Cancer Moonshot LUND

GYORGY MARKO-VARGA

***Lund University Hospital**

***Division of Clinical Protein Science & Imaging, Dep. BioMedical Engineering, Lund University, Lund, Sweden,**

***First Department of Surgery, Tokyo Medical University, Tokyo, Japan**

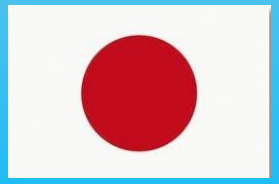
Lecture Content

1. European Cancer Moonshot Lund Center
2. Functional Cancer Impact
3. Clinical Studies
4. Drug Imaging
5. Targeting Tumor Clones

European Cancer Moonshot Lund TEAM






European Cancer Moonshot Lund Center

"EU Spalation Center-Lund Univ"

MAX IV Laboratries

LU-Institute of Technology Structure Labs

EU-Spallation Source "ESS

Interreg Öresund-Kattegat-Skagerrak European Regional Development Fund — EUROPEAN UNION — REGION SKANE — LUND UNIVERSITY — ESS & MAX IV: Cross Border Science and Society

Cancer Moonshot Program
Biggest Cancer Initiative EVER..

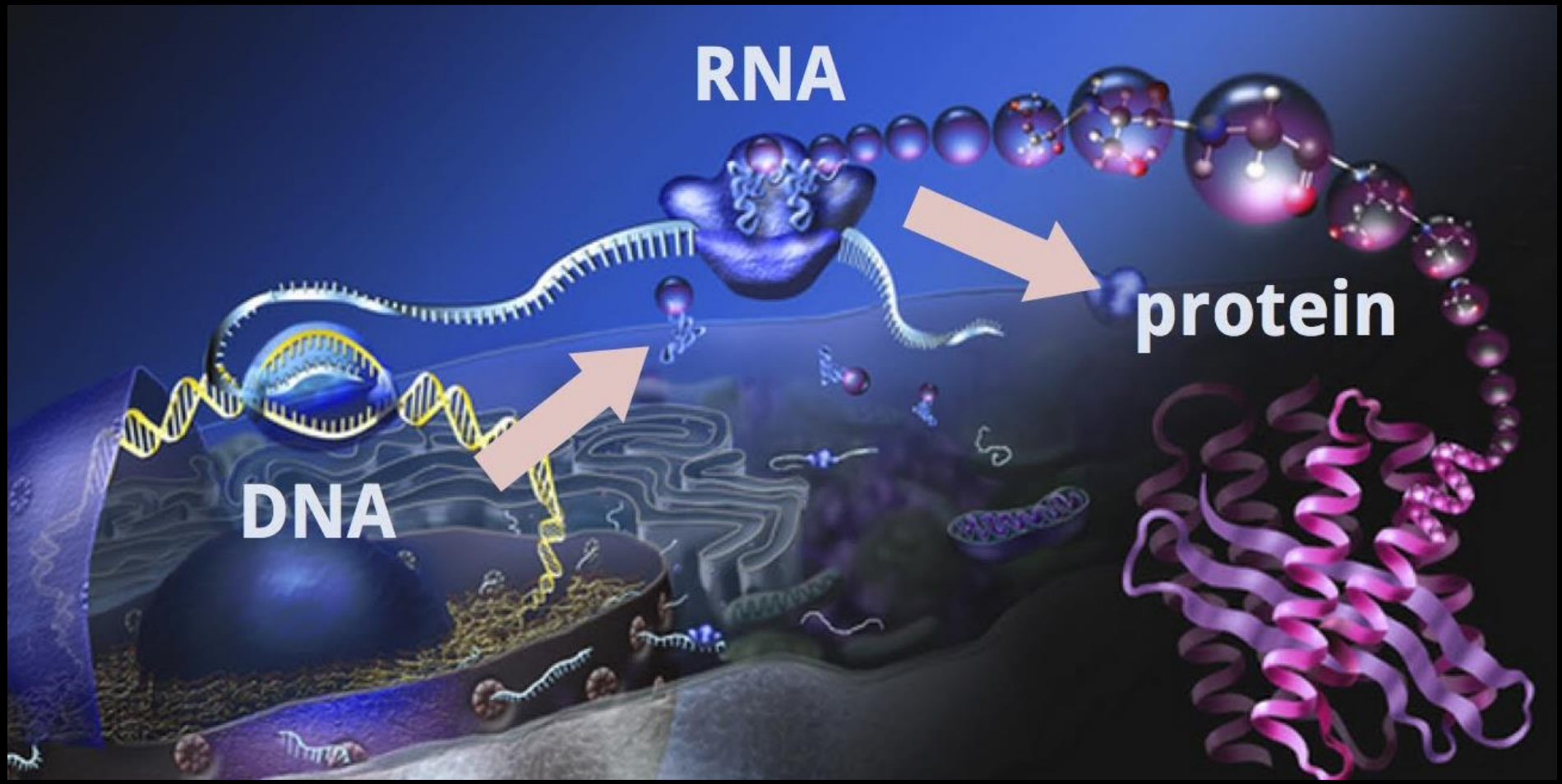
Phase 2 - 2022-2027

I believe that this Nation should commit itself to achieving the goal, before this decade is out, of landing a man on the moon and returning him safely to earth.

CANCER MOONSHOT

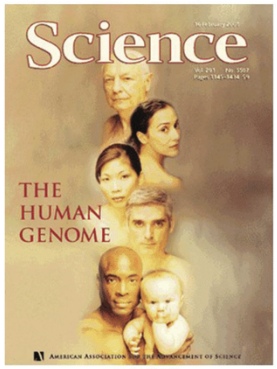
- Catalyse/Unleash Proteogenomic Big Data Breakthroughs
- Detect Cancer Earlier
- Accelerate Trials of New Cancer Therapies/PHARMA
- Better Match Patients to Drugs/PHARMA

Central Dogma of Life



The Human Proteome Bluepint-2020

The Human Genome



In – 2000

nature COMMUNICATIONS

PERSPECTIVE

https://doi.org/10.1038/s41467-020-19045-9 OPEN

A high-stringency blueprint of the human proteome

Subash Adhikari et al.#

"Nov 2020"

The Human Proteome Organization (HUPO) launched the Human Proteome Project (HPP) in 2010, creating an international framework for global collaboration, data sharing, quality assurance and enhancing accurate annotation of the genome-encoded proteome. During the subsequent decade, the HPP established collaborations, developed guidelines and metrics, and undertook reanalysis of previously deposited community data, continuously increasing the coverage of the human proteome. On the occasion of the HPP's tenth anniversary, we here report a 90.4% complete high-stringency human proteome blueprint. This knowledge is essential for discerning molecular processes in health and disease, as we demonstrate by highlighting potential roles the human proteome plays in our understanding, diagnosis and treatment of cancers, cardiovascular and infectious diseases.

A decade after the release of the draft Human Genome Project (HGP), the Human Proteome Organization (HUPO) leveraged this genomic encyclopedia to launch a visionary international scientific collaboration called the Human Proteome Project (HPP)[1–4]. Utilizing substantial community data, the HPP connects scientists, clinicians, industry, institutions and

Building Human Global Libraries

Adhikari et al, Nature com., 2020,

The European Cancer Moonshot Center Labs

Fully Automated Biobank -80°C
Robotic Processing
Electronc Surveilance
2D-Barcoding
LINKED TO
Sothern SWEDISH HEALTHCARE

Fully Automated Biobank -80°C
Robotic Processing
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2D-Barcoding
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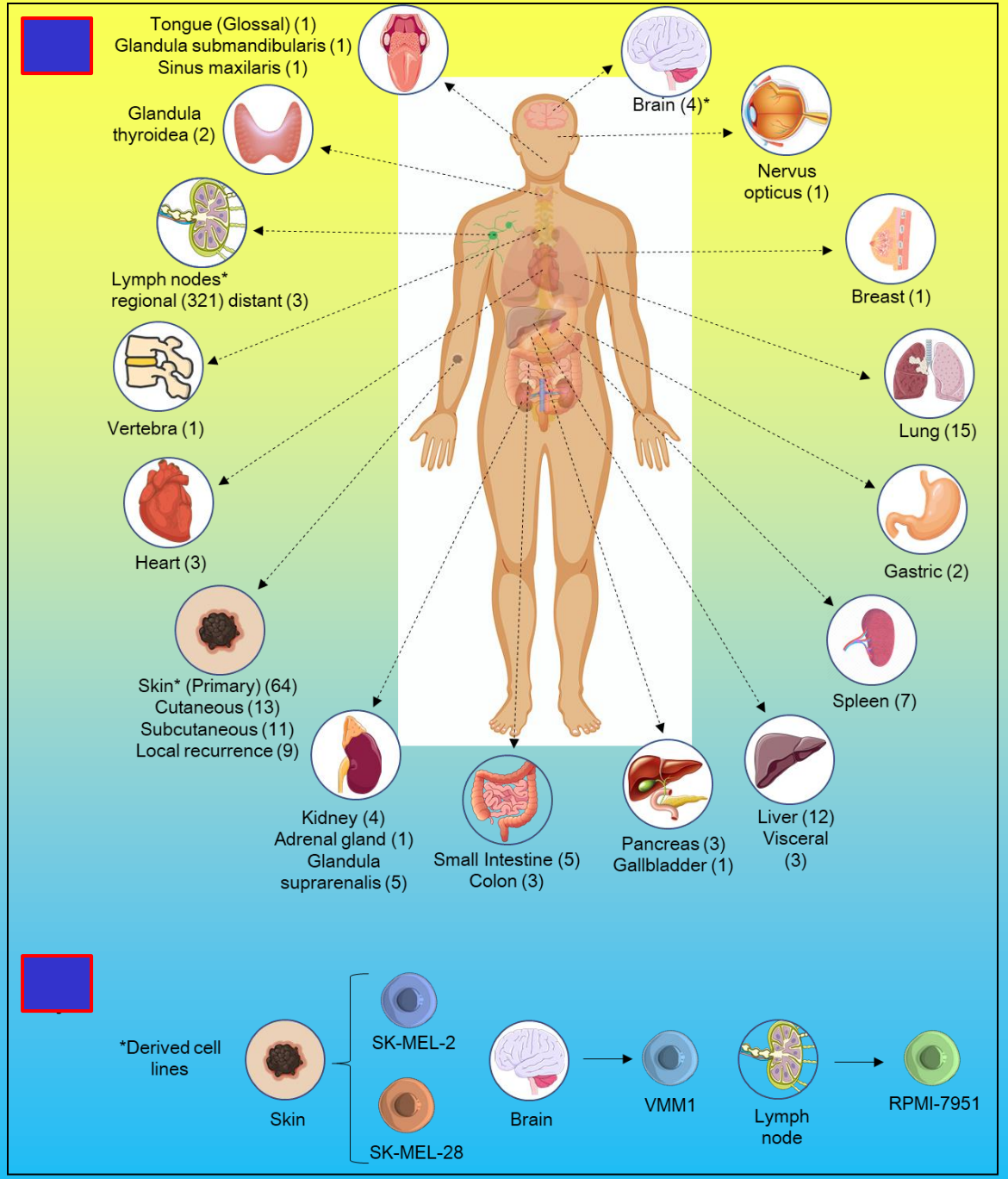
Melanoma Proteome Atlas



