



tebubio

Facilitators of Life Sciences Research

Decoding the Tumor Microenvironment: Advanced Proteomics for Biomarker Discovery & Immunotherapy Insights

Dr Valerie Jones

Sales, Marketing & Technical support Director @ RayBiotech



Our Team Today



Speaker

Valerie Jones , PhD

Sales, Marketing & Technical support
Director @ Raybiotech



Session Moderator

Frédéric Samazan

Event Manager

Webinar Agenda

1. | Tebubio at a glance
2. | Speaker Introduction
3. | Raybiotech presentation

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We facilitate Life Sciences Research everyday

and contribute to a brighter future



We are Pan-European

- Founded in 1953
- Family-owned
- 100+ Employees
- Local offices across Europe



We Act for Life Sciences

- Innovation is in our DNA
- Contract Research Services Lab
- Part of EU Life Sciences ecosystems



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- Ethical, compliant and transparent sourcing (from OEMs only)
- Animal welfare policy
- Corporate Social Responsibility (ISO 14001 / ISO 9001, Decarbonation Program)

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Based in Europe

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A **PhD project manager** ensures the success of your project from A to Z.

Strong expertise in Life sciences

- **RNA based** therapeutic discovery
- **in vitro** modeling
- **Biomarker** mapping
- **Data analysis**

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- **Sourcing outside** existing suppliers
- **Warehousing** services

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Tailored agreements

From specific **one-off terms** to **procure-to-pay**, supported by **e-procurement** solutions.

Tebubio CRS : Facilitators of Life Sciences Research

What do you want to talk about?



RNA based therapeutic
discovery

Production | Delivery | Expression



in vitro modeling

Organoids | Microfluidics | 2&3D
Models



Biomarker mapping

Target identification | Profiling |
Quantification



Data analysis

Biostatistics | NGS | Custom

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Our Speaker



Speaker

Valerie Jones , PhD

Sales, Marketing & Technical support
Director @ Raybiotech

- Dr. Valerie Jones, PhD, has a background in protein biochemistry, enzymology, and experimental pathology. Prior to joining RayBiotech, she received her post-doctoral training at Emory University where she was awarded an NRSA (National Research Service Award) grant through the National Institutes of Health to support her research on host-pathogen interactions within the intestinal epithelium.
- Prior to this, she earned her Ph.D. in Biochemistry from Louisiana State University with a focus on the enzyme kinetics of biotin carboxylase.
- At RayBiotech, she serves as Director of Sales, Marketing, and Technical Support. In her current position, Dr. Jones has been instrumental in elucidating complex biotechnological concepts, and her efforts contribute significantly to RayBiotech's mission of advancing proteomic research and applications.

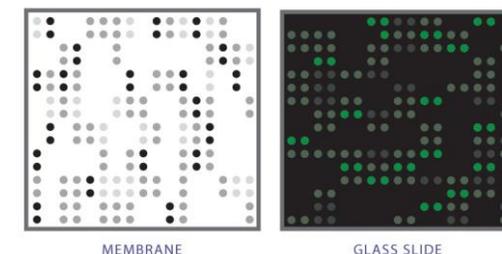
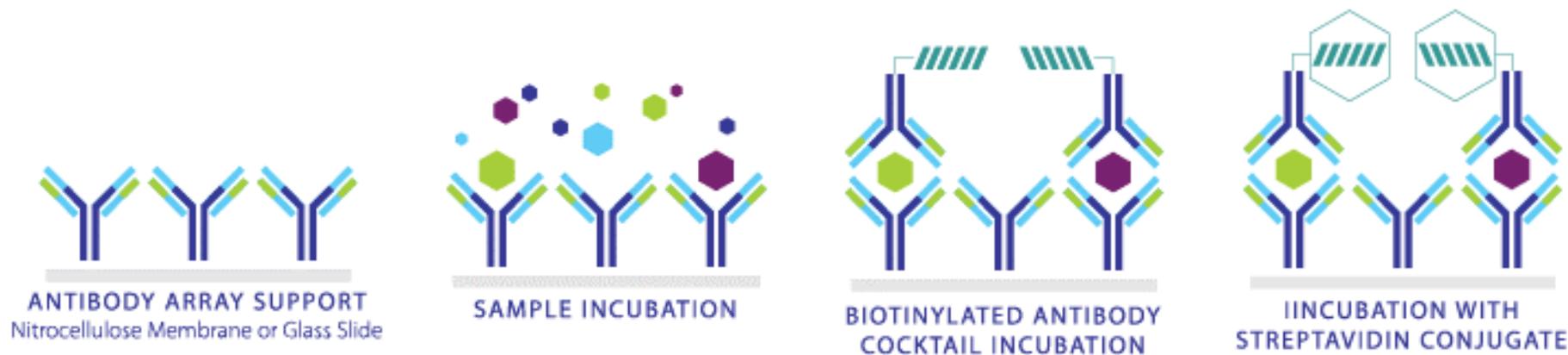
Webinar Agenda

1. | Tebubio at a glance

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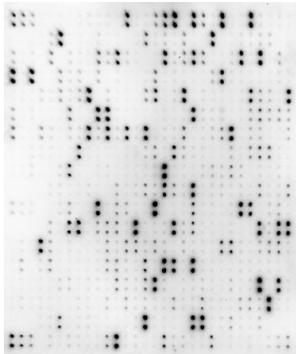
RayBiotech antibody arrays: how they work



- Allow for efficient, non-biased identification of protein profiles
- Objective screens for precise identification of key pathways and biomarkers in cancer biology
- Can be quantitative or semi-quantitative
- Antibody panels can be small & focused (10-100 proteins) or high-density (up to 8000 proteins)

