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Backing visionary entrepreneurs

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2023 EIC Accelerator Challenge:

Novel biomarker-based assays to guide personalised cancer treatment

3 February 2023

Iordanis Arzimanoglou, EIC Programme Manager for Health and Biotechnology

Table of Contents

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EIC Accelerator Challenge Call

Scope

(EIC Work Programme 2023 pg.83)

European innovation Council

To bring new effective biomarkers (predictive and prognostic) at clinical stage, in order to then be used for biomarker-guided cancer treatment, eventually leading to improved efficacy of current or new treatment (new therapeutic protocols) against refractory cancers

EIC Accelerator Challenge Call

Key objectives

(EIC Work Programme 2023 pg.83)

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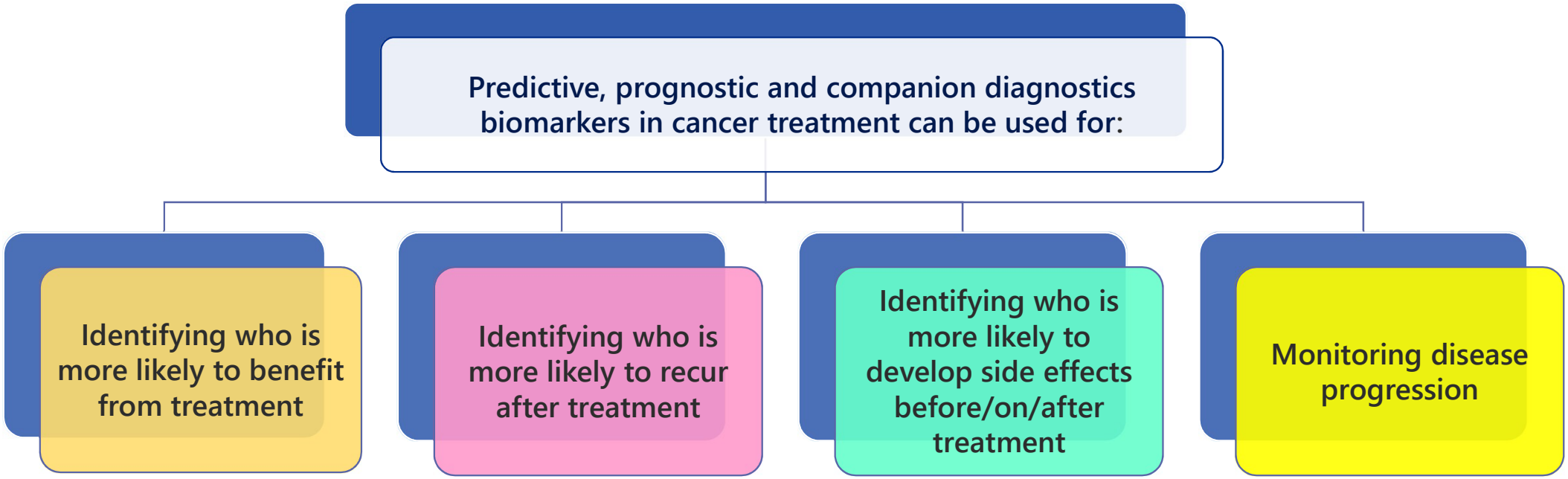

EIC Accelerator Challenge Call

Expected Impact (I)

(EIC Work Programme 2023 pg.84)

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Clinical establishments

Bio-Industry

Bio-Investment world

- Through the work to be funded with this Call, we expect to gain critical insights how to design novel and effective ways to predict, monitor and guide Ca treatment to patients afflicted by refractory cancers
- All the above three sectors will benefit in one way or another, from the novel biomarker assays to guide and monitor cancer treatment

EIC Accelerator Challenge
Expected Clinical Impact (II)
(EIC Work Programme 2023 pg.84)

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Expected outcomes from this Challenge:

Clinicians will be able to identify:

- Who among cancer patients, is more likely to benefit from a given treatment (guided treatment)
- Who among patients with potentially precancerous lesions, is more likely to develop cancer
- Who among the cancer patients having underwent treatment, is more likely to recur
- Who among the cancer patients receiving treatment, is more likely to develop side effects as a result of the treatment, affecting their quality of life and
- More effectively monitor the clinical course of the disease.

