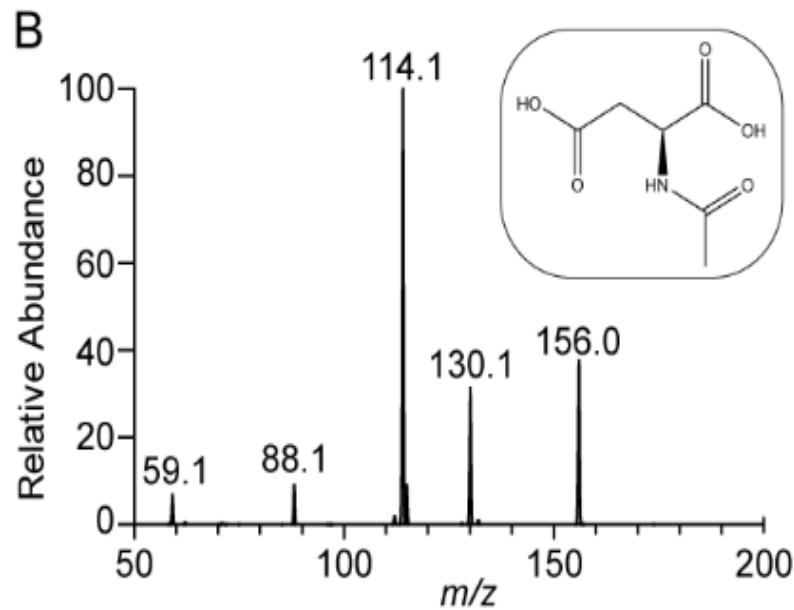
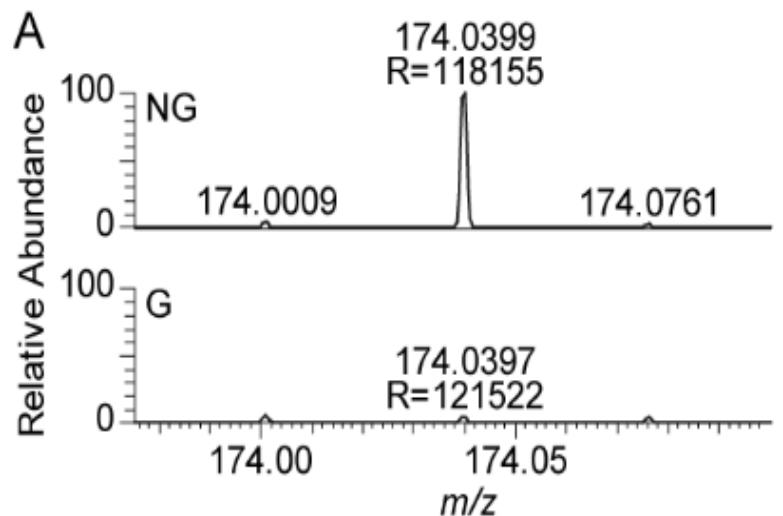