Human Melanoma Protein Atlas

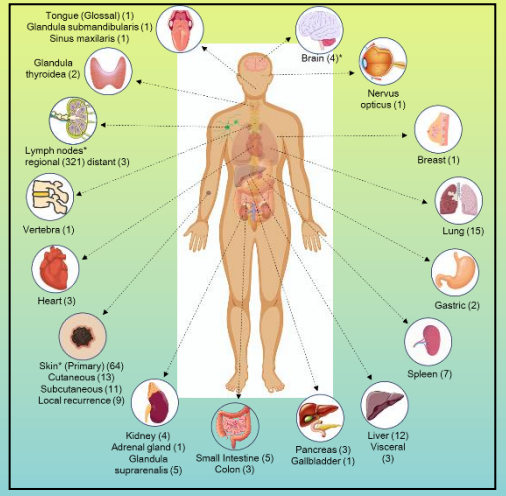
DOI: 10.1002/ctm2.451

RESEARCH ARTICLE

CLINICAL AND TRANSLATIONAL MEDICINE Open Access WILEY

The Human Melanoma Proteome Atlas—Complementing the melanoma transcriptome

Lazaro Hiram Betancourt[1] | Jeovanis Gil[1] | Aniel Sanchez[2] | Viktória Doma[3,4] |



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DOI: 10.1002/ctm2.473

RESEARCH ARTICLE

CLINICAL AND TRANSLATIONAL MEDICINE Open Access WILEY

The human melanoma proteome atlas—Defining the molecular pathology

Lazaro Hiram Betancourt[1] | Jeovanis Gil[1] | Yonghyo Kim[1] | Viktória Doma[2,3] |

8 Global Medical Centers

Lazaro Hiram Betancourt[1] | Jeovanis Gil[1] | Aniel Sanchez[2] | Viktória Doma[3,4]
Magdalena Kuras[3] | Jimmy Rodriguez Murillo[5] | Erika Velasquez[2] |
Uğur Çakır[4] | Yonghyo Kim[1] | Yutaka Sugihara[1] | Indira Pla Parada[2] |
Beáta Szeitz[6] | Roger Appelqvist[1] | Elisabet Wieslander[1] | Charlotte Welinder[1]
Natália Pinto de Almeida[7,8] | Nicole Woldmar[7,8] | Matilda Marko-Varga[1] |
Jonatan Eriksson[1] | Krzysztof Pawłowski[4,9,10] | Bo Baldetorp[1] |
Christian Ingvar[11,12] | Håkan Olsson[1,11] | Lotta Lundgren[1,11] | Henrik Lindberg[1]
Henriett Oskolas[1] | Boram Lee[1] | Ethan Berge[1] | Marie Sjögren[1] |
Carina Eriksson[1] | Dasol Kim[13] | Ho Jeong Kwon[13] | Beatrice Knudsen[14] |
Melinda Rezeli[8] | Johan Malm[2] | Runyu Hong[15] | Peter Horvath[16] |
A. Marcell Szász[17,18] | József Tímár[3] | Sarolta Kárpáti[4] | Peter Horvatovich[19] |
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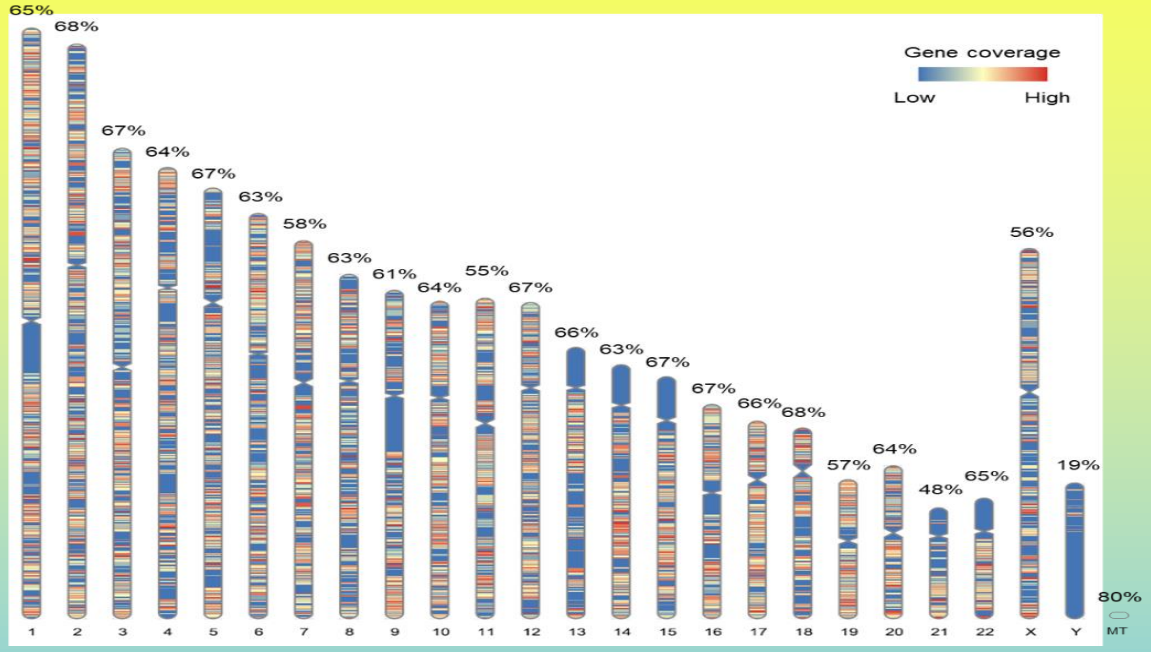
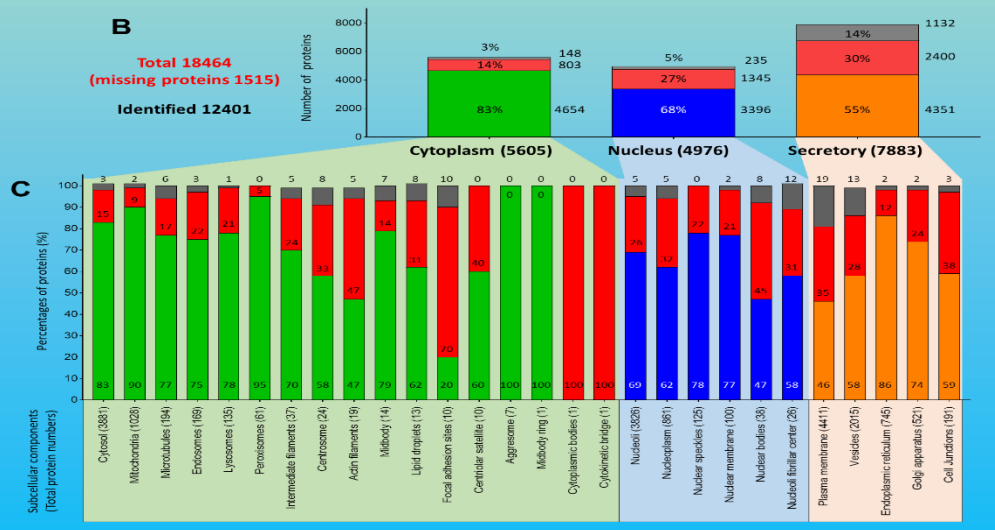
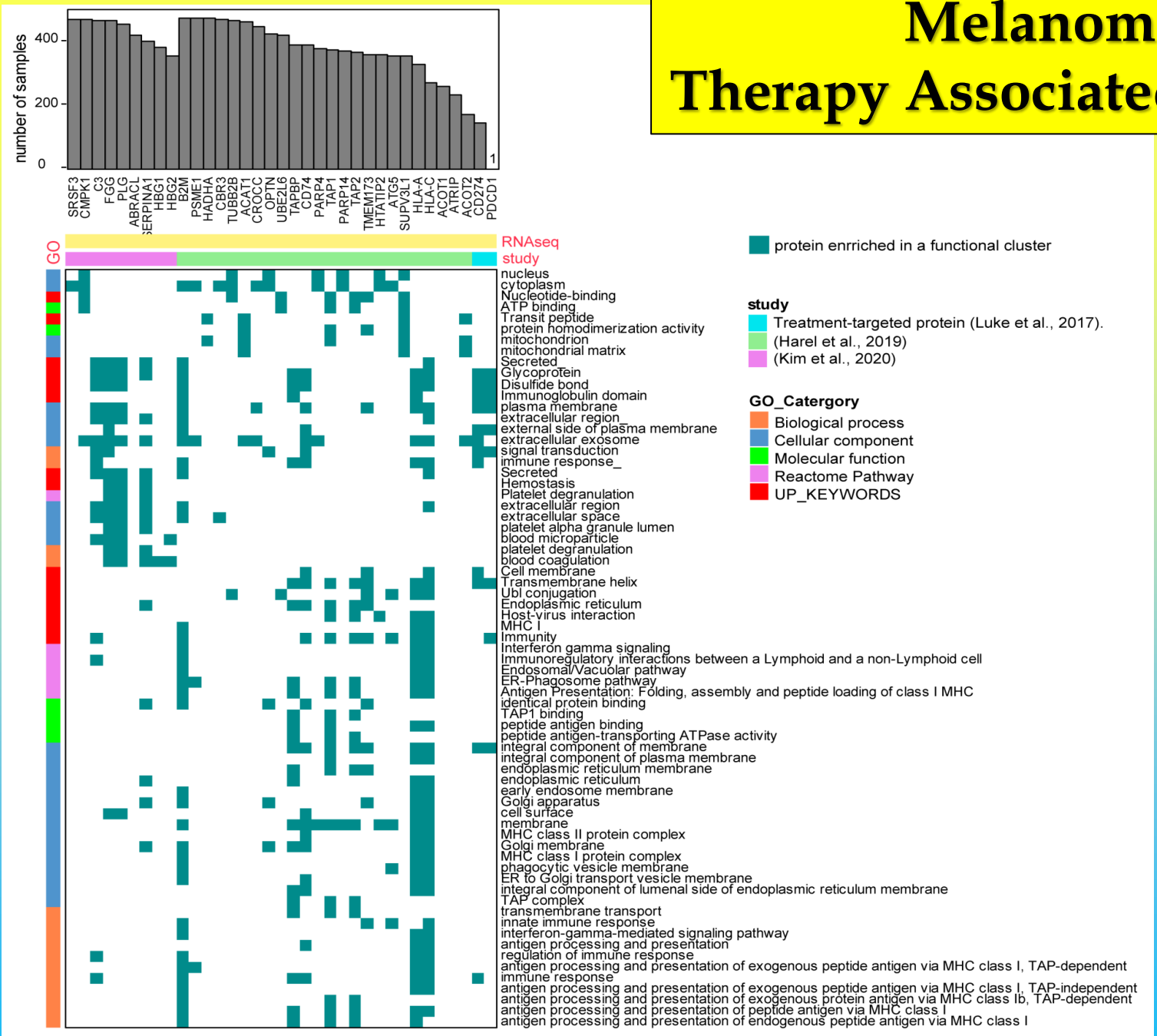
Madalina Oppermann[23] | Ken Miller[23] | Francesco Florindi[24] | Quimin Zhou[25] |
Gilberto B. Domont[7] | Luiciana Pizzatti[7] | Fábio C. S. Nogueira[7] |
Leticia Szadai[26] | István Balázs Németh[26] | Henrik Ekedahl[1,11] | David Fenyö[15] |
György Marko-Varga[8,13,22]