EIC Accelerator Challenge

Expected industry Outcome and Impact (II)

(EIC Work Programme 2023 pg.84)

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Expected outcome from this Challenge:

EIC biotech portfolio on biomarker guided-cancer treatment

- Despite ample participation of health-tech startups in Health Cluster calls, the outcome of this Challenge-based Call is essential for Europe to establish a globally competitive biotech portfolio composed of startups and scaling up SMEs targeted to novel biomarker-guided cancer treatment
- In addition, the portfolio could set the basis for a future critical mass in this area, potentially leading to gain technological autonomy for Europe in the same area

EIC Accelerator – The evaluation process

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We will help **you** to prepare your **business plan** and draft a **proposal** with AI tool and coaching

You submit your full **proposal** which will be **assessed** by Remote evaluators

You have a disruptive / deep tech **idea** with a potential to **scale up** and you need **financial support**

Tell us your story in 5 pages

You will **pitch** your innovation in front of EIC Jury Members

If selected, you will sign the **contract**

A four-steps process

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Challenges to bring liquid biomarkers in the clinic

https://www.mdpi.com/2075-4418/12/3/748/htm

Liquid profiling (LP) enables real-time assessment of tumor mutational profile for clinical management of cancer patients. However, LP is not yet integrated into daily clinical routine to the extent that might be expected due to the lack of:

- Harmonization and standardization of preanalytical and analytical workflows
- The lack of proper quality controls
- Limited evidence of its clinical utility
- Heterogeneous study results
- The uncertainty of clinicians regarding the value and appropriate indications for LP and its interpretation, and finally,
- The lack of reimbursement for most LP tests

Regulatory framework for biomarkers

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https://www.ema.europa.eu/en/glossary/biomarker-qualification

EMA requires qualification of biomarkers

EMA gives opinions on biomarker qualifications

Certification of the acceptability of a biomarker for a specific use in pharmaceutical research and development

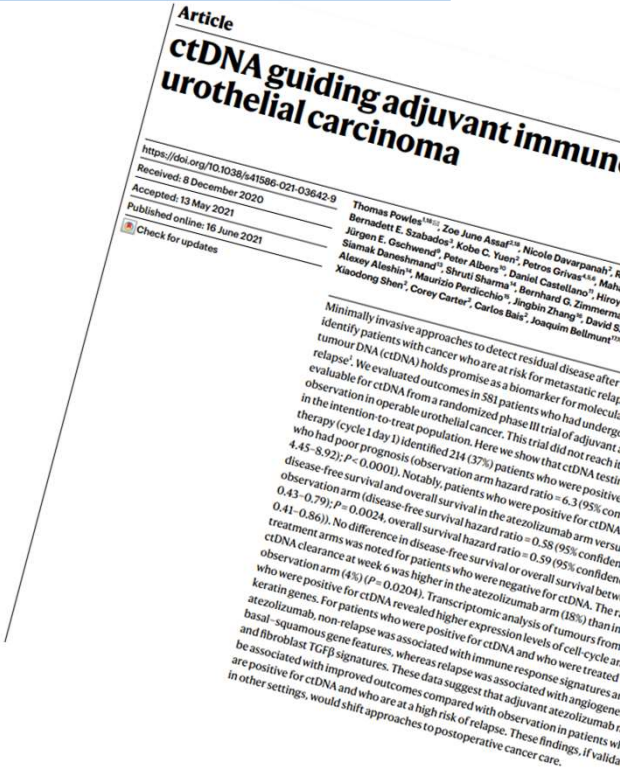
2023 EIC Accelerator Challenge Call
Underpinning Evidence

European Innovation Council

Selected examples of biomarkers under development (predictive, prognostic and companion diagnostics), potentially applicable to guide cancer treatment, in support of this Challenge Call

Tiny amounts of ctDNA can inform about the need for additional treatment in bladder Ca

https://www.nature.com/articles/s41586-021-03642-9


Article

ctDNA guiding adjuvant immun
urothelial carcinoma

https://doi.org/10.1038/s41586-021-03642-9
Received: 8 December 2020
Accepted: 13 May 2021
Published online: 16 June 2021
Check for updates

- Detection of tiny amounts of circulating tumor DNA (ctDNA) to identify the risk of cancer recurrence and guide precision treatment in bladder cancer following surgery.
- Patients with urothelial cancer who had ctDNA fragments that escaped into their bloodstream following surgery to remove their tumor, had a higher likelihood of cancer relapse. These patients could benefit from subsequent treatment with an immunotherapy called atezolizumab.

Underpinning Evidence

Detection of ultra low risk for recurrence would allow breast Ca patients to skip chemotherapy

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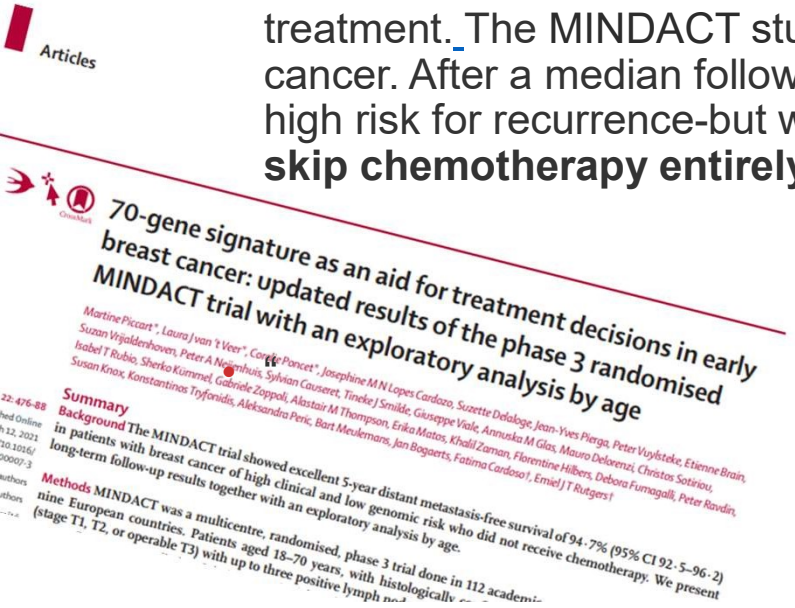
https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045%2821%2900007-3/fulltext