- Glioma
- Grey matter
- White matter



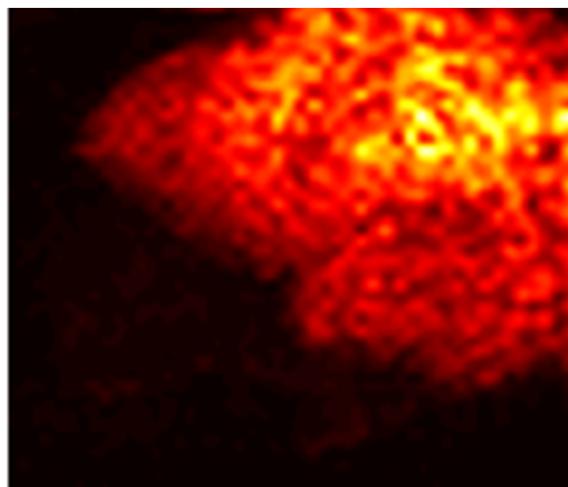
# NAA, N-acetyl-aspartic acid



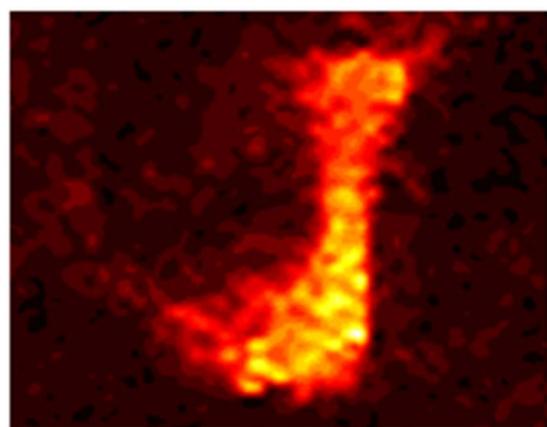
# NAA distribution within tissue sections

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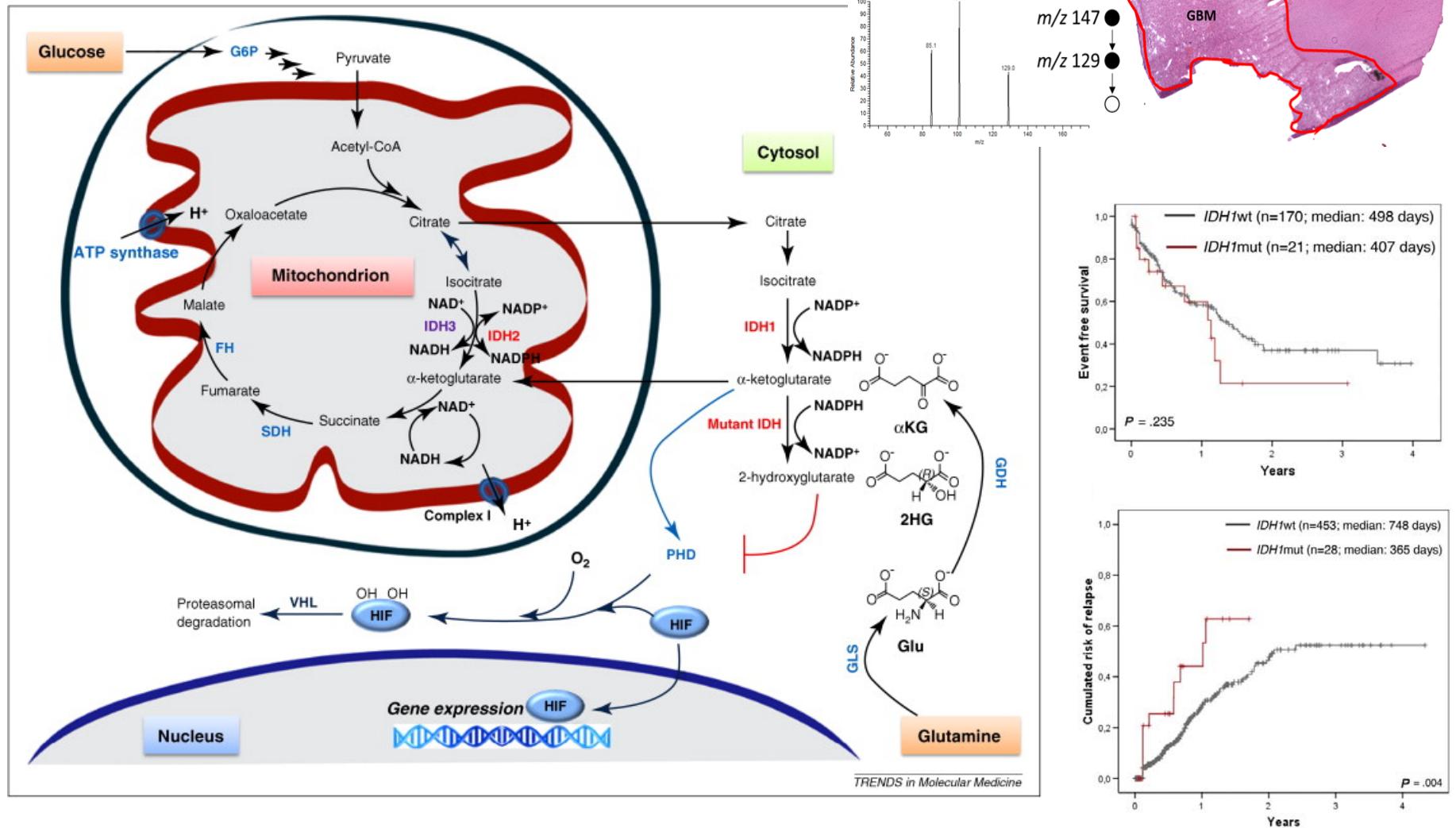
*m/z* 174