Melanoma ProteinExpression & Localisation

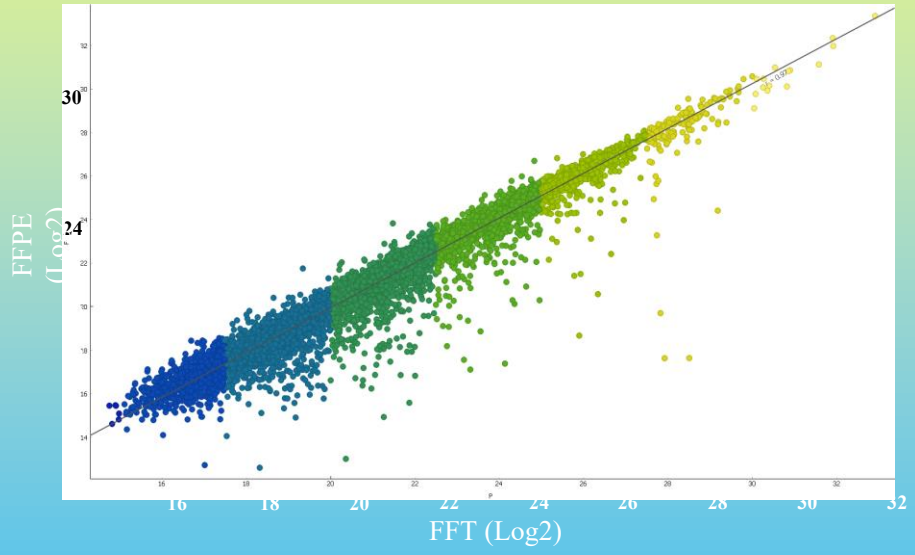


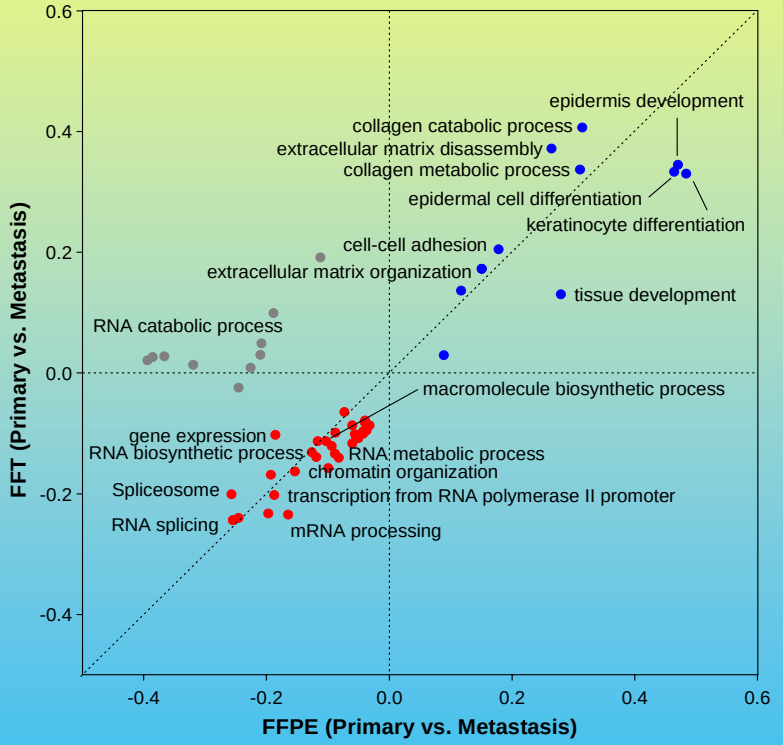


Melanoma Therapy Associated Proteins

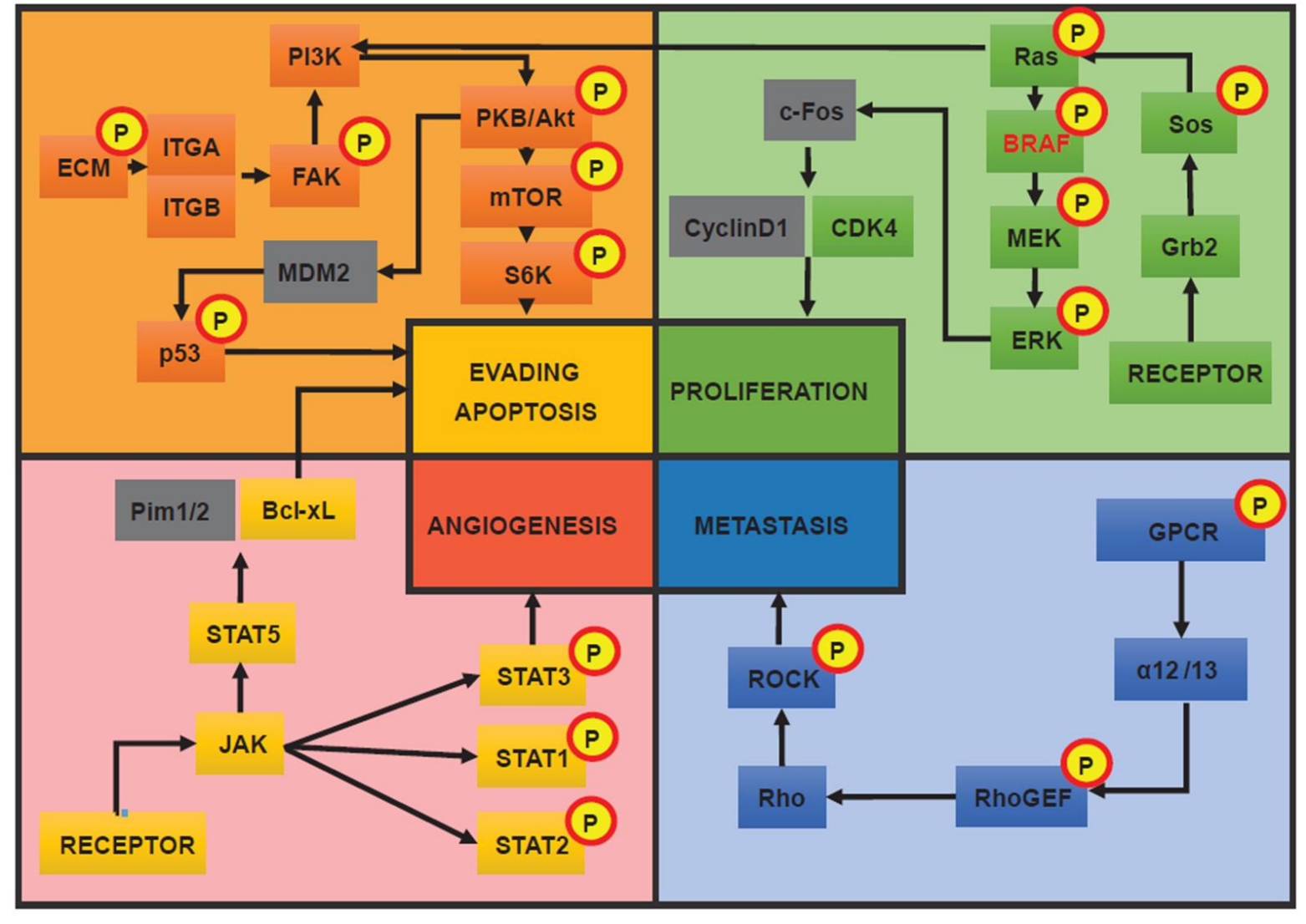


Global proteome analysis of FFPE and FFT

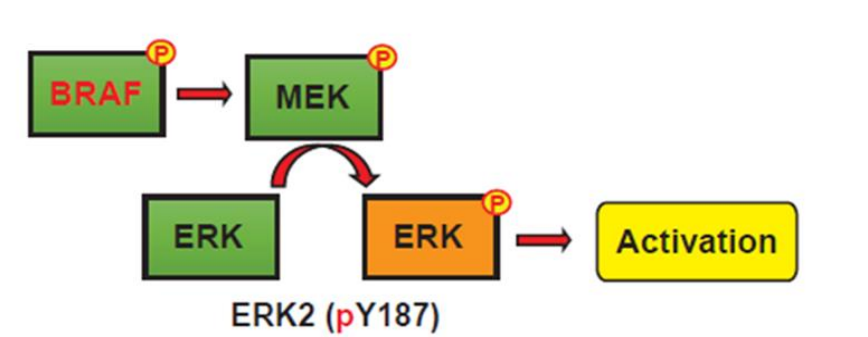


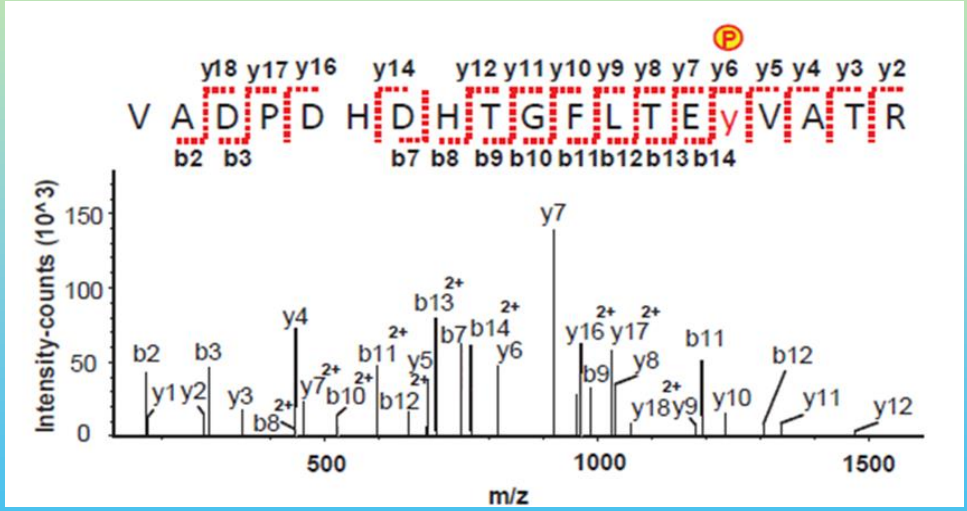


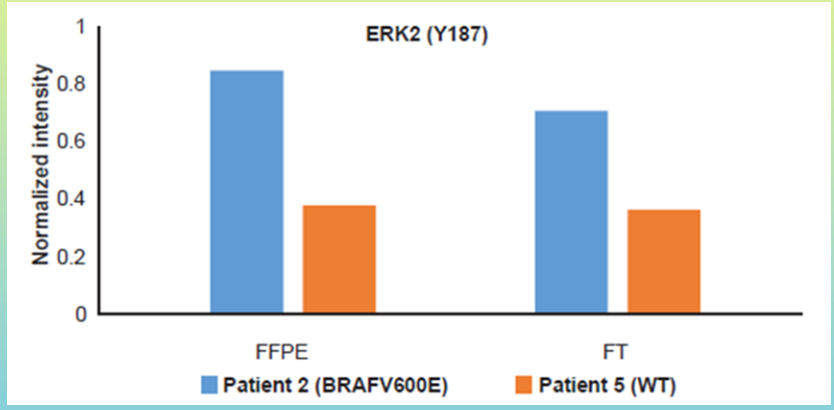
Mapping Cancer-Specific Pathways