- Through the EU-funded MINDACT trial, Agendia has delivered new data showing its MammaPrint genomic diagnostic can help identify patients at an ultralow risk of recurrence
- 99% of breast cancer patients in this category survived at least 8 years, regardless of other clinical risks-while 97% saw no distant tumor metastases over the same amount of time
- The Ultra Low threshold identifies patients who may be candidates for further de-escalation of treatment. The MINDACT study enrolled nearly 7,000 patients with newly diagnosed breast cancer. After a median follow-up of nearly 9 years, 46% of patients shown to be at a clinically high risk for recurrence-but who had a low-risk result from the MammaPrint **test-were able to skip chemotherapy entirely without hurting their outcome**.


Articles

70-gene signature as an aid for treatment decisions in early breast cancer: updated results of the phase 3 randomised MINDACT trial with an exploratory analysis by age

Summary

Background The MINDACT trial showed excellent 5-year distant metastasis-free survival of 94·7% (95% CI 92·5–96·2) in patients with breast cancer of high clinical and low genomic risk who did not receive chemotherapy. We present long-term follow-up results together with an exploratory analysis by age.

Methods MINDACT was a multicentre, randomised, phase 3 trial done in 112 academi- nine European countries. Patients aged 18–70 years, with histologically (stage T1, T2, or operable T3) with up to three positive lymph

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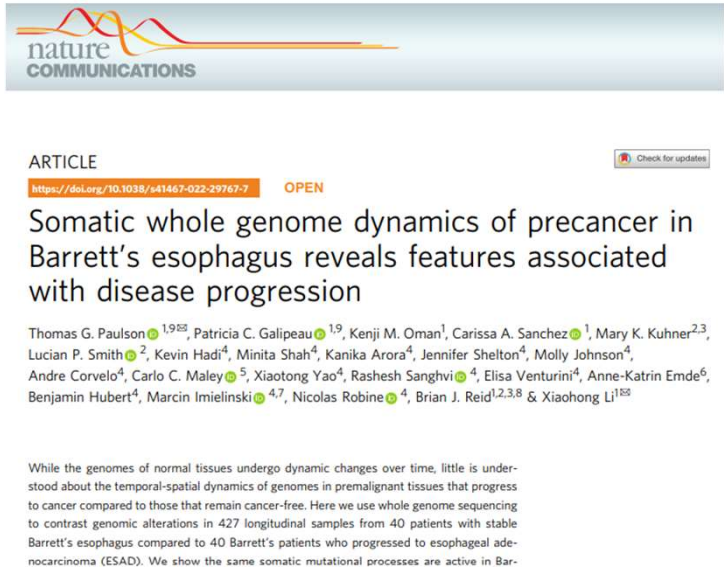
Predictive biomarkers in Barrett's esophagus

https://www.nature.com/articles/s41467-022-29767-7

- WGS to contrast genomic alterations from 40 patients with stable Barrett's esophagus compared to 40 Barrett's patients who progressed to esophageal adenocarcinoma (ESAD)
- It was found that the same somatic mutational pattern (focal chromosomal alterations and similar mutational signatures) were active in Barrett's tissue regardless of outcome
- The critical distinction between stable Barrett's versus those who progress to cancer was the acquisition and expansion of cell populations with TP53−/−, complex structural variants and high-level amplifications, which are **detectable up to six years prior to a cancer diagnosis.**



Underpinning Evidence

Genetic alterations in a single pathology slide using AI can guide cancer treatment

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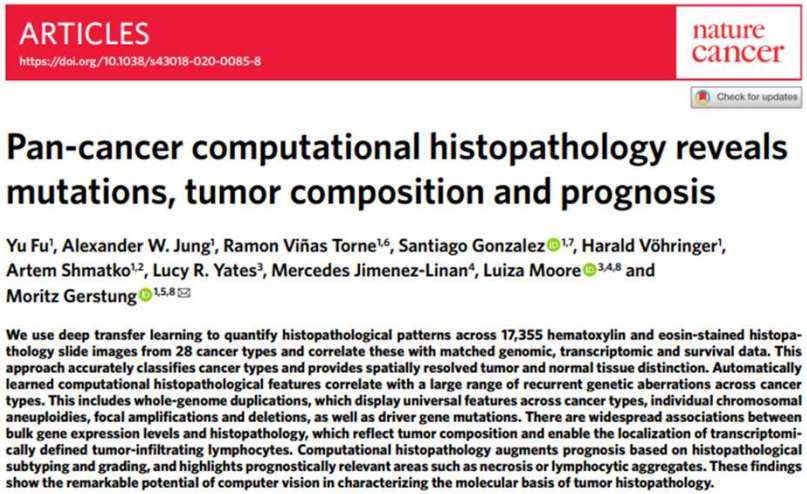
https://www.nature.com/articles/s43018-020-0085-8