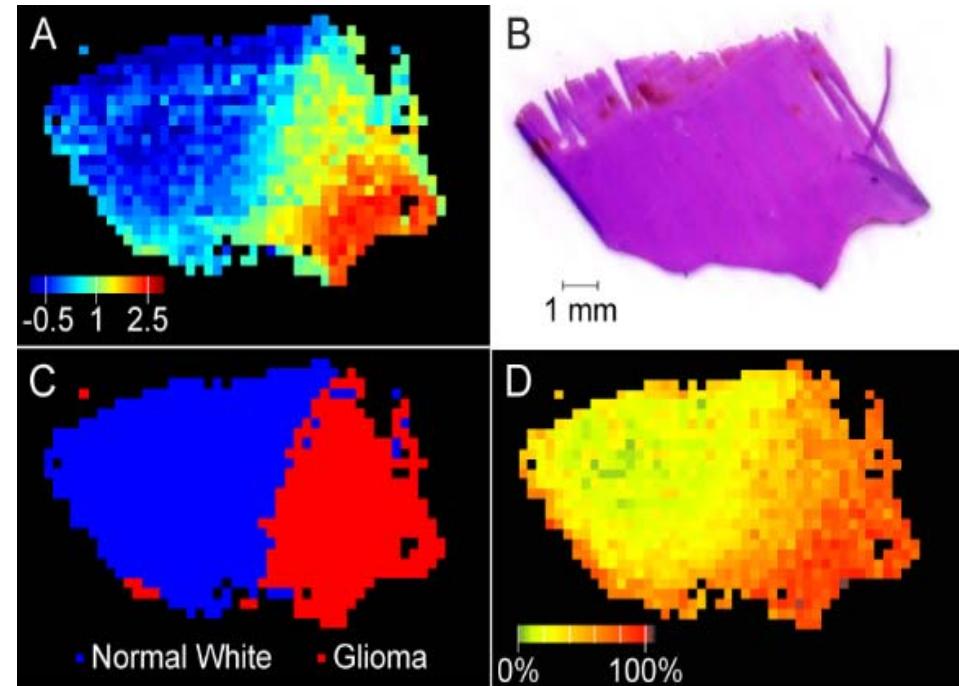
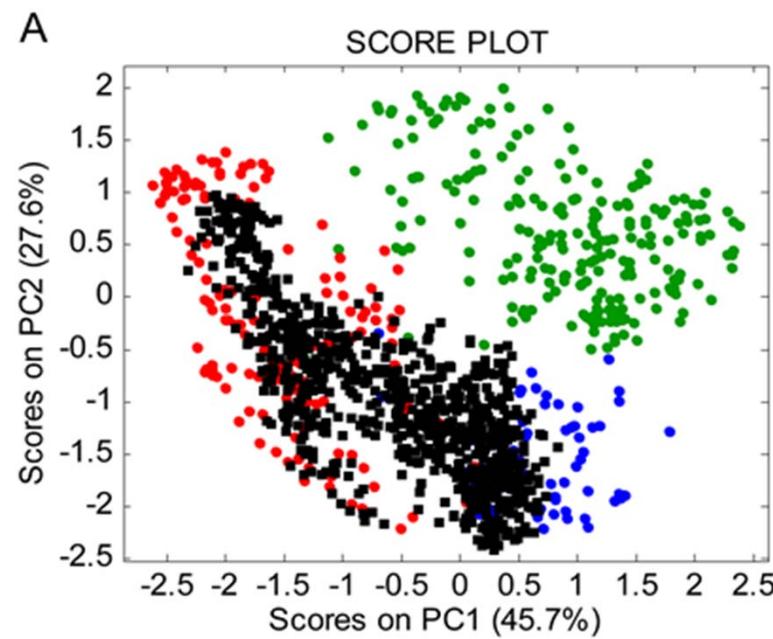
H&E Stain Slide