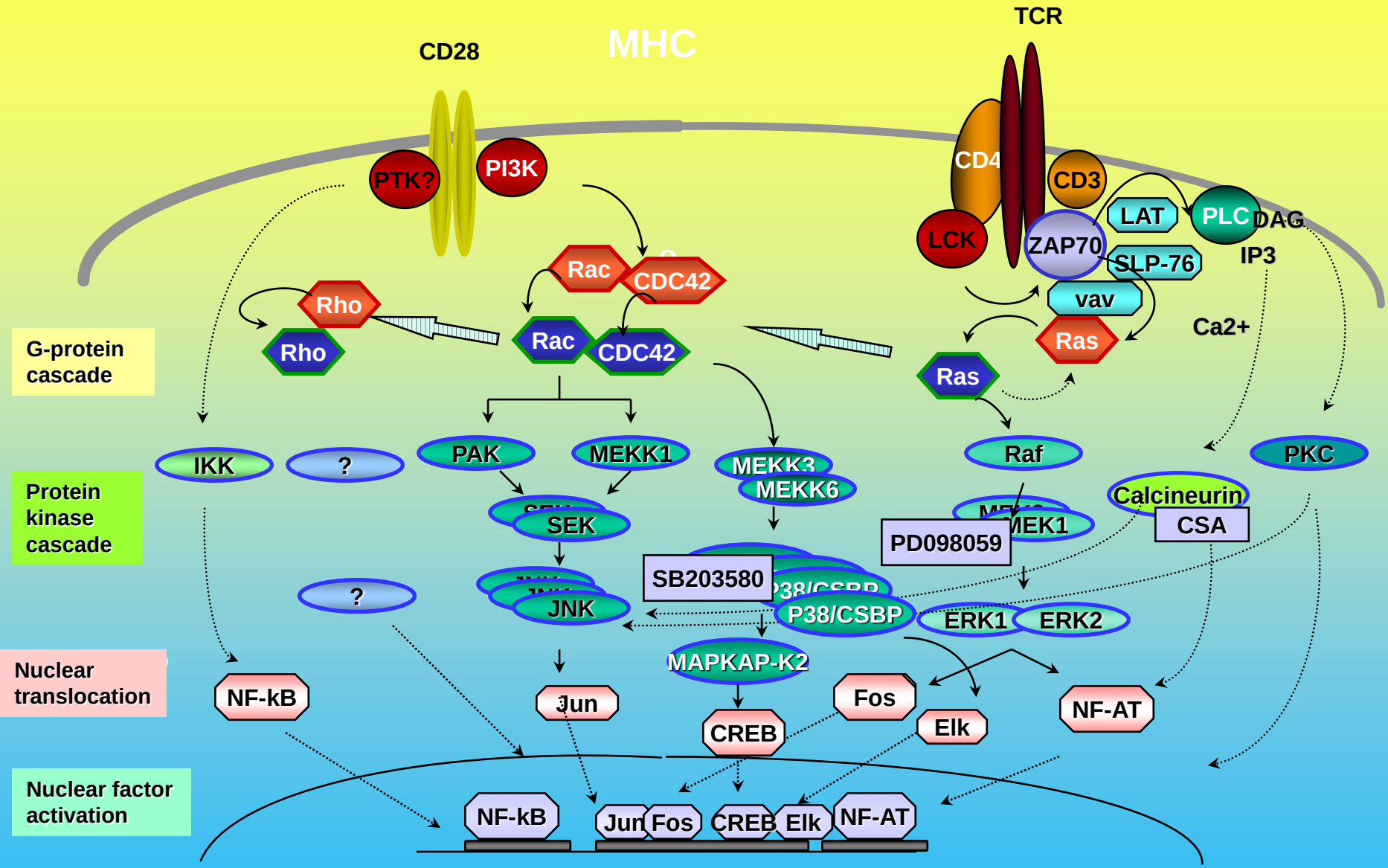
Personalized Treatment Monitoring





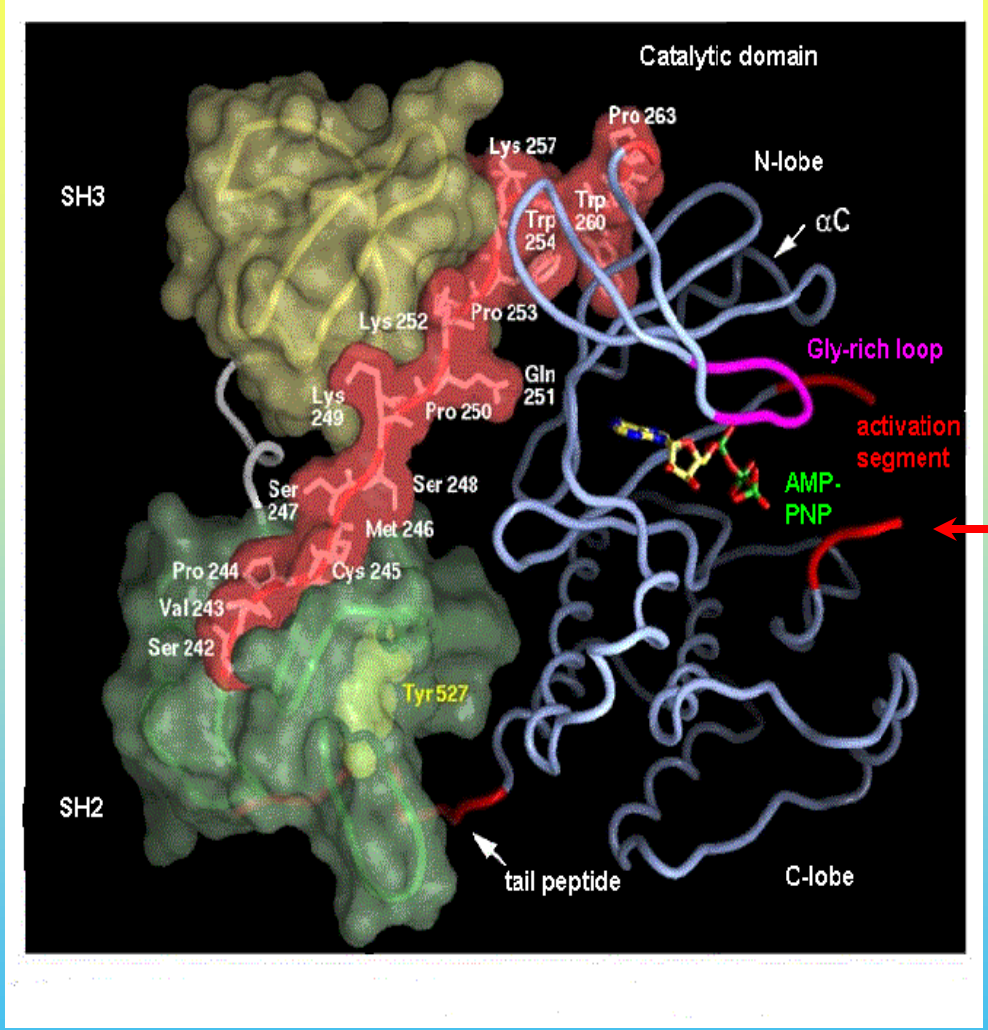


Components of Signaling Pathways Through TCR and CD28



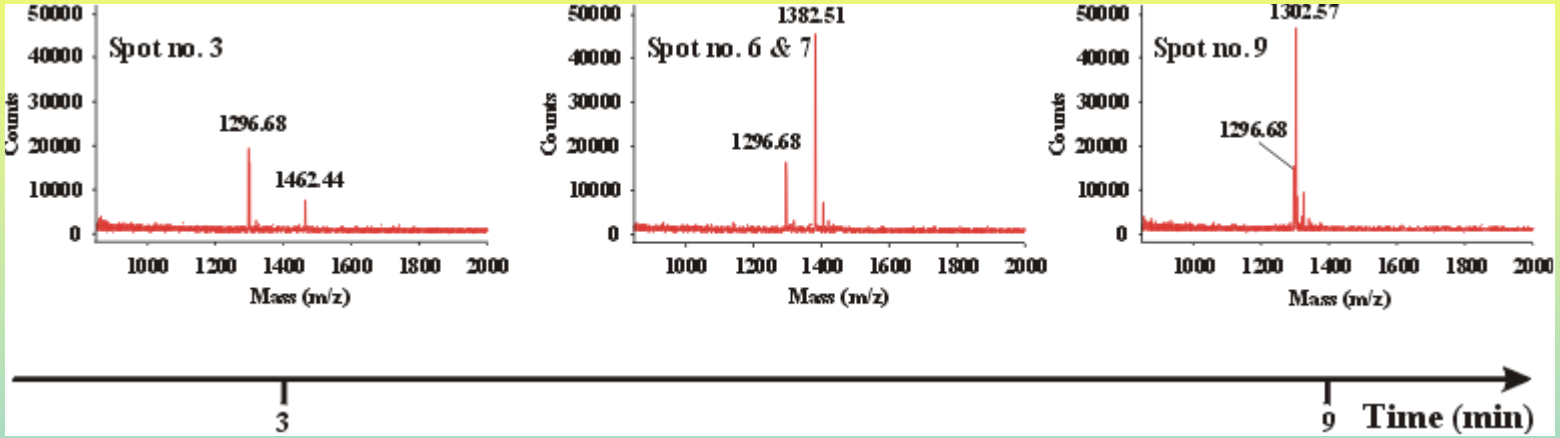
Jacinto et al Immunity 8, 31-41, 1998, Kaga et al J Immunol 160, 4182-89, 1998, Cantrell Annu Rev Immunol 14, 259-74, 1996, Cohen Trends in Cell Biology 7, 353-361, 1997