- Information gained from accurately screening of cancer patient biopsies for certain genetic alterations may inform about their treatment options and likelihood to respond to specific therapies



ARTICLES
https://doi.org/10.1038/s43018-020-0085-8

nature cancer

Check for updates

Pan-cancer computational histopathology reveals mutations, tumor composition and prognosis

Yu Fu[1], Alexander W. Jung[1], Ramon Viñas Torne[1,6], Santiago Gonzalez[1,7], Harald Vöhringer[1], Artem Shmatko[1,2], Lucy R. Yates[3], Mercedes Jimenez-Linan[4], Luiza Moore[3,4,8] and Moritz Gerstung[1,5,8]

We use deep transfer learning to quantify histopathological patterns across 17,355 hematoxylin and eosin-stained histopathology slide images from 28 cancer types and correlate these with matched genomic, transcriptomic and survival data. This approach accurately classifies cancer types and provides spatially resolved tumor and normal tissue distinction. Automatically learned computational histopathological features correlate with a large range of recurrent genetic aberrations across cancer types. This includes whole-genome duplications, which display universal features across cancer types, individual chromosomal aneuploidies, focal amplifications and deletions, as well as driver gene mutations. There are widespread associations between bulk gene expression levels and histopathology, which reflect tumor composition and enable the localization of transcriptomically defined tumor-infiltrating lymphocytes. Computational histopathology augments prognosis based on histopathological subtyping and grading, and highlights prognostically relevant areas such as necrosis or lymphocytic aggregates. These findings show the remarkable potential of computer vision in characterizing the molecular basis of tumor histopathology.

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- Ability to detect these genetic alterations almost instantly from a single slide (with the help of AI too), instead of requiring additional testing post-biopsy, has the potential to significantly improve the effectiveness of treatment across cancer types, provided that this model is validated and deployed at scale

Underpinning Evidence

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Breast Ca subtypes can help guide treatment and maximize response, especially for high-risk patients

https://www.cell.com/cancer-cell/fulltext/S1535-6108(22)00216-1

Using comprehensive multi-omic molecular characterization of all tumors and the diverse drugs targeting different molecular pathways, the researchers were able to create breast cancer subtypes to match current treatments (Predictive biomarkers across 10 cancer treatments)

They found they could improve treatment efficacy and patient outcomes, particularly by using immune, DNA repair, luminal, and HER2 phenotypes.

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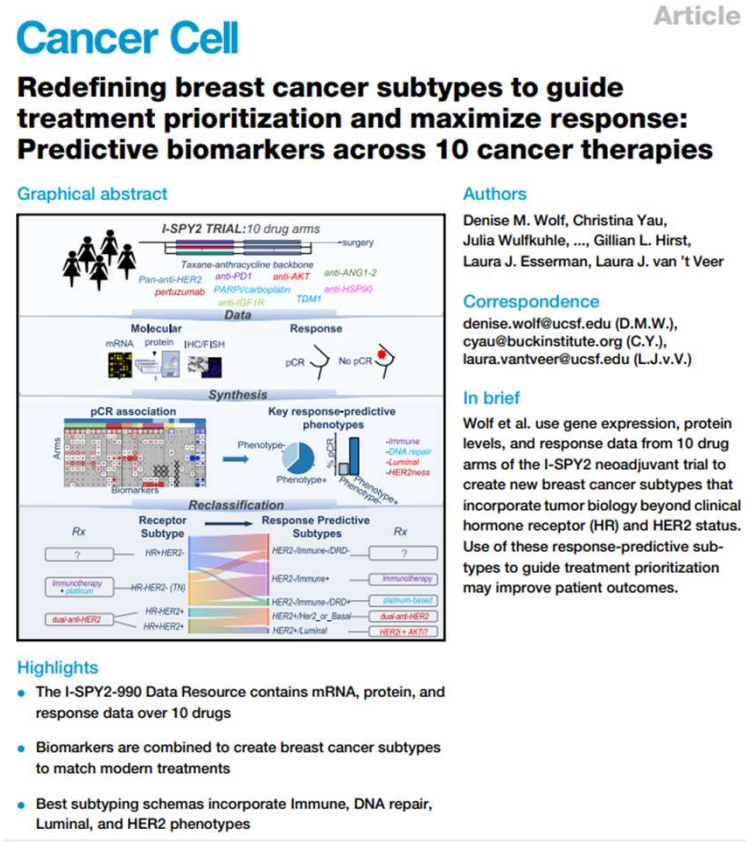


Article

Cancer Cell

Redefining breast cancer subtypes to guide treatment prioritization and maximize response: Predictive biomarkers across 10 cancer therapies

Graphical abstract

Authors

Denise M. Wolf, Christina Yau, Julia Wulfkuhle, ..., Gillian L. Hirst, Laura J. Esserman, Laura J. van 't Veer

Correspondence

denise.wolf@ucsf.edu (D.M.W.), cyau@buckinstitute.org (C.Y.), laura.vantveer@ucsf.edu (L.J.v.V.)