Antibody Array Formats

Membrane



- Easy to handle
- Chemiluminescent detection
- Semi-quantitative

1 ml

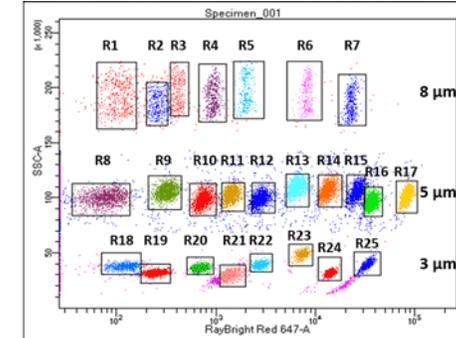
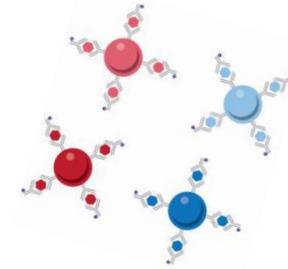
Glass Slide



- Miniaturized – saves sample
- Fluorescent detection (scanner)
- Quantitative or semi-quantitative

100 μ l

Fluorescent Microspheres



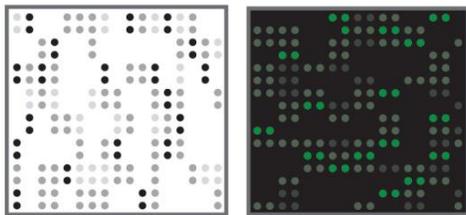
- Low sample consumption
- Fluorescent detection (flow cytometer)
- Quantitative

25 μ l

RayBio[®] Array Technologies

Unmatched content in multianalyte immunodetection

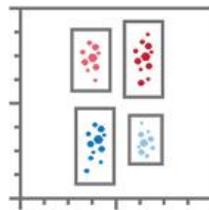
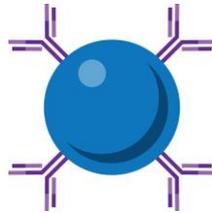
PLANAR ARRAYS



MEMBRANE

GLASS SLIDE

BEAD ARRAYS

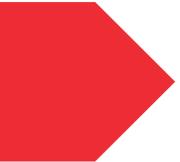


RayPlex[®]

> 700 array panels in-stock for finding

- Cytokine profiles
- Autoantibody profiles
- Protein-protein interactions
- Pathway activation
- Post-translational modification profiles

25,000 publications since 2001



How do antibody arrays help?

1. An affinity proteomic tool: Most **cost-effective** way to profile protein expression precisely
2. A screening tool: Keeps you from missing something important
3. A hypothesis generation tool: determine **where to focus next**.
4. Sensitive enough to detect many clinically relevant proteins
5. Efficient: No sample depletion required