Phosphorylation of Y493 in the activation loop



Autophosphorylation-site Y493

Capillary LC coupled to MALDI-TOF MS



PP
| |

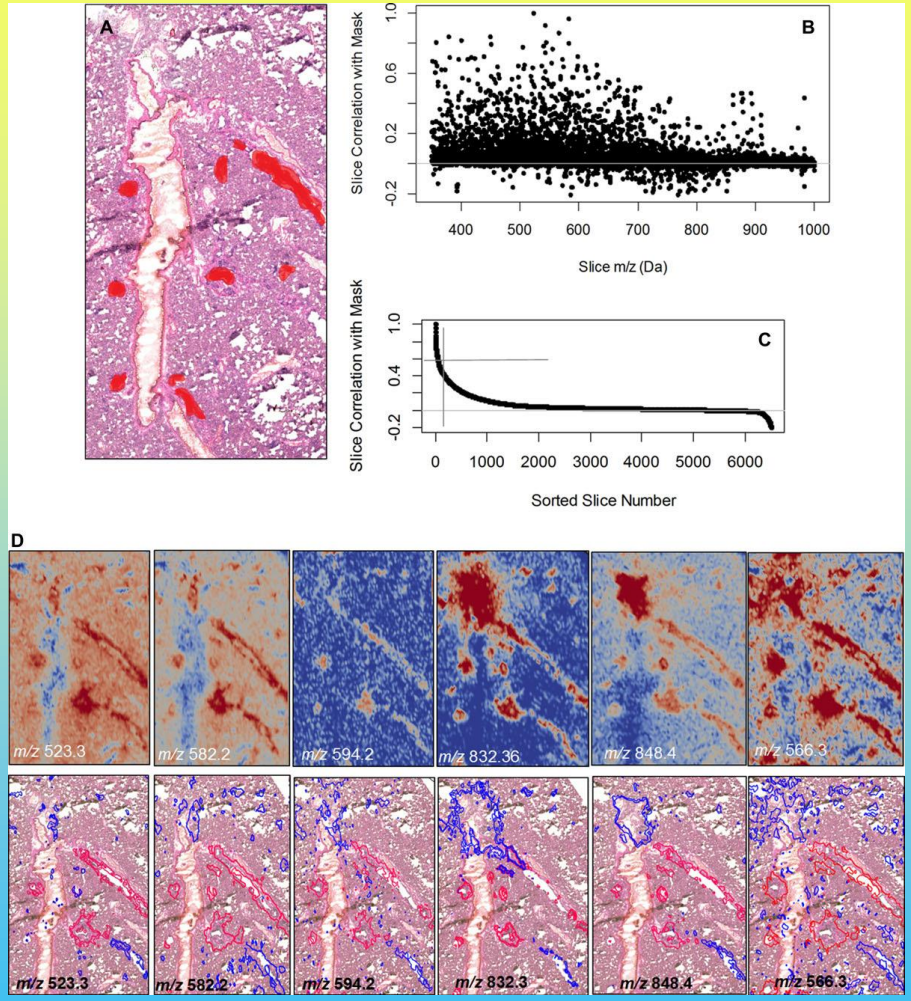
- **Detection of; ALGADDSYYTAR its phosphorylation states**
- **Fractions correspond to 5 fmol - sensitivities down to 50 attomoles achieved**

Mass Spectrometry Imaging

CROSS-OVER HISTOLOGY & MS-IMAGING
ID-of specific metabolites Lung Cancer Function

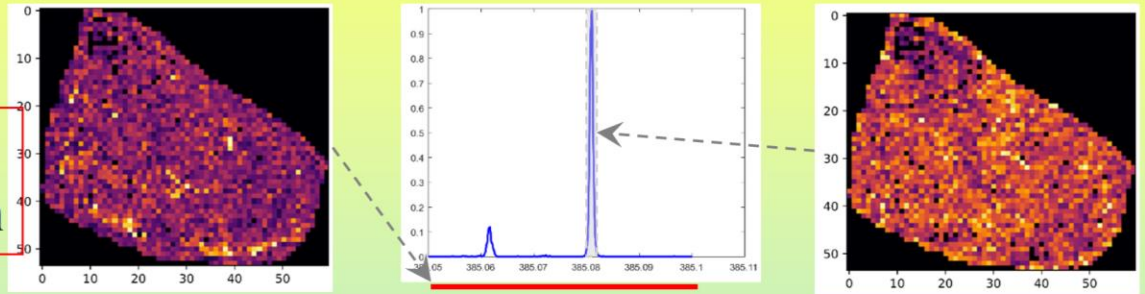
Fehniger, Marko-Varga

*Mask location (red) on H&E image showing bronchioles
*Pearson's correlation index of individual m/z values
*Pearson's correlation sorted according to Pearson's correlation.
*Upper row: representative m/z distribution associated with the mask
*Lower row: H&E image with m/z intensity contour of the mask (red) and other locations (blue)



Detection of Vemurafenib in human Melanoma Lung Metastasis

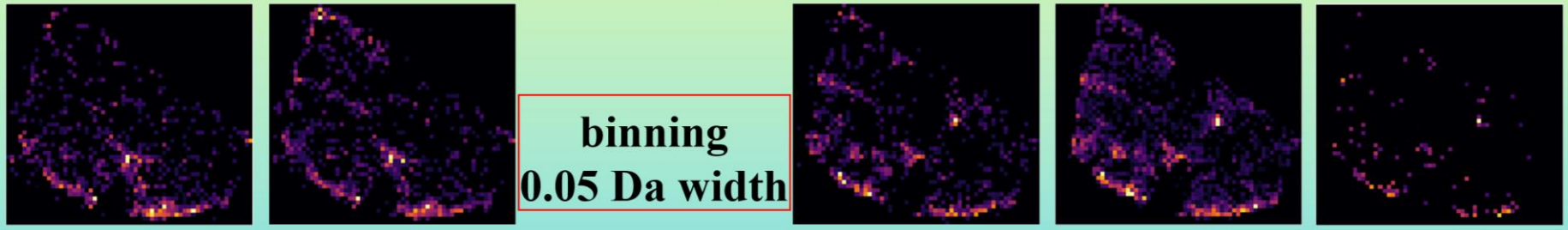
Single Cell spatial resolution



KDE peak cluster 385 Da

Isotopes and fragments.

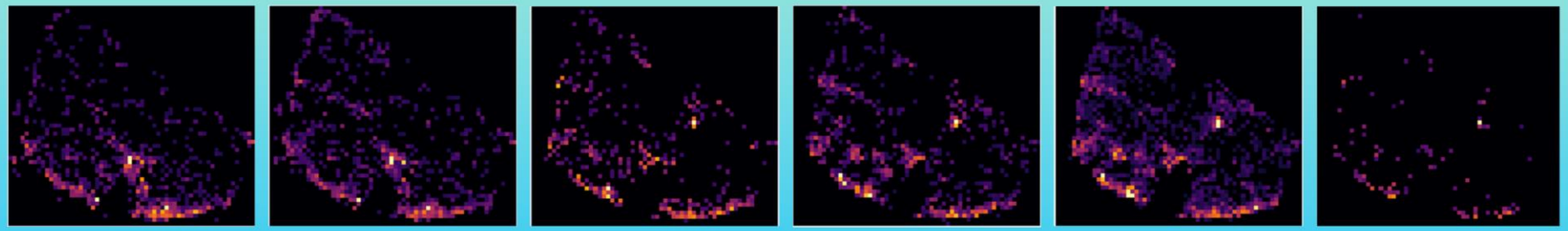
Binning



357.125 Da | 371.175 Da | 491.075 Da | 492.075 Da | 493.075 Da

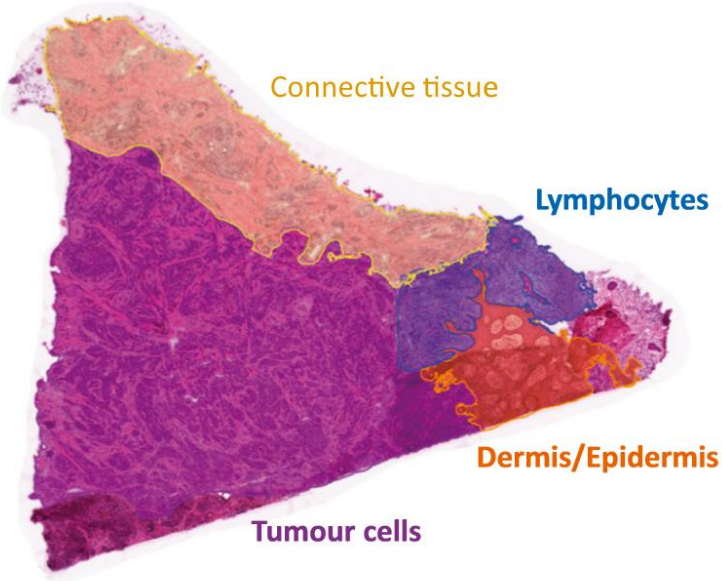
binning 0.05 Da width

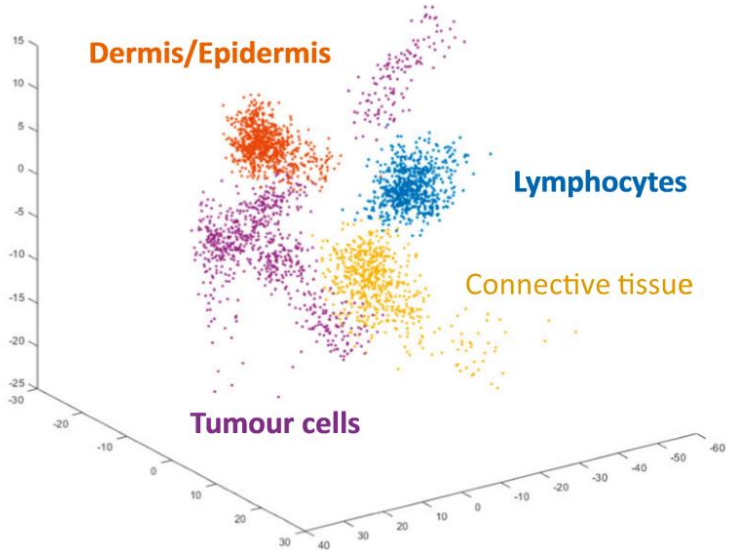
Cluster wise



357.148 Da | 371.164 Da | 385.062 Da | 491.085 Da | 492.078 Da | 493.082 Da

Mass Spec IMAGING – Surgically Isolated Tumor





H&E-stained Tumor from Cancer Patient

Principal Component analysis - MALDI Spectra - Compartments

Betancourt et al, Sci Rep, 2019

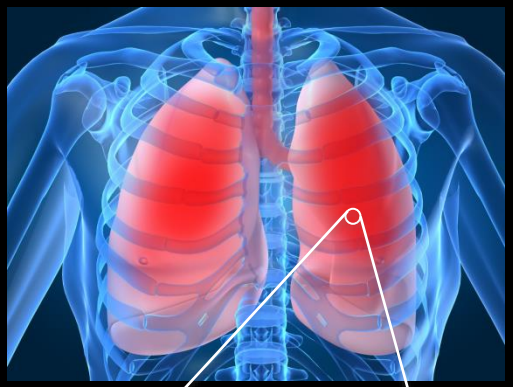
BIG3 Study AstraZeneca & Region Skåne -2022