In brief

Wolf et al. use gene expression, protein levels, and response data from 10 drug arms of the I-SPY2 neoadjuvant trial to create new breast cancer subtypes that incorporate tumor biology beyond clinical hormone receptor (HR) and HER2 status. Use of these response-predictive subtypes to guide treatment prioritization may improve patient outcomes.

Highlights

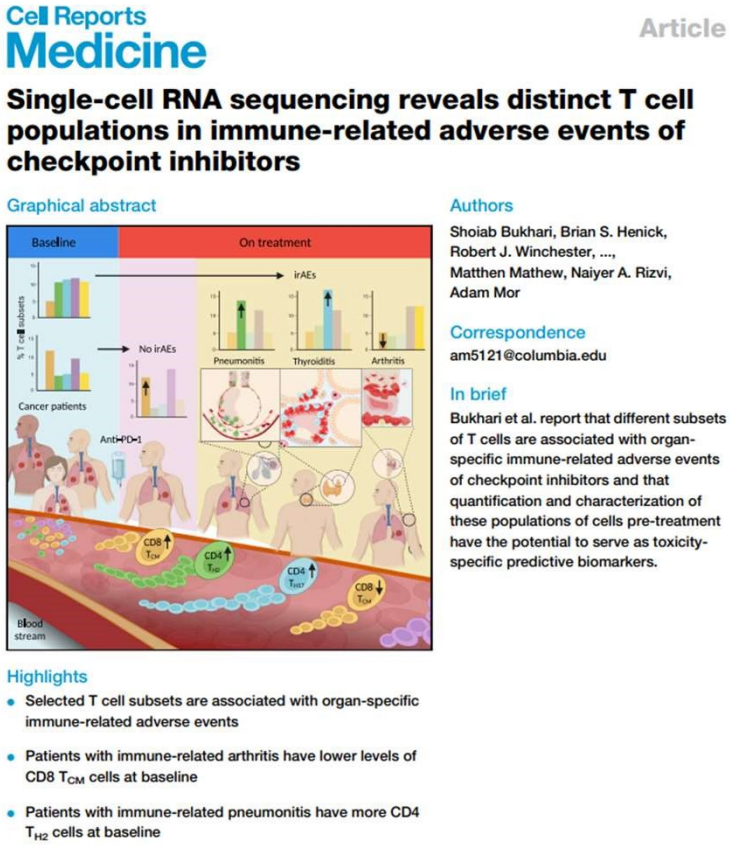
- The I-SPY2-990 Data Resource contains mRNA, protein, and response data over 10 drugs
- Biomarkers are combined to create breast cancer subtypes to match modern treatments
- Best subtyping schemas incorporate Immune, DNA repair, Luminal, and HER2 phenotypes

Underpinning Evidence

T-Cell Subpopulations in Blood May Help Predict Treatment Side Effects

European Innovation Council

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(22)00432-3 Dec 12, 2022



Cell Reports Medicine

Article

Single-cell RNA sequencing reveals distinct T cell populations in immune-related adverse events of checkpoint inhibitors

Graphical abstract

Authors

Shoiab Bukhari, Brian S. Henick, Robert J. Winchester, ..., Matthen Mathew, Naiyer A. Rizvi, Adam Mor

Correspondence

am5121@columbia.edu

In brief

Bukhari et al. report that different subsets of T cells are associated with organ-specific immune-related adverse events of checkpoint inhibitors and that quantification and characterization of these populations of cells pre-treatment have the potential to serve as toxicity-specific predictive biomarkers.

Highlights

- Selected T cell subsets are associated with organ-specific immune-related adverse events
- Patients with immune-related arthritis have lower levels of CD8 T_{CM} cells at baseline
- Patients with immune-related pneumonitis have more CD4 T_{H2} cells at baseline

- Immune cell gene expression patterns and subtypes may hold clues to immune-related adverse effects that cancer patients develop after immunotherapy (immune checkpoint blockade)
- Investigators used single-cell RNA sequencing to profile circulating T cells in pre-treatment peripheral blood samples from two dozen individuals undergoing anti-PD-1, anti-PD-L1, or anti-CTLA-4 immunotherapy cancer treatment, including 18 lung adenocarcinoma patients. They identified gene expression patterns and T-cell subgroups that corresponded to grade 2 or grade 3 immune-related adverse events after four to six weeks of treatment

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Association of Inflammatory Biomarkers With Survival Among Patients With Stage III Colon Cancer

Cancer Biomarkers | JAMA Oncology | JAMA Network

- A large cohort study of patients with stage III colon cancer demonstrated that higher levels of inflammatory biomarkers (IL-6, soluble TNF, and high sensitivity C-reactive protein) were significantly associated with increased risk of recurrence and mortality, even after adjustment for a wide range of potentially confounding variables.