Array Categories

Screening Arrays



1200-8000 analytes

Proteome profiling:
Unbiased queries

Targeted Arrays



10-500 analytes

Probe a **specific** pathway or
molecule type:
Hypothesis-driven queries

PTM Arrays



500-8000 analytes

Post-translational
modification profiling:
Unbiased queries

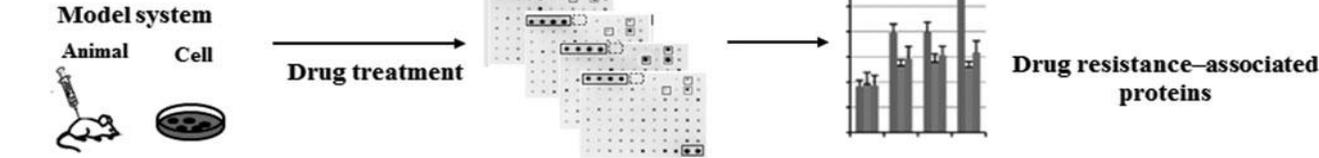
Paths to Advancement

- In Vitro Models
- Animal Models
- Clinical Trials

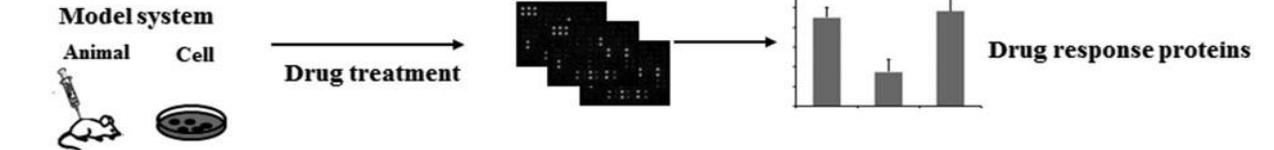
1. Identify right target



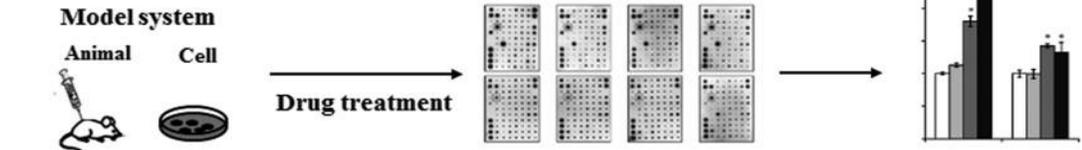
2. Drug resistance



3. Drug action



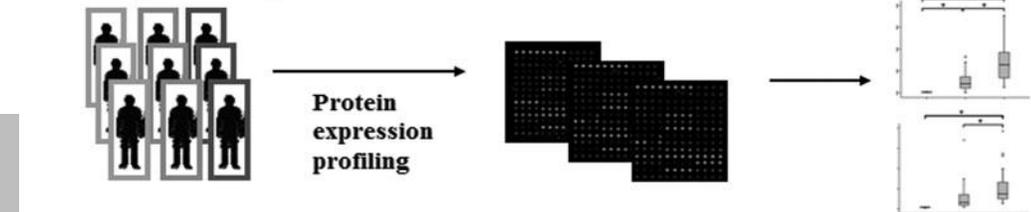
4. Drug side effects



5. Clinical trials

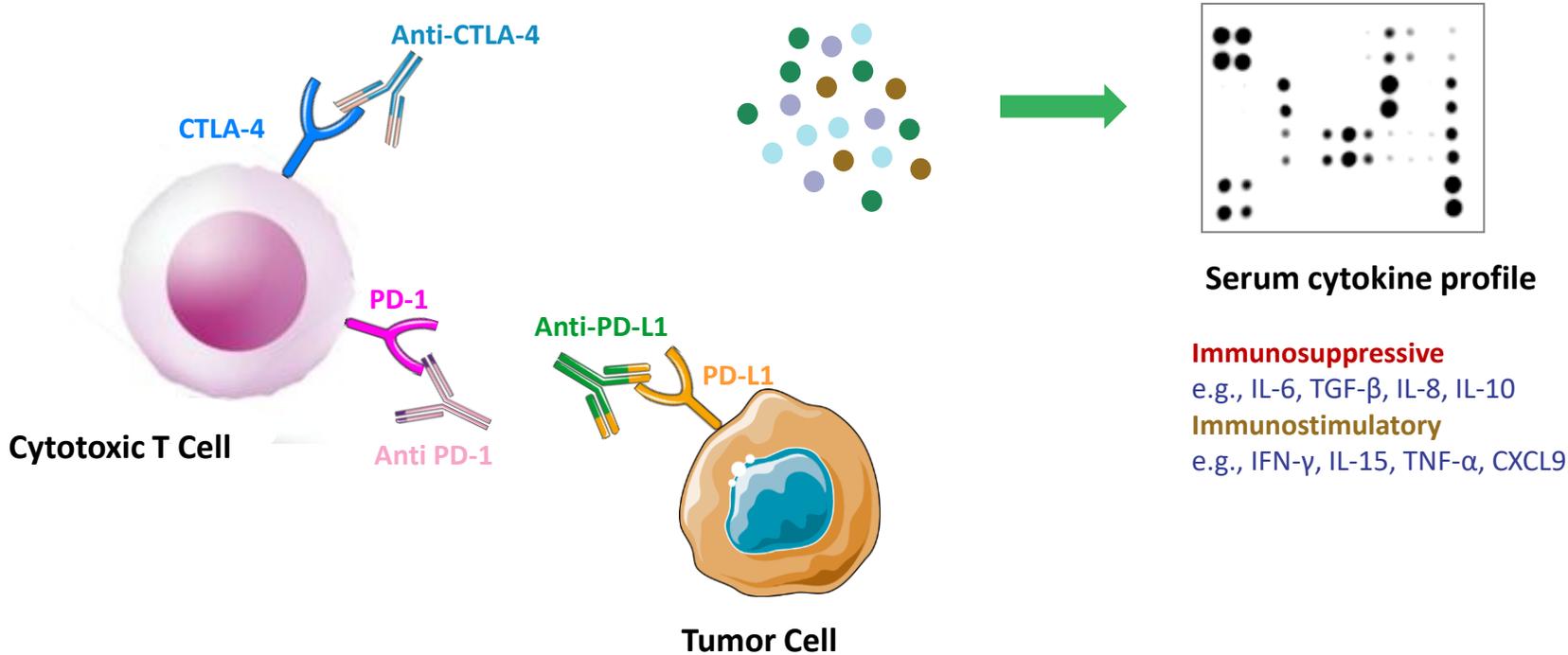


6. Management of patients care



Predicting Immunotherapy Outcomes

How do we distinguish ICT responders from non-responders?

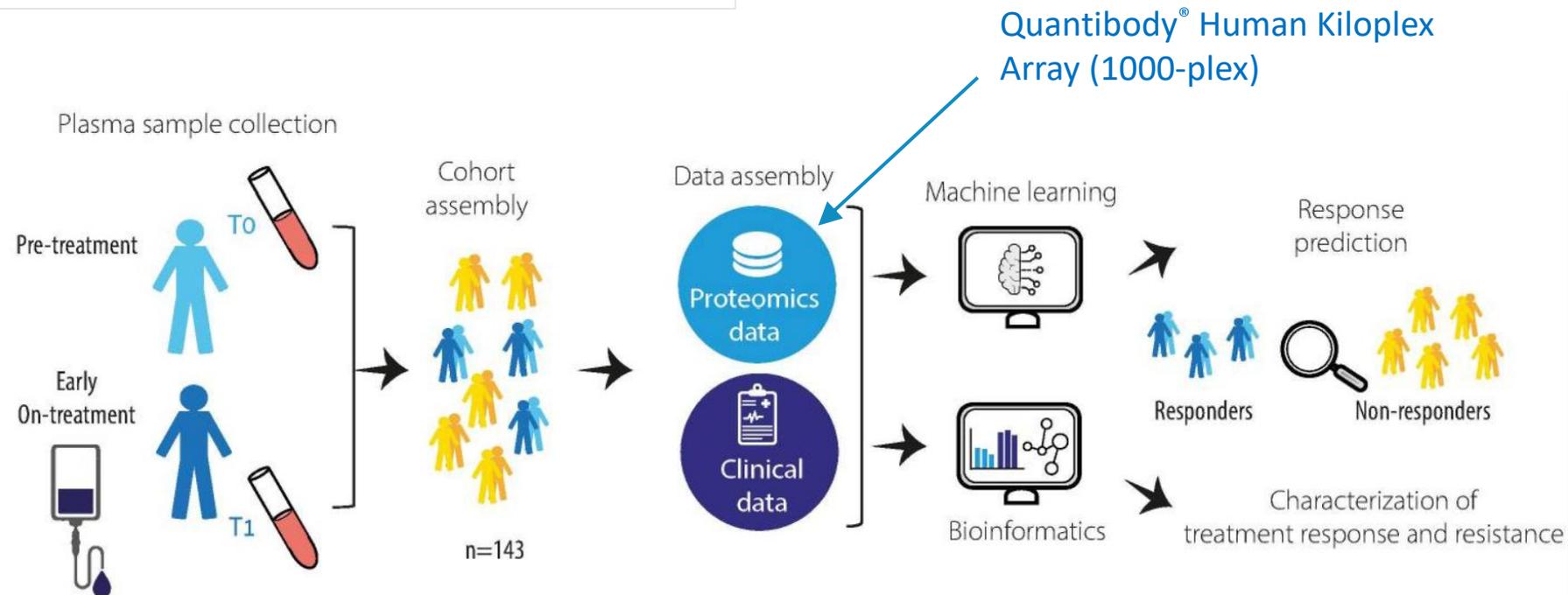


Longitudinal plasma proteomic profiling of patients with non-small cell lung cancer undergoing immune checkpoint blockade