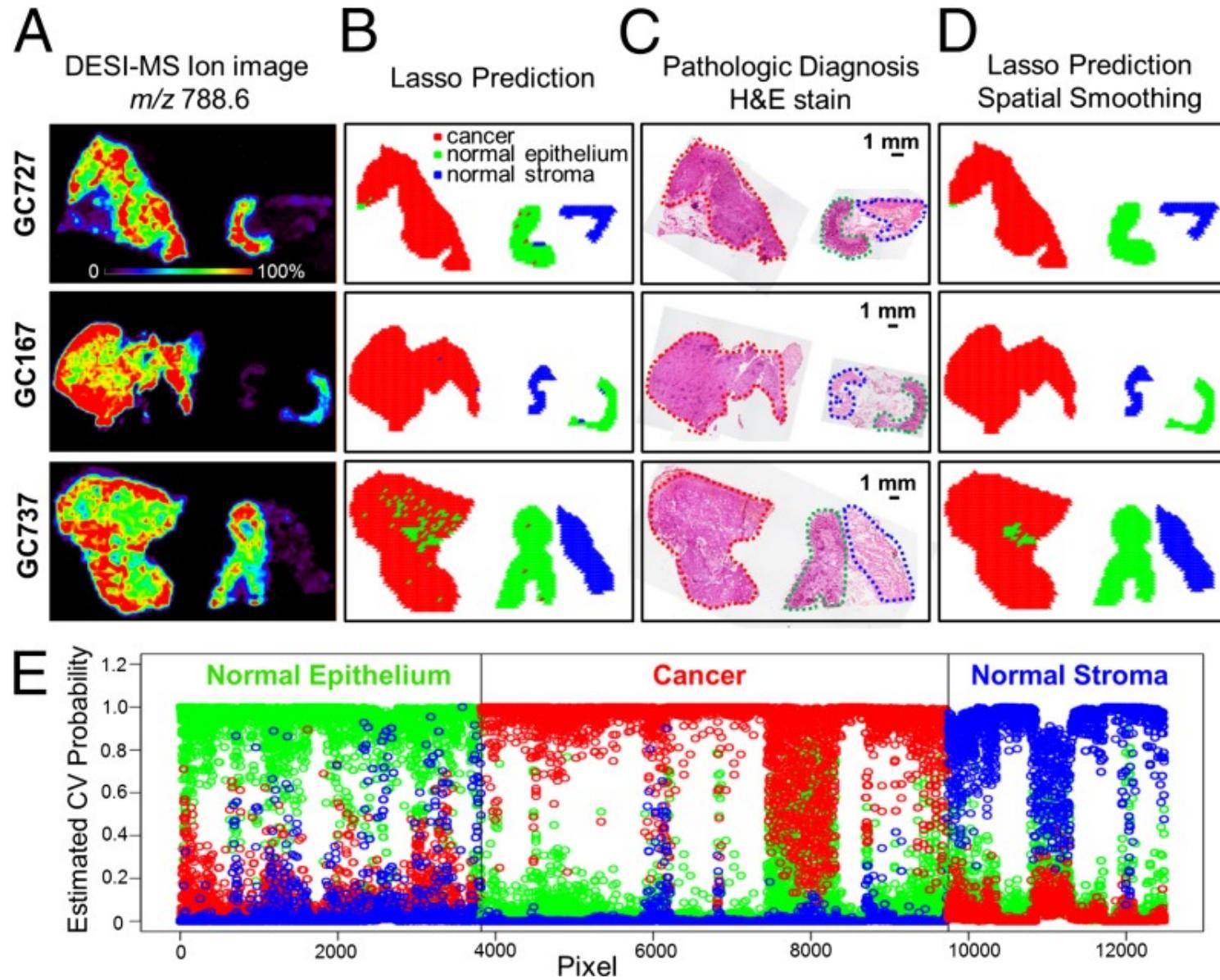
# 2HG, 2-hydroxyglutaric acid



# Classification strategy to predict the tissue state for unknown samples....

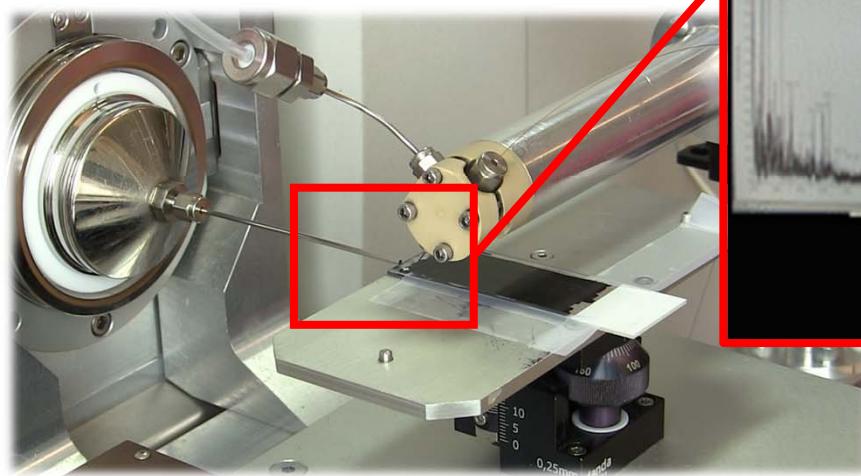


❖ LASSO discriminant technique