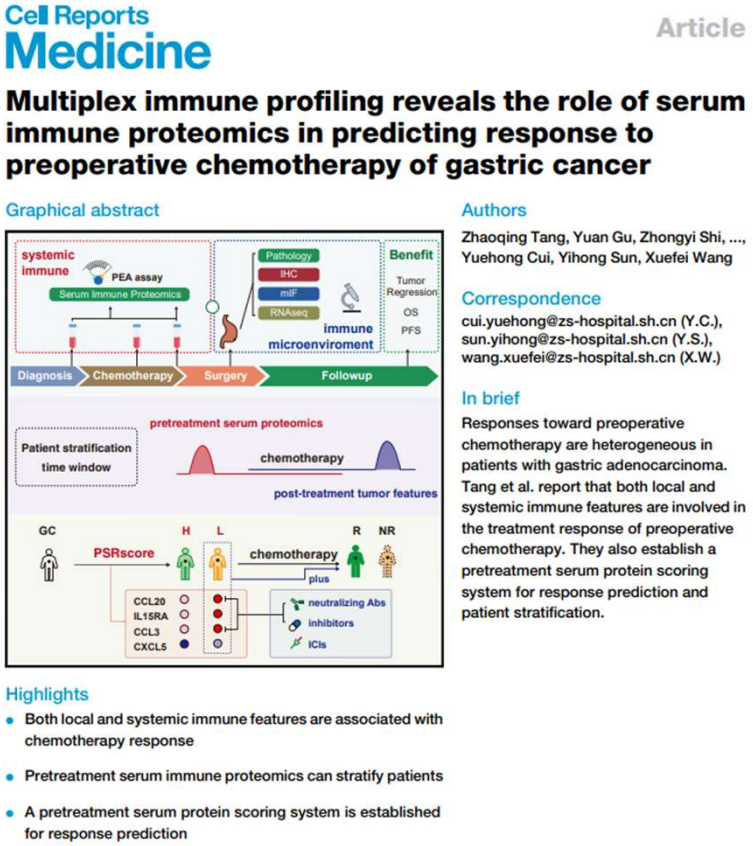
Underpinning Evidence

Immune Proteomic biomarkers in blood can predict response to treatment in Gastric Cancer

European Innovation Council

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(23)00023-X

- Immune proteomic profiles present in blood serum samples taken prior to treatment can provide prognostic clues in gastric cancer patients receiving chemotherapy ahead of surgery
- This work emphasized the rather underestimated, role of systemic immunity in the preoperative chemotherapy of gastric cancer," supporting a patient stratification strategy based on pretreatment serum immune proteomic biomarkers and highlighting the importance of profiling immunity as a whole in future studies



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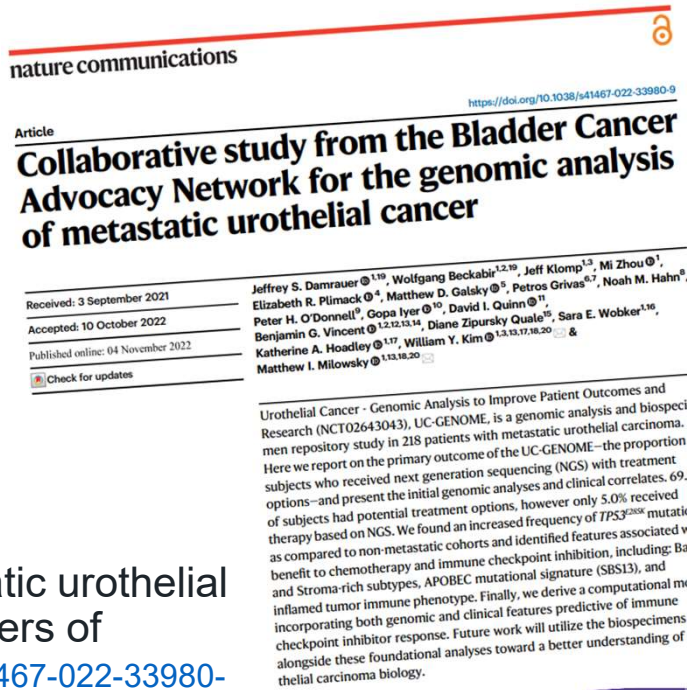
New biomarker-guided treatment strategies
Targeted therapy in bladder Ca

- Only 5% of patients with metastatic bladder cancer with potentially actionable mutations, received targeted therapy. There is only one targeted therapy approved in the US for bladder Ca (Janssen's FGFR inhibitor erdafitinib, for patients with locally advanced or metastatic bladder cancer that has FGFR2 or FGFR3 gene alteration)



nature communications

https://doi.org/10.1038/s41467-022-33980-9

Article

Collaborative study from the Bladder Cancer Advocacy Network for the genomic analysis of metastatic urothelial cancer