Michal Harel,¹ Coren Lahav,¹ Eyal Jacob,¹ Nili Dahan,¹ Itamar Sela,¹ Yehonatan Elon,¹ Shani Raveh Shoval,¹ Galit Yahalom,¹ Iris Kamer,² Alona Zer,³ Ofer Sharon,¹ David P Carbone,⁴ Adam P Dicker,⁵ Jair Bar,^{2,6} Yuval Shaked ⁷

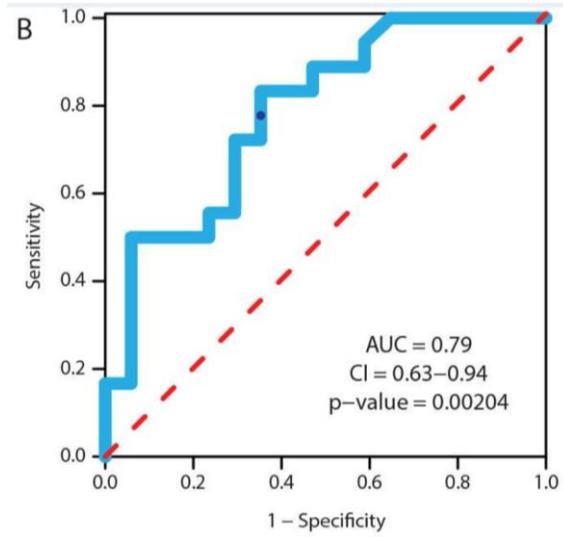
Problem:

ICI therapy achieves only 20-50% response rate in NSCLC patients. Might therapy resistance be predicted prior to treatment?



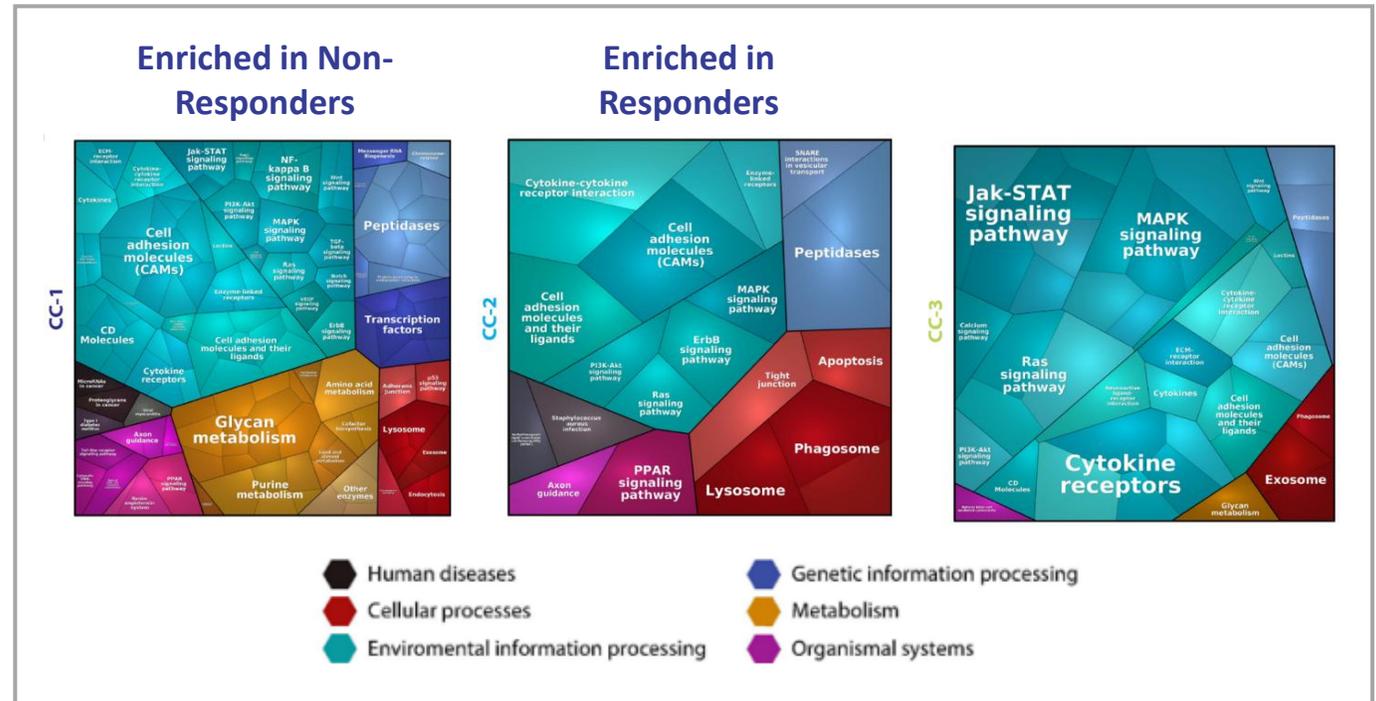
Plasma proteomes were collected longitudinally from 143 NSCLC patients treated with anti-PD-1/PD-L1.

CXCL8 and CXCL10, along with sex and age, predicts clinical outcome.