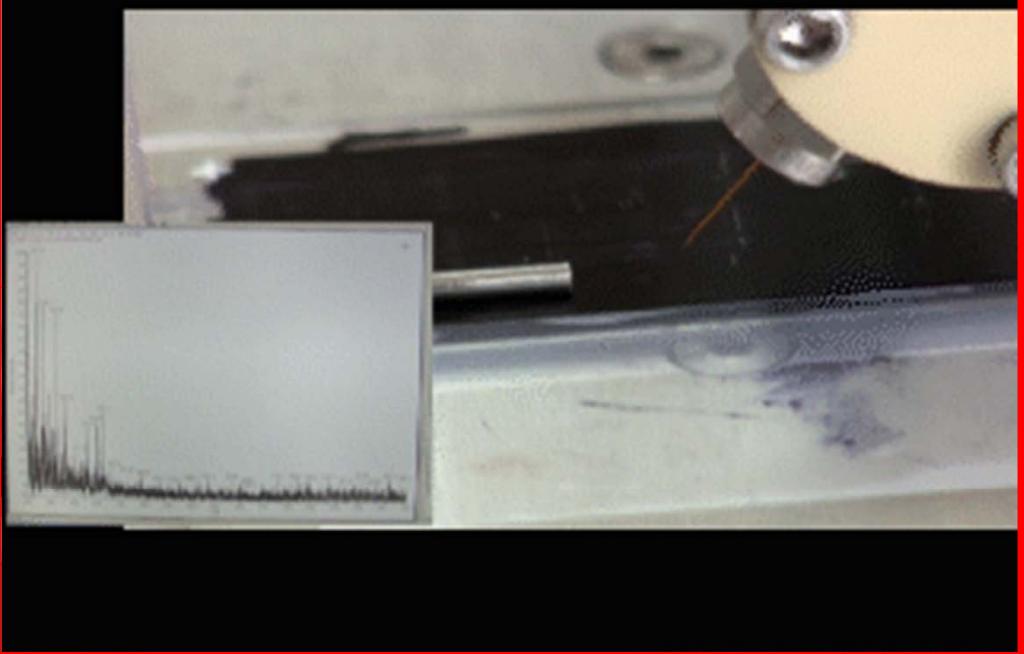


# DESI analysis of tissue smears

3D printed device



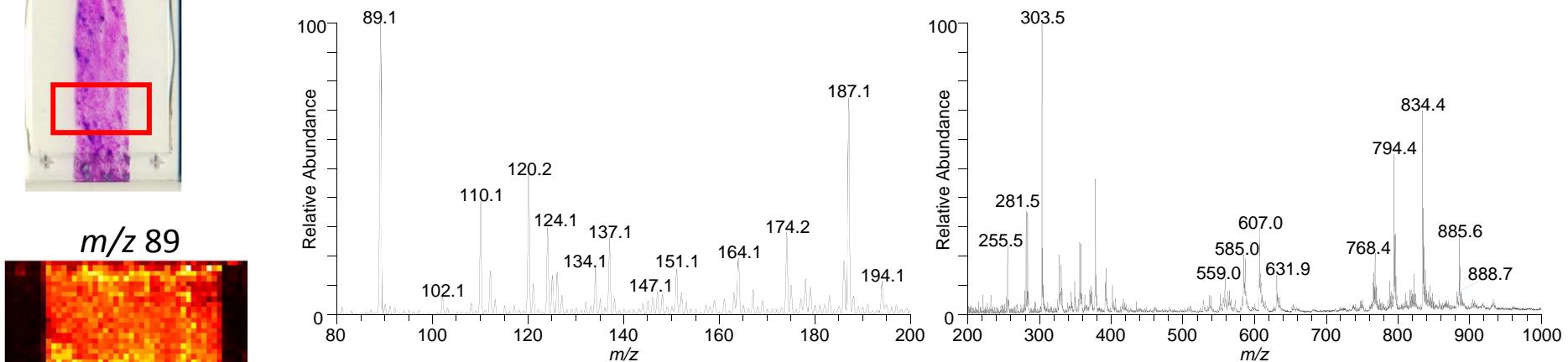
Rapid DESI-MS Analysis



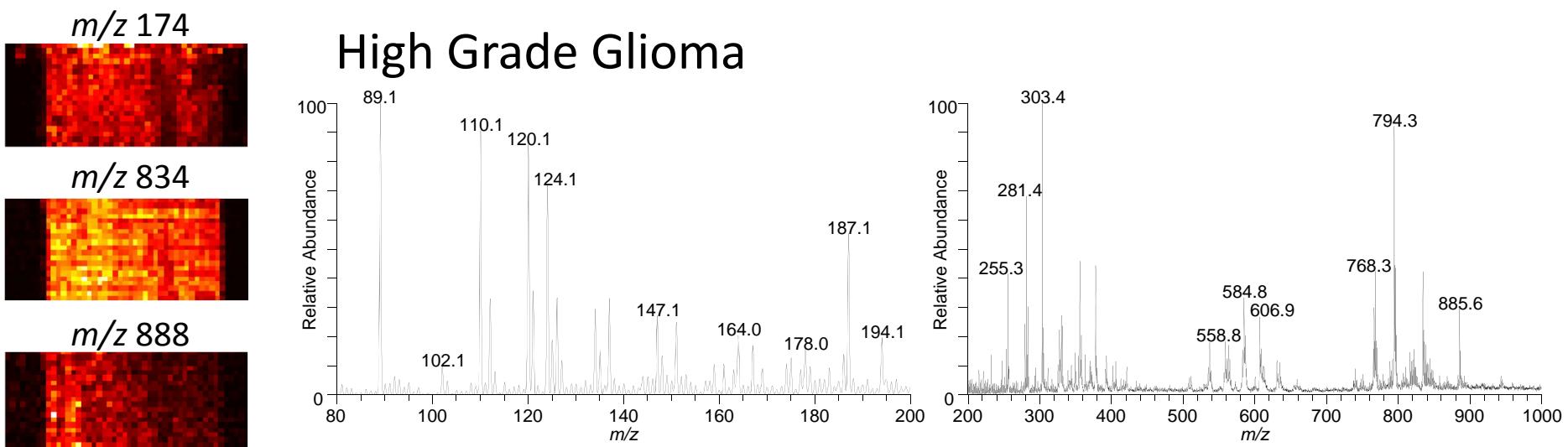


Smears are chemically homogeneous and provide high quality spectra

Normal Grey with 2° infiltration (~10%)



High Grade Glioma



# DESI analysis of tissue smears and tissue sections yield equivalent information

Canonical correlation analysis (CCA) supports the chemical information is equivalent