Received: 3 September 2021

Accepted: 10 October 2022

Published online: 04 November 2022

Check for updates

Jeffrey S. Damrauer[1,19], Wolfgang Beckabir[1,2,19], Jeff Klomp[1,3], Mi Zhou[1], Elizabeth R. Plimack[4], Matthew D. Galsky[5], Petros Grivas[6,7], Noah M. Hahn[8], Peter H. O'Donnell[9], Gopa Iyer[10], David I. Quinn[11], Benjamin G. Vincent[1,2,12,13,14], Diane Zipursky Quale[15], Sara E. Wobker[1,16], Katherine A. Hoadley[1,17], William Y. Kim[1,3,13,17,18,20] & Matthew I. Milowsky[1,13,18,20]

Urothelial Cancer - Genomic Analysis to Improve Patient Outcomes and Research (NCT02643043), UC-GENOME, is a genomic analysis and biospeci men repository study in 218 patients with metastatic urothelial carcinoma. Here we report on the primary outcome of the UC-GENOME–the proportion subjects who received next generation sequencing (NGS) with treatment options–and present the initial genomic analyses and clinical correlates. 69. of subjects had potential treatment options, however only 5.0% received therapy based on NGS. We found an increased frequency of *TP53*[R285K] mutatio as compared to non-metastatic cohorts and identified features associated w benefit to chemotherapy and immune checkpoint inhibition, including: Ba and Stroma-rich subtypes, APOBEC mutational signature (SBS13), and inflamed tumor immune phenotype. Finally, we derive a computational mo incorporating both genomic and clinical features predictive of immune checkpoint inhibitor response. Future work will utilize the biospecimens alongside these foundational analyses toward a better understanding of thelial carcinoma biology.

- New biomarker-guided treatment strategy involved 218 patients with metastatic urothelial Ca aimed to identifying potential actionable mutations and exploring biomarkers of response to immunotherapy and chemotherapy: https://www.nature.com/articles/s41467-022-33980-9#Sec10

Immunotherapies approved for bladder Ca patients, include Merck's Keytruda, BMS Opdivo, Genentech's Tecentriq, and Merck KGaA and Pfizer's Bavencio (avelumab). Immunotherapies are an option as an adjuvant or neoadjuvant therapy and for patients who are ineligible for platinum-based chemo.

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Targeted therapy in NSCLC: How to interpret actionable mutations for clinical use

- According to current guidelines, it's essential to perform broad molecular testing in patients with advanced adenocarcinoma
- Mutations in the biomarkers EGFR, ALK, ROS1, KRAS, are most commonly seen in adenocarcinomas but some of these can arise in squamous cell carcinomas as well. Can we distinguish between the two types based on mutation panel?
- Biomarker EGFR: The heterogeneity between the various EGFR exon 20 mutations seen in patients with NSCLC, can inform clinician's about the patient's actionable mutation status

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3D Genome Analysis may influence AML treatment

Nature. 2022 Nov;611(7935):387-398

Changes in three-dimensional (3D) chromatin structure and related methylation alterations may provide subtype-specific clues for understanding and treating acute myeloid leukemia (AML)

› Nature. 2022 Nov;611(7935):387-398. doi: 10.1038/s41586-022-05365-x. Epub 2022 Oct 26.

Subtype-specific 3D genome alteration in acute myeloid leukaemia

Jie Xu [#1,2], Fan Song [#1,3], Huijue Lyu [1], Mikoto Kobayashi [1], Baozhen Zhang [1,4], Ziyu Zhao [5], Ye Hou [1], Xiaotao Wang [1], Yu Luan [1], Bei Jia [6], Lena Stasiak [1], Josiah Hiu-Yuen Wong [1], Qixuan Wang [1], Qi Jin [1], Qiushi Jin [1], Yihao Fu [1], Hongbo Yang [1], Ross C Hardison [7], Sinisa Dovat [6], Leonidas C Platanias [8,9], Yarui Diao [10], Yue Yang [5], Tomoko Yamada [5], Aaron D Viny [11], Ross L Levine [12], David Claxton [6], James R Broach [2], Hong Zheng [13], Feng Yue [14,15]