AUC = 0.79

Functional groups of proteins for each patient consensus cluster (CC) at T1



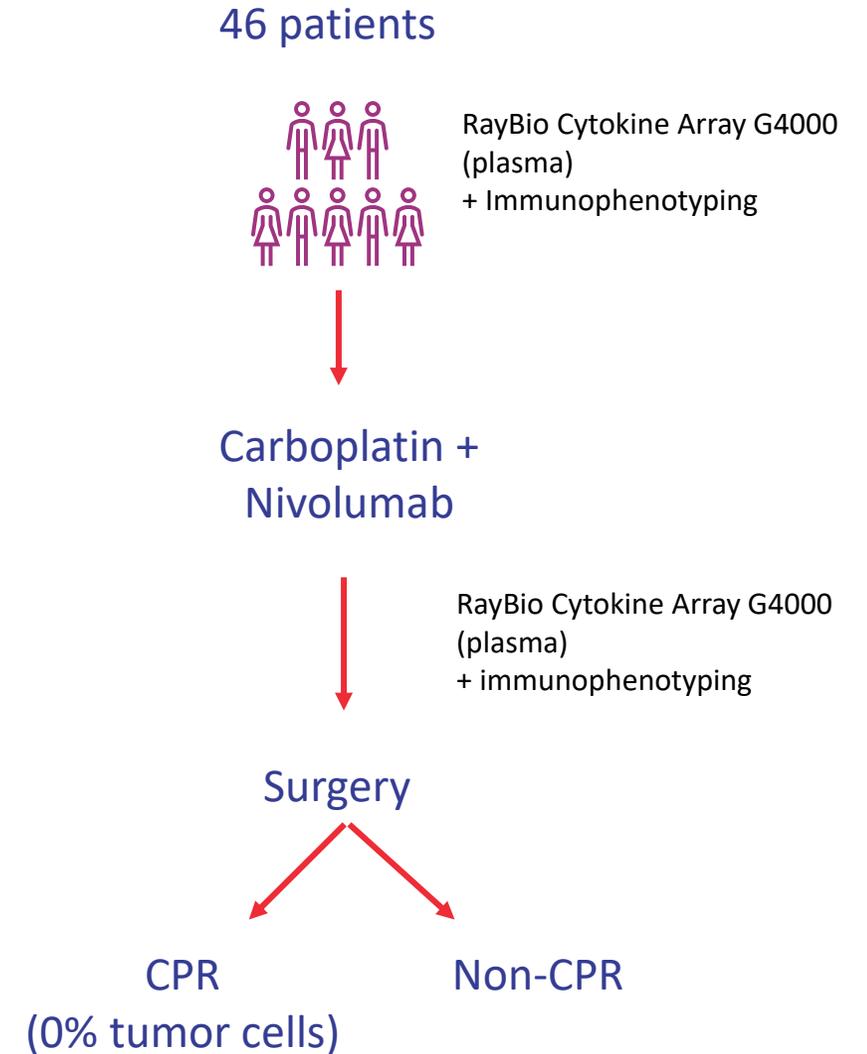
Non-responders:

- ↑ expression of neutrophil proteins (GRO, PLAUR, PILRA) tied to immune evasion pathways (MAPK, NF-κB, JAK-STAT)
- Enriched in cell proliferation and immunosuppression promoting proteins (e.g. pyrimidine metabolism)

Blood biomarkers associated to complete pathological response on NSCLC patients treated with neoadjuvant chemoimmunotherapy included in NADIM clinical trial

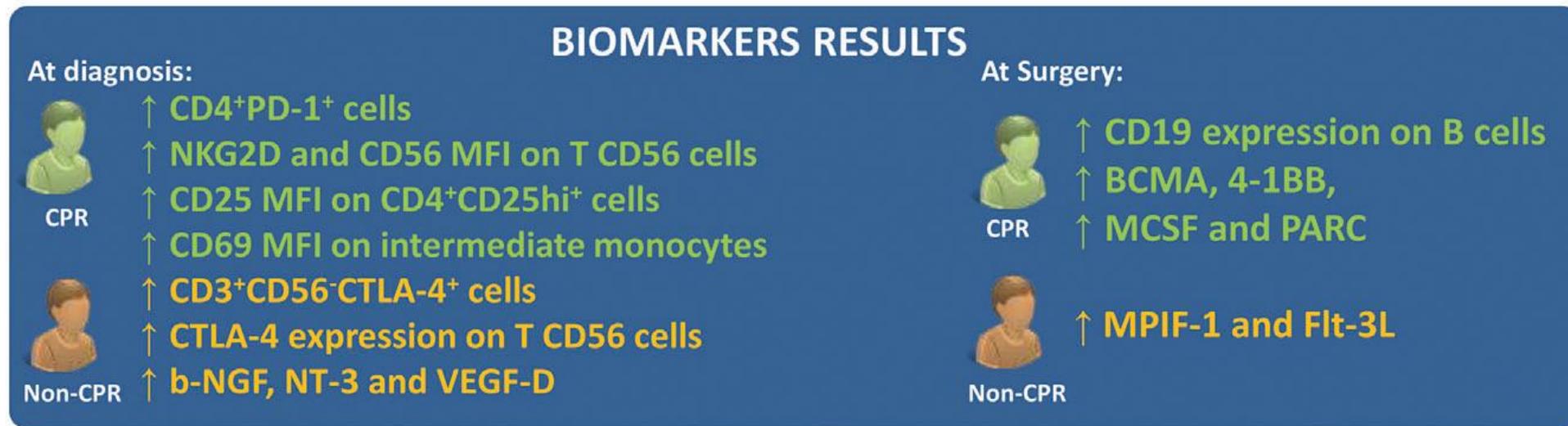
Problem:

Current biomarkers for monotherapy (TMB; PD-L1 TPS) may be useless for predicting CPR in neoadjuvant therapy (chemo + immunotherapy).



Complete response predicted by a less immunosuppressive cytokine profile

At baseline, CPR patients had lower levels of neurotrophins and VEGF-D, indicating a less suppressive immune environment.