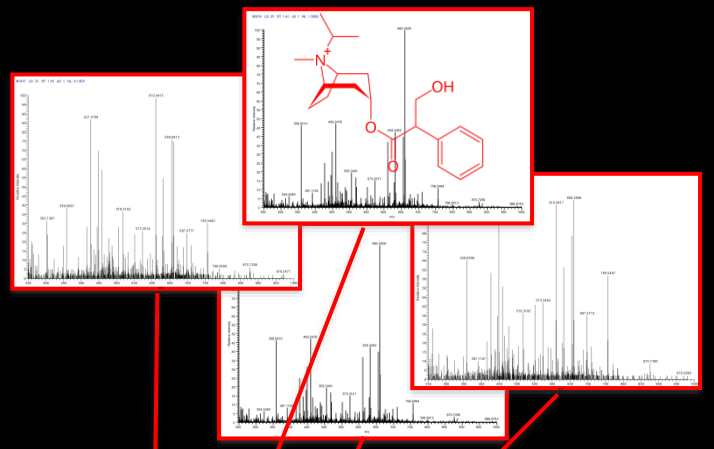
Lung Cancer/COPD/Cardiovascular

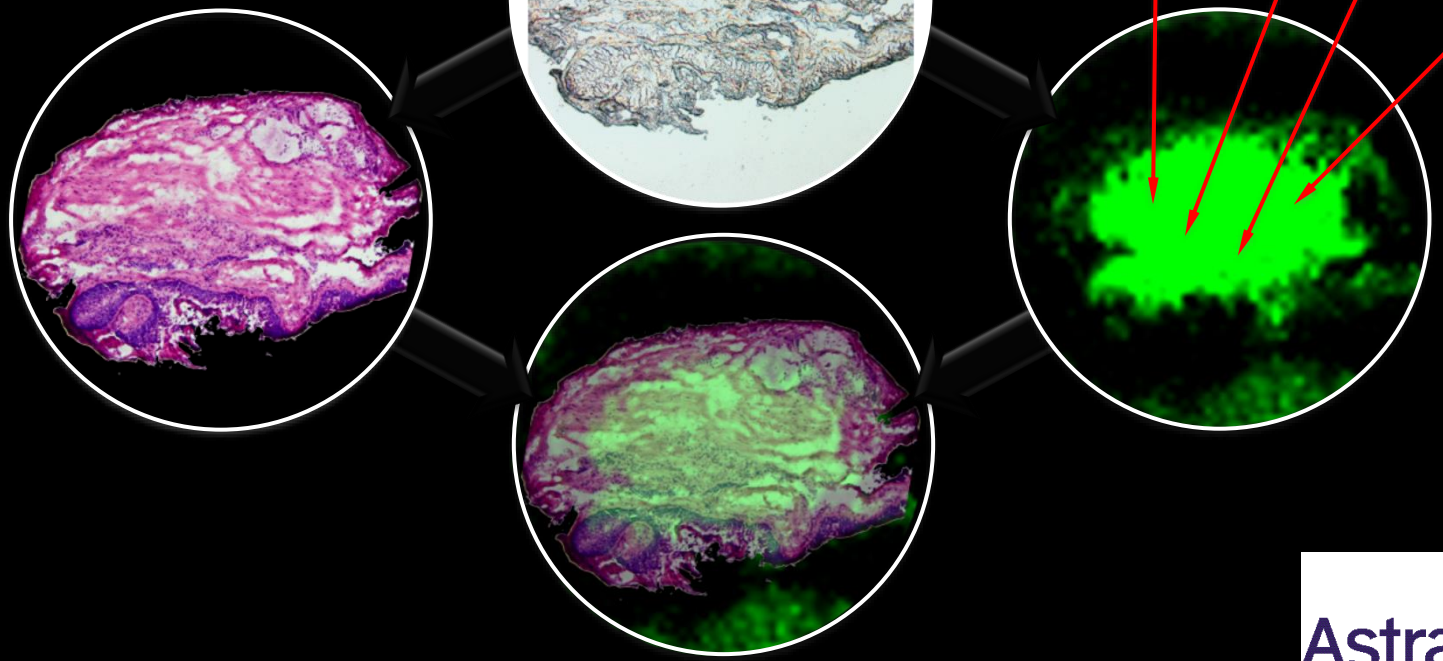
* Contacted more than 60.000 Patients
* 10.000 passed Questionnaire
* 5.000 Patients Heart & Lung test
* 2300 passed CT Imaging
* 3.7 Million Blood Samples

AstraZeneca

First LUNG CANCER /COPD Drug Imaging Study
- Single Cell View

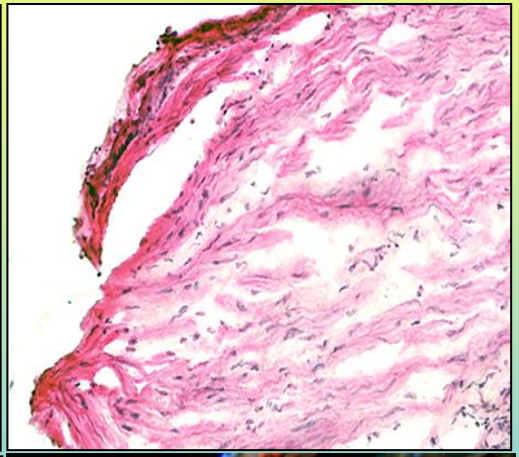


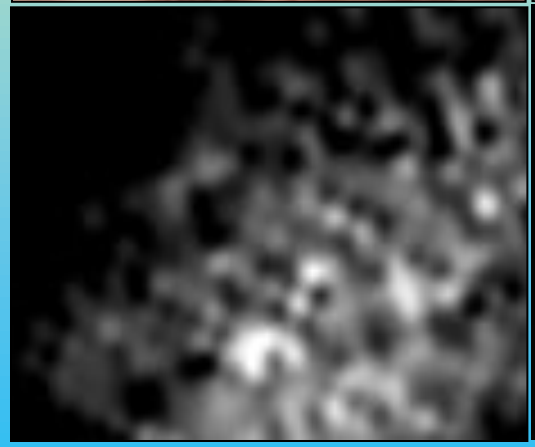


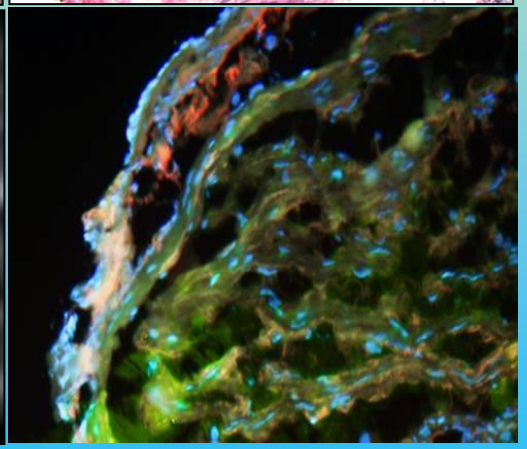


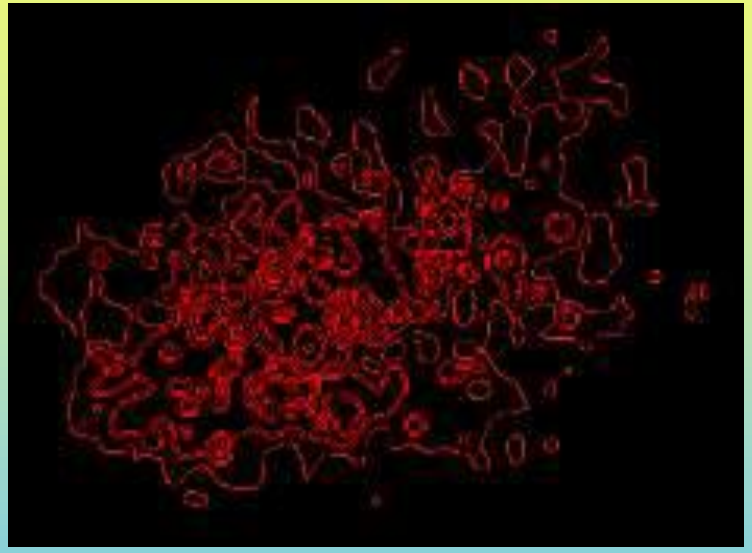
AstraZeneca

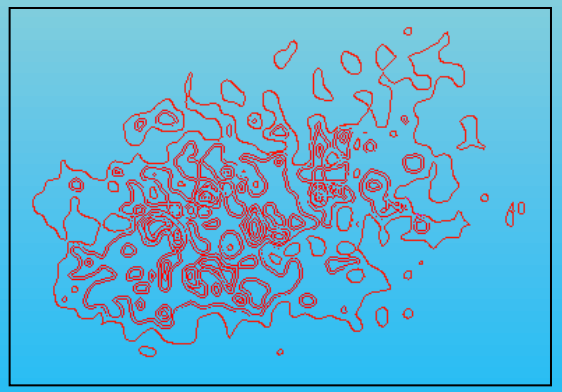
Co-Localization Drug and Protein Target Study