CPR patients exhibited enhanced anti-tumor responses through immune reprogramming

communications biology

ARTICLE



<https://doi.org/10.1038/s42003-022-04403-8>

OPEN

TLR5 agonists enhance anti-tumor immunity and overcome resistance to immune checkpoint therapy

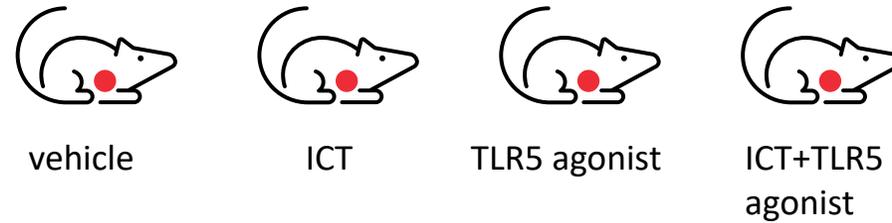
Caleb Gonzalez¹, Sarah Williamson¹, Seth T. Gammon ¹, Sarah Glazer¹, Joon Haeng Rhee ² & David Piwnica-Worms ¹✉

Problem:

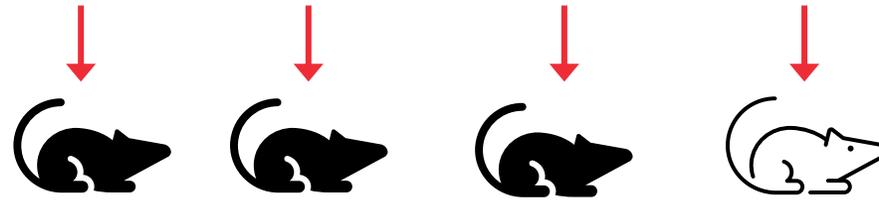
ICT resistance in triple-negative breast cancer and melanoma.

Can a TLR5 agonist enhance survival when combined with anti-CTLA-4 or PD-1?

Syngeneic 4T1 mammary carcinoma / B16-F10 melanoma murine models



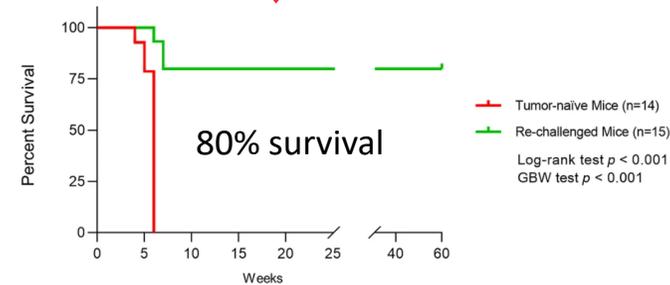
Mouse 32-plex (serum) + tumor infiltrate profiling



20-25% survival

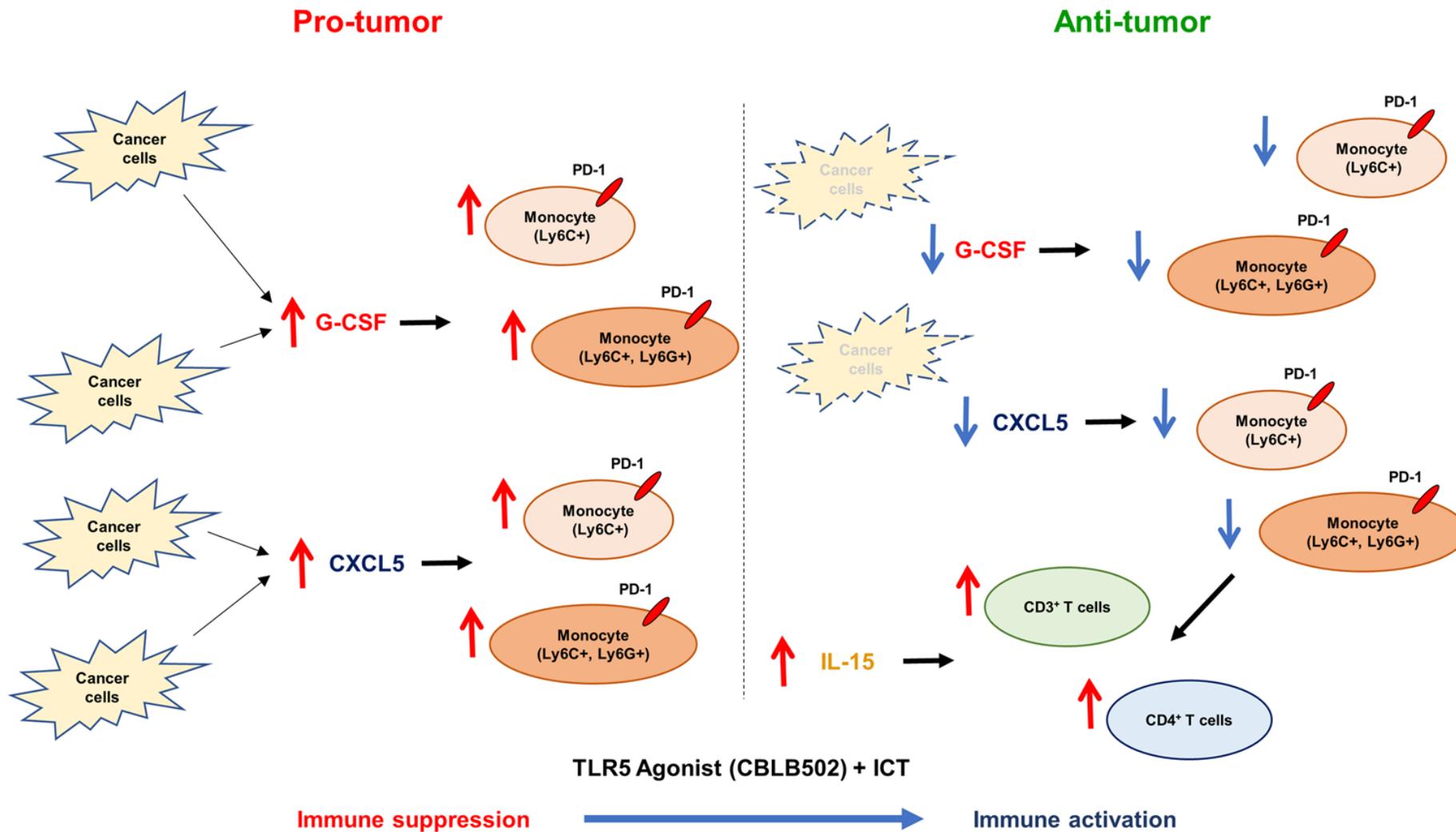
Tumor re-challenge

Mouse 32-plex (serum) + tumor infiltrate profiling



ICT = anti-PD-1 + anti-CTLA-4

TLR5 agonist = flagellin or CBLB502



Combined treatment shifts the tumor microenvironment from immune suppression to immune activation.

Biomarker Studies

 | Frontiers in **Immunology**

Biomarkers in the early stage of PD-1 inhibitor treatment have shown superior predictive capabilities for immune-related thyroid dysfunction

Jinyu Liu¹, Mengli Chen¹, Shu Li¹, Le Cai¹, Liang Ma¹, Qiuliang Yang², Xiaoxuan Zhang¹, Nan Bai¹, Xiaodong Wu³, Zhihui Tang¹ and Tianlin Wang^{1*}



Cytokine

Volume 125, January 2020, 154810



Extensive serum cytokine analysis in patients with prostate cancer

Daoyuan Gong^{a,1}, Yunuo Wang^{b,1}, Yong Wang^{a,1}, Xin Chen^a, ShenYuan Chen^a, Ruixue Wang^a, Lian Liu^a, Chaohui Duan^{d,e,f,g,h}, Shuhong Luo^{a,i,j}

Cancer Medicine

Open Access

ORIGINAL RESEARCH |  Open Access |  

Serum biomarker panels for the diagnosis of gastric cancer

Dan Wu, Pinglu Zhang, Ji Ma, Jinbo Xu, Li Yang, Weidan Xu, Haifeng Que, Meifen Chen , Hongtao Xu 

First published: 14 March 2019 | <https://doi.org/10.1002/cam4.2055> | Cited by: 1

Autoantibody Signatures as a Biomarker Panel for the Detection of Nasopharyngeal Carcinoma

Qian-Ping Shi,^{a,b,c} Xuan Wang,^{a,c} Zhi-Xi Liu,^{a,b,c} Jian-Jun Zhang,^{b,1,*} and Zhao-Yang Wang^{d,1,**}

^aKey Laboratory of Molecular Biology in High Cancer Incidence Coastal Chaoshan Area of Guangdong Higher Education Institutes, Shantou University Medical College, Shantou, Guangdong, China, 515041

^bDepartment of Preventive Medicine, Shantou University Medical College, Shantou, Guangdong, China, 515041

^cDepartment of Biochemistry and Molecular Biology, Shantou University Medical College, Shantou, Guangdong, China, 515041

^dDepartment of Radiation Oncology, Shenzhen People's Hospital, Second Clinical Medicine College of Jinan University, Shenzhen, Guangdong, China,

Clinical Proteomics

REVIEW

Open Access



Circulating proteins as predictive and prognostic biomarkers in breast cancer

Hugo Veysi re^{1,2,3}, Yannick Bidet^{1,5†}, Frederique Penault-Llorca^{1,6}, Nina Radosevic-Robin^{1,6††} and Xavier Durando^{1,2,3,4†}

Cancer Prevention Research

Research Article

Simultaneous Measurement of 92 Serum Protein Biomarkers for the Development of a Multiprotein Classifier for Ovarian Cancer Detection

Amy P.N. Skubitz, Kristin L.M. Boylan, Kate Geschwind, Qing Cao, Timothy K. Starr, Melissa A. Geller, Joseph Celestino, Robert C. Bast Jr., Karen H. Lu, and Joseph S. Koopmeiners

DOI: 10.1158/1940-6207.CAPR-18-0221 Published March 2019 

Mechanisms of Disease or Drug Action

Cell

LETTER

doi:10.1038/nature11183

Tumour micro-environment elicits innate resistance to RAF inhibitors through HGF secretion

Ravid Straussman¹, Teppei Morikawa², Kevin Shee¹, Michal Barzily-Rokni¹, Zhi Rong Qian², Jinyan Du¹, Ashli Davis¹, Margaret M. Mongare¹, Joshua Gould¹, Dennie T. Frederick³, Zachary A. Cooper³, Paul B. Chapman⁴, David B. Solit^{4,5}, Antoni Ribas^{6,7}, Roger S. Lo^{7,8}, Keith T. Flaherty³, Shuji Ogino^{2,9}, Jennifer A. Wargo³ & Todd R. Golub^{1,10,11,12}

Microenvironment and Immunology

Cancer Research

Gr-1+CD11b+ Myeloid Cells Tip the Balance of Immune Protection to Tumor Promotion in the Premetastatic Lung

Hannah H. Yan¹, Michael Pickup^{2,4}, Yanli Pang¹, Agnieszka E. Gorska^{2,4}, Zhaoyang Li¹, Anna Chytil^{2,4}, Yipeng Geng^{2,3}, Jerome W. Gray³, Harold L. Moses^{2,4}, and Li Yang¹

Metformin and simvastatin exert additive antitumour effects in glioblastoma via senescence-state: clinical and translational evidence

Antonio C. Fuentes-Fayos^{a,b,c,d,*}, Miguel E. G-García^{a,b,c,d}, Jesús M. Pérez-Gómez^{a,b,c,d}, Antonio J. Montero-Hidalgo^{a,b,c,d}, Julia Martín-Colom^{a,b,e}, Carlos Doval-Rosa^{a,b,e}, Cristóbal Blanco-Acevedo^{a,b,e}, Encarnación Torres^{a,b,c,d}, Álvaro Toledano-Delgado^{a,b,e}, Rafael Sánchez-Sánchez^{a,b,f}, Esther Peralbo-Santaella^{a,g}, Rosa M. Ortega-Salas^{a,b,f}, Juan M. Jiménez-Vacas^{a,b,c,d}, Manuel Tena-Sempere^{a,b,c,d}, Miguel López^{d,h}, Justo P. Castaño^{a,b,c,d}, Manuel D. Gahete^{a,b,c,d}, Juan Solivera^{a,b,e} and Raúl M. Luque^{a,b,c,d,**}