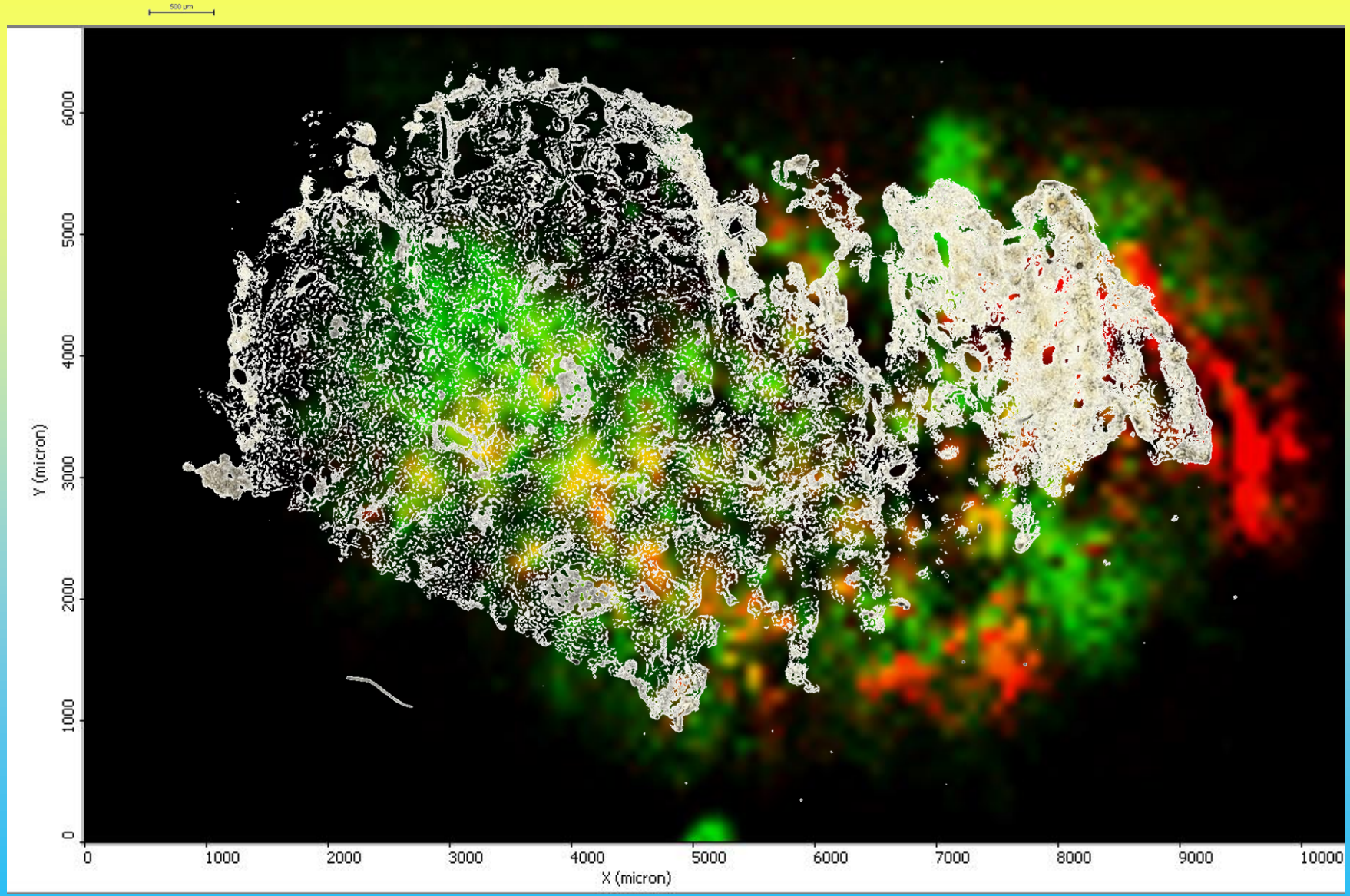




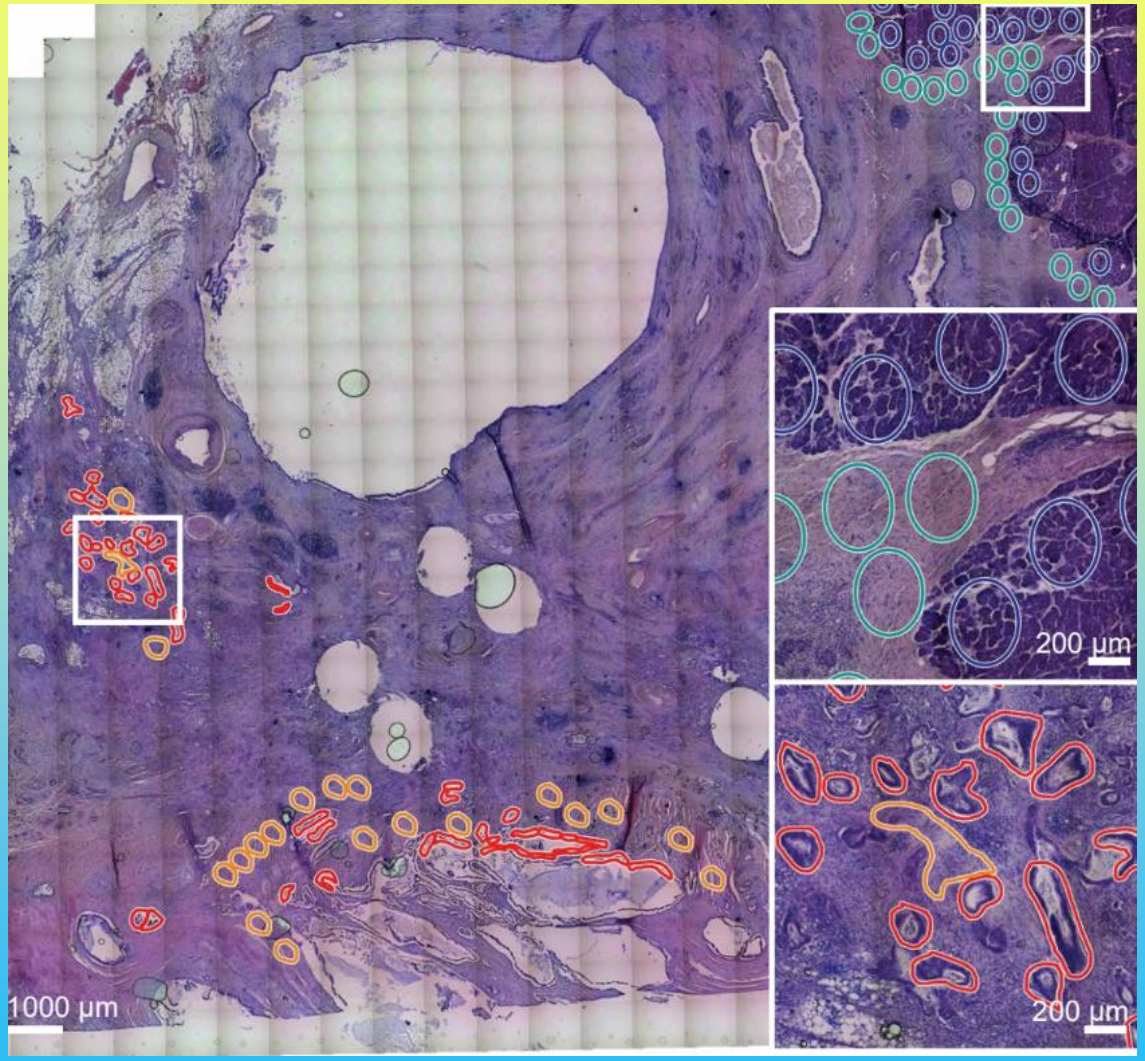




Localization of Gefitinib “IRESSA”& Ipratropium



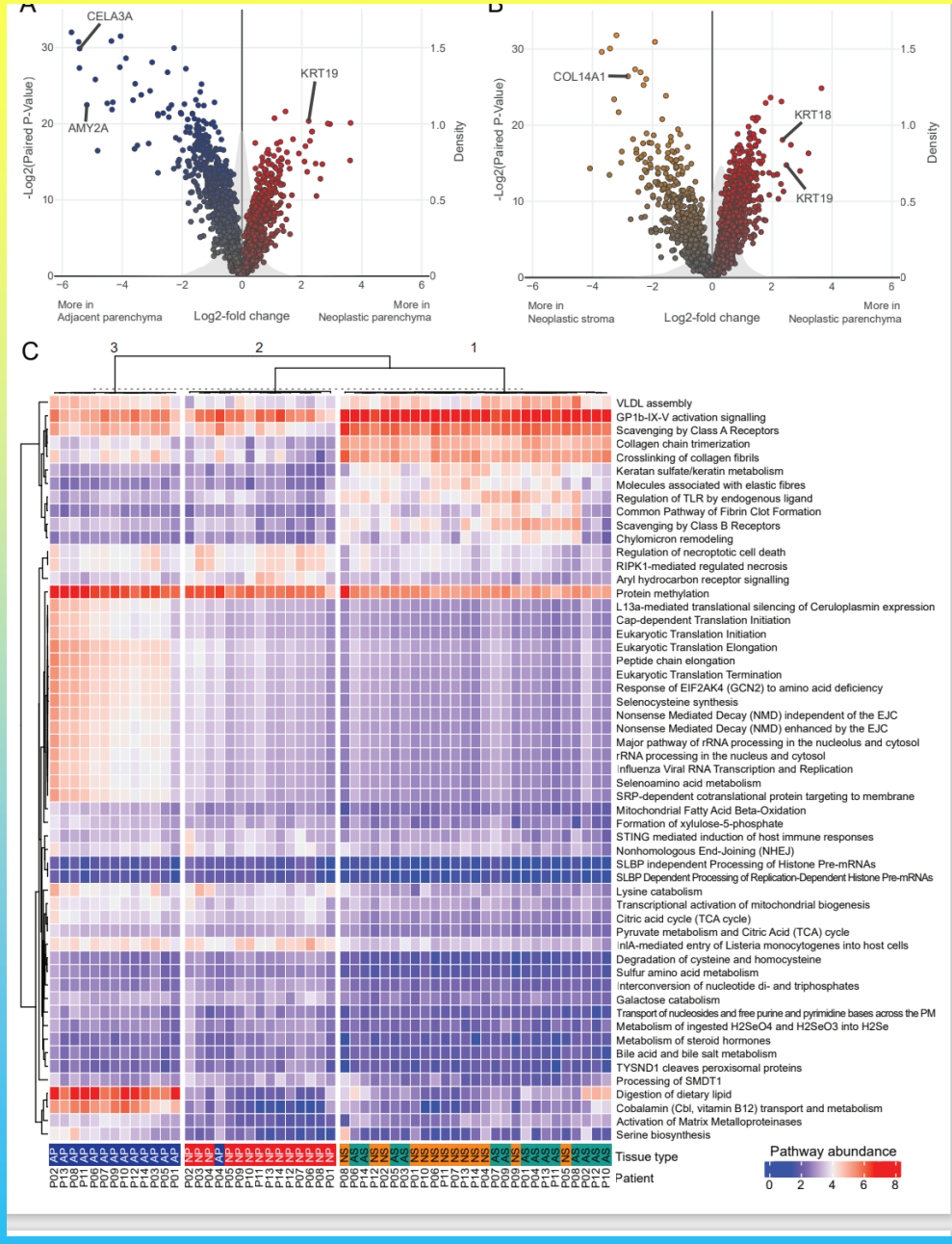
Pancreatic Cancer – Targeting Single Cell isolations



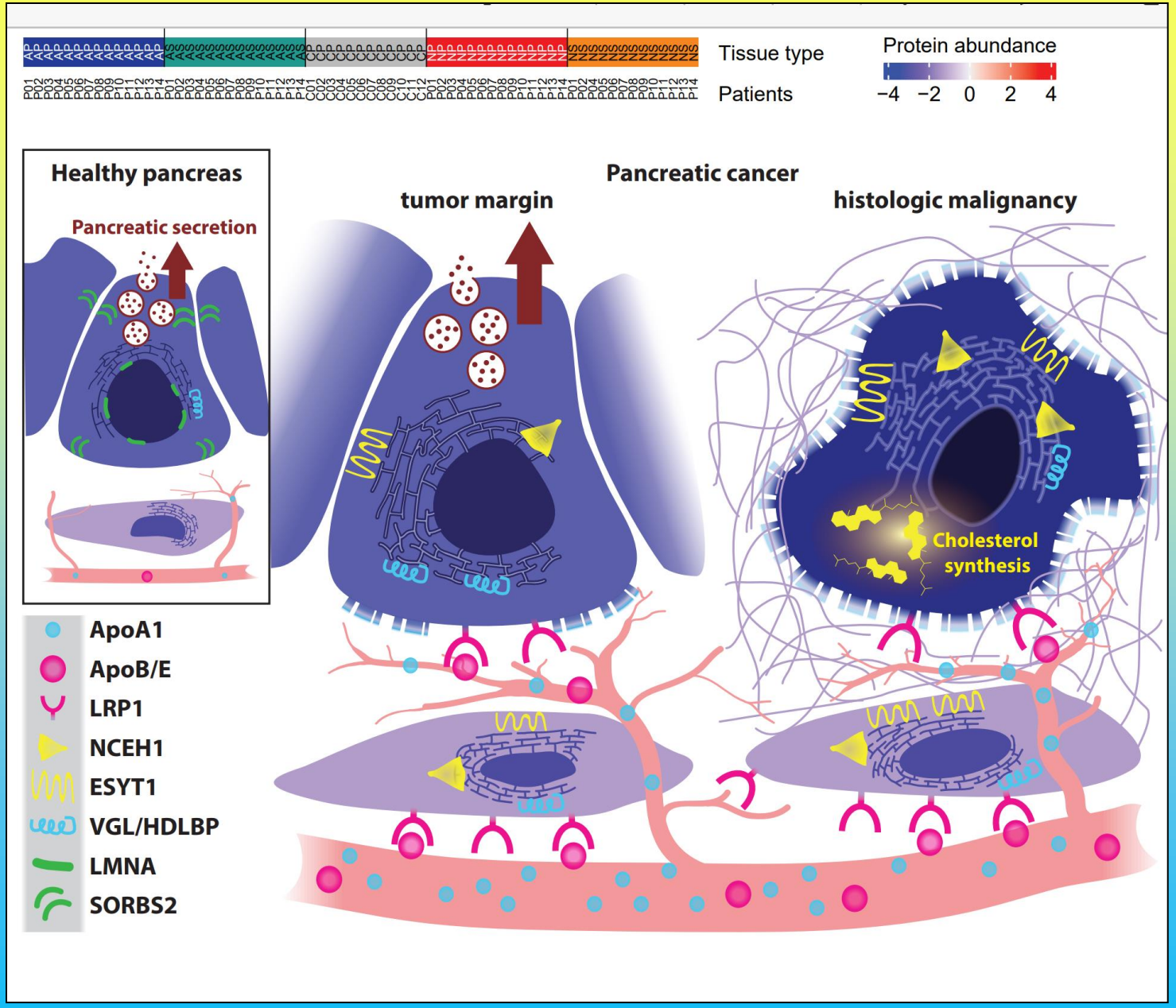
Pirhonen et al., Cancer Res 2022

Regions Distant from malignant cells already display Protein Expression **Changes**

<u>Related to lipid transport and metabolism</u>



Pancreatic Metabolicalic Cross-Talks with its Environment



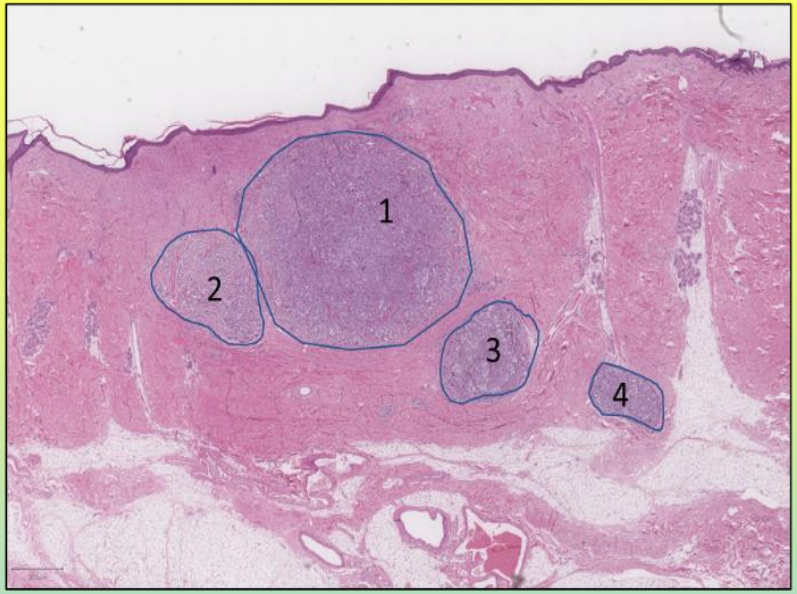
Discovery within the Study with Impact *NOVELTY*

***Deep Proteomic Analyses from diagnostic specimens of operable, treatment naïve PDAC patients**

***Widespread Downregulation of Pancreatic Secretory Functions Paralleled by High Cholesterol Biosynthetic activity**

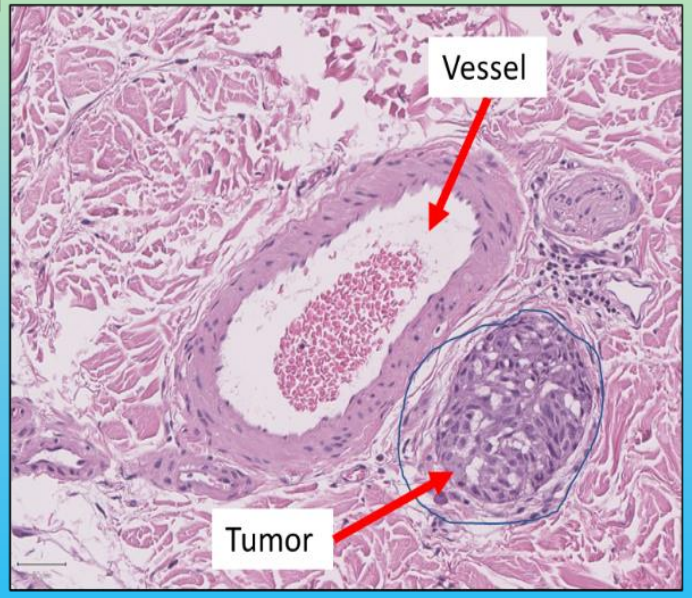
***Lack of Prominent Lipid Storage in the Neoplastic Cells**

TARGETING Clone Heterogeneity – Melanoma Primary Tumor

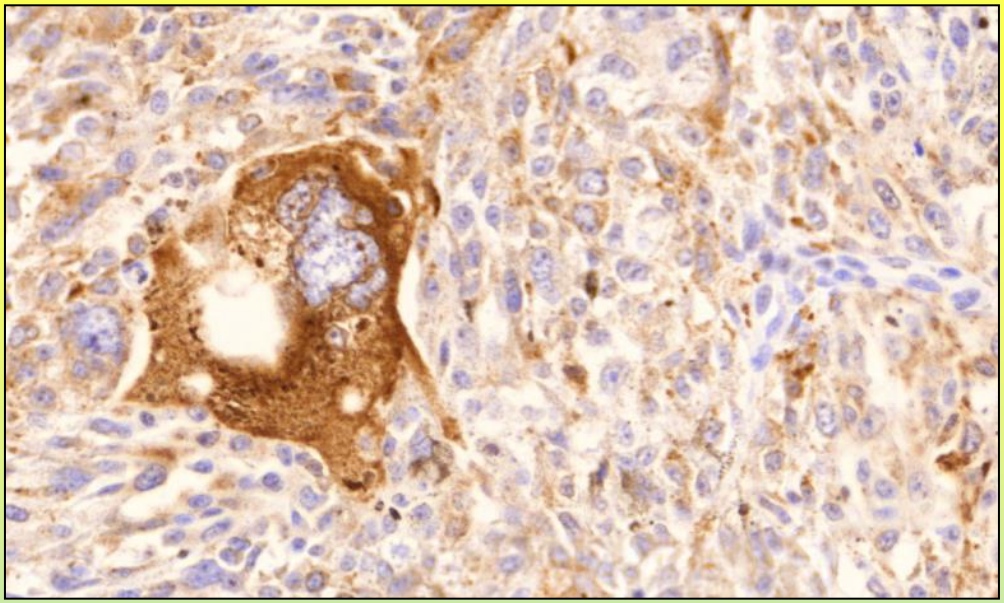


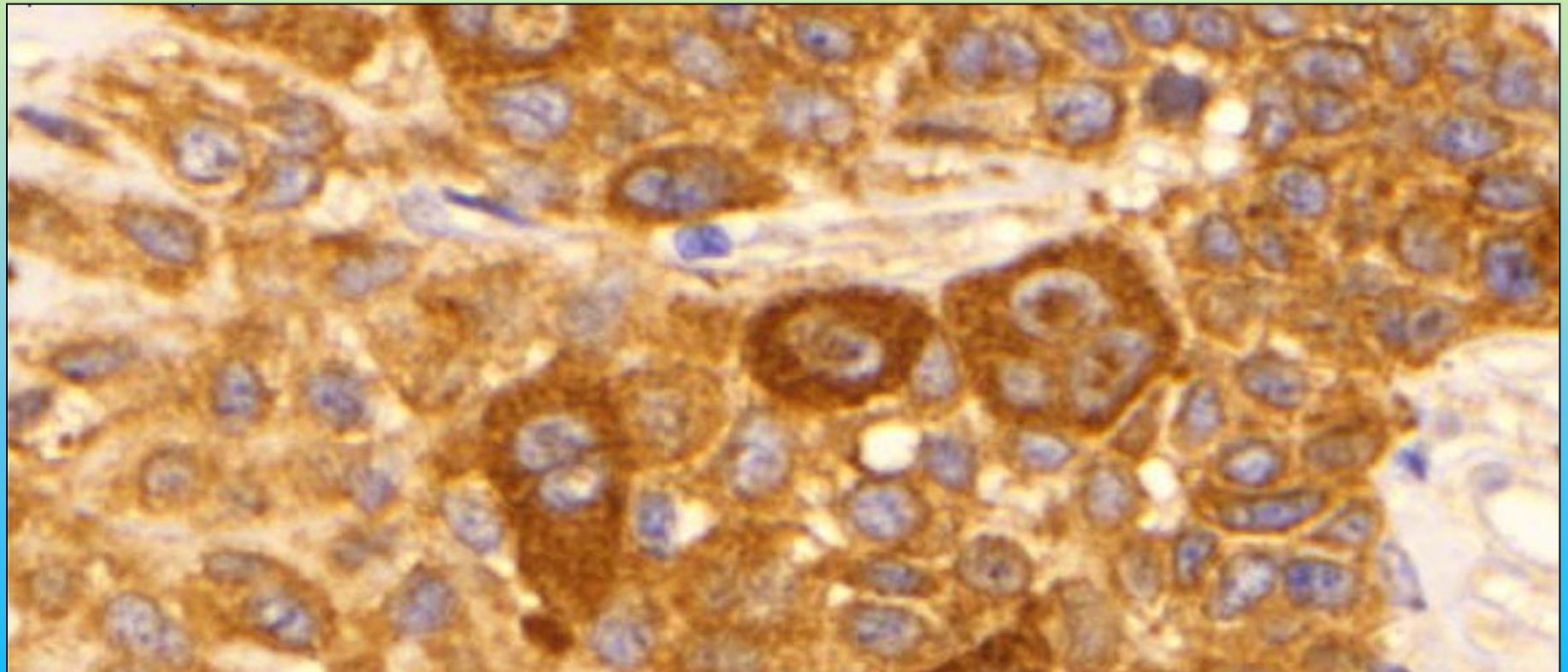
“Our New Direction”

Followig Patient Relapses



Tumor Heterogeneity Adressing Single Cells/Clones





In Summary

- Protein Functionality and variants thereof is KEY in Cancer treatment
- Drug Imaging by MS and Single Cell resolution – FDA standard
- Tumor Clone disposition is a Future focus for improved patient outcome
- Current work: adding digital pathology layers and AI-based characterization – provide complement understanding – improved treatment

European Cancer Moonshot

@europeancancermoonshotlund

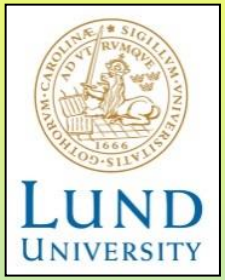
@europeancancermoonshot

@CancerLund

European Cancer Moonshot Lund

www.cancermoonshotlund.com

Funding & Support



Fru Berta Kamprad Stiftelse

THE WALL STREET JOURNAL.

Coal's Decline Spreads Far Beyond Appalachia

Democrats Seek Upset in South Carolina Special Election

Senate GOP Plans Health-Care Vote Next Week

BREAKING NEWS U.K. charges Barclays, four former executives with fraud related to crisis-era fundraising with Qatar

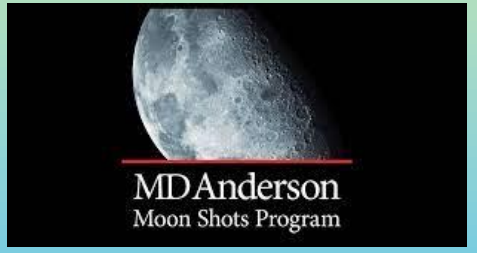
THE EXPERTS

Why the 'Moon Shot' to Cure Cancer Might Work

Feb 17, 2016 7:00 am ET

ATUL GROVER: Widespread praise for Vice President Joseph Biden's "Moon Shot to Cure Cancer" is another positive development

Recommended Videos



Thank You
For
Your attention