Tumor Self-Seeding by Circulating Cancer Cells

Mi-Young Kim,¹ Thordur Oskarsson,¹ Swarnali Acharyya,¹ Don X. Nguyen,¹ Xiang H.-F. Zhang,¹ Larry Norton,² and Joan Massagué^{1,3,*}

¹Cancer Biology and Genetics Program

²Department of Medicine

³Howard Hughes Medical Institute

Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA

*Correspondence: massagu@mskcc.org

DOI 10.1016/j.cell.2009.11.025

Cancer Cell

Article

Tissue factor is a critical regulator of radiation therapy-induced glioblastoma remodeling



KISS1 tumor suppressor restricts angiogenesis of breast cancer brain metastases and sensitizes them to oncolytic virotherapy in vitro

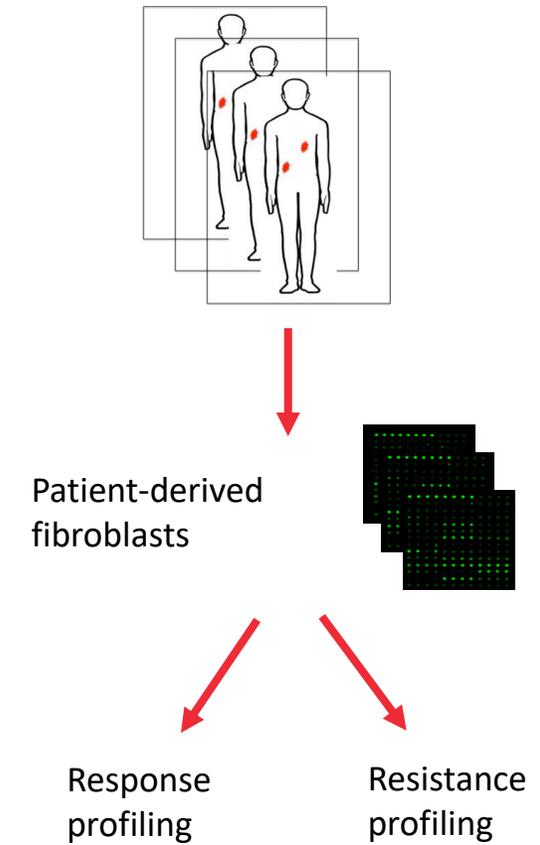
Mikhail E. Platonov, Anton V. Borovjagin, Natalya Kaverina, Ting Xiao, Zaira Kadagidze, Maciej Lesniak, Marya Baryshnikova, Ilya V. Ulasov.

Cancer Cell

Article

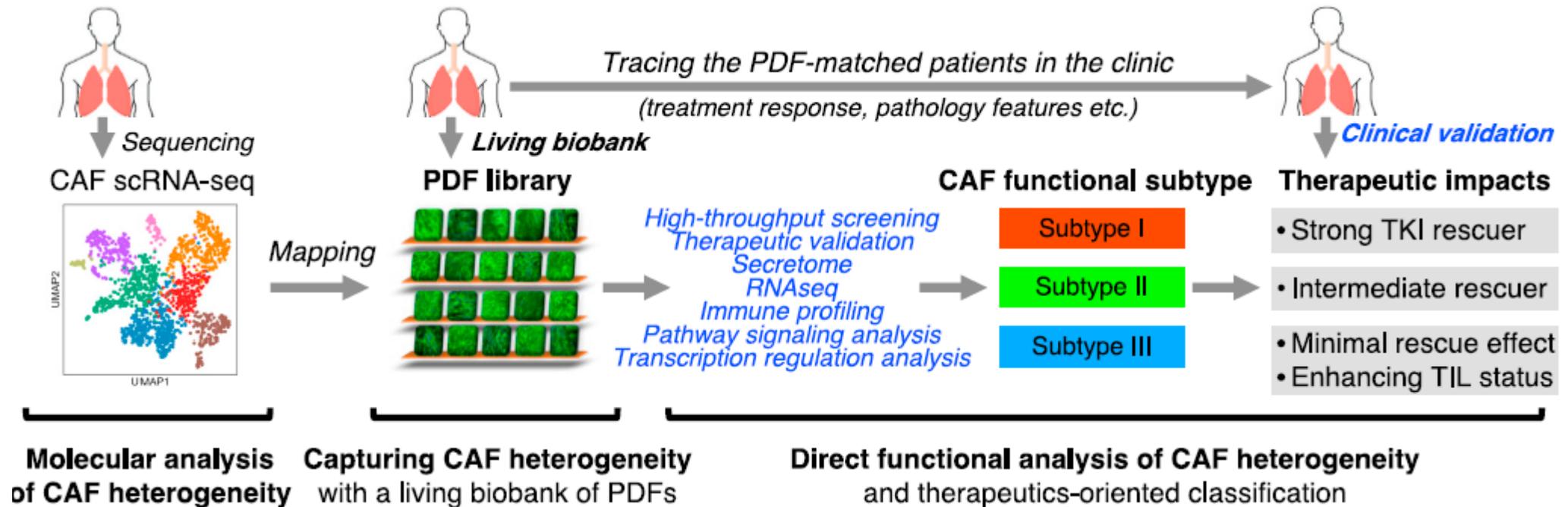
Three subtypes of lung cancer fibroblasts define distinct therapeutic paradigms

Can CAF phenotypes reveal distinct clinical patient responses to targeted therapies?



Subtype I: HGF and FGF7 are upregulated
Subtype II: Only FGF7 is upregulated
Subtype III: Neither is upregulated

CAF secretomes: mapping patients' clinical response to targeted therapy



For large arrays, we recommend service

- **Tebubio** serves researchers throughout Europe with local offices in France, Belgium, U.K, Spain, Portugal, Italy, Germany, Netherlands, and Nordics



thank you for your attention



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Facilitators of Life Sciences Research