Affiliations + expand

PMID: 36289338 DOI: 10.1038/s41586-022-05365-x

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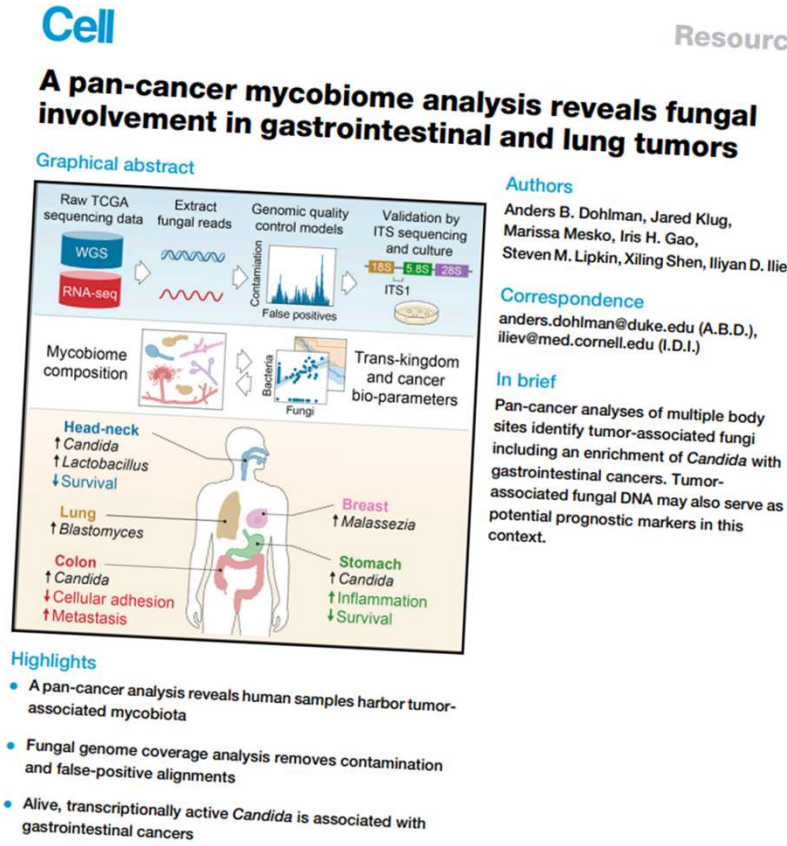
New concept: Microbes are associated with tumor's favorable or non prognosis

https://www.cell.com/cell/fulltext/S0092-8674(22)01173-4

- New research reveals that cancer is rife with bacteria and fungi, from seven parts of the body, including the mouth, esophagus, stomach, colon, rectum, breasts, and lungs and that specific microbes are associated with tumor's favorable or non prognosis (e.g. people were more likely to die of stomach cancer if their tumors contained the fungus Candida tropicalis)

- The results also point to the possibility of using antifungal treatments to reinforce conventional cancer treatments in some cases



Cell

Resourc

A pan-cancer mycobiome analysis reveals fungal involvement in gastrointestinal and lung tumors

Graphical abstract

Authors

Anders B. Dohlman, Jared Klug, Marissa Mesko, Iris H. Gao, Steven M. Lipkin, Xiling Shen, Iliyan D. Ilie

Correspondence

anders.dohlman@duke.edu (A.B.D.), iliev@med.cornell.edu (I.D.I.)

In brief

Pan-cancer analyses of multiple body sites identify tumor-associated fungi including an enrichment of *Candida* with gastrointestinal cancers. Tumor-associated fungal DNA may also serve as potential prognostic markers in this context.

Highlights

- A pan-cancer analysis reveals human samples harbor tumor-associated mycobiota
- Fungal genome coverage analysis removes contamination and false-positive alignments
- Alive, transcriptionally active *Candida* is associated with gastrointestinal cancers

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Relevance to EU health cluster policies in cancer

No overlap between the present EIC Accelerator and relevant EC Health Cluster Calls

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- HORIZON-HLTH-2021-DISEASE-04-01: Improved supportive, palliative, survivorship and end-of-life care of cancer patients *closed 21.09.21*
- HORIZON-HLTH-2021-CARE-05-02: Data-driven decision-support tools for better health care delivery and policy-making with a focus on cancer *closed 21.09.21*
- HORIZON-INFRA-2021-EOSC-01-06: FAIR and open data sharing in support of cancer research *closed 23.09.21*
- HORIZON-INFRA-2021-SERV-01-01: Research infrastructures services to support research addressing cancer *closed 20.10.21*
- HORIZON-MISS-2021-CANCER-02-01: Develop new methods and technologies for cancer screening and early detection *closed 26.04.22*
- HORIZON-MISS-2021-CANCER-02-02: Develop and validate a set of quality of life and patient preference measures for cancer patients and survivors *closed 26.04.22*
- HORIZON-MISS-2021-CANCER-02-03: Better understanding of the impact of risk factors and health determinants on the development and progression of cancer *closed 26.04.22*
- DIGITAL-2022-CLOUD-AI-02-CANCER-IMAGE: Federated European infrastructure for cancer images data *closed 17.05.22*
- HORIZON-MISS-2022-CANCER-01-01: Improving and upscaling primary prevention of cancer through implementation research
- HORIZON-MISS-2022-CANCER-01-03: Pragmatic clinical trials to optimise treatments for patients with refractory cancers

Relevance to EU health cluster policies in cancer
No overlap between the present EIC Accelerator and relevant IHI Calls

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- **Scope**: The scope of the below IHI Calls is to help achieve the IHI JU specific objective: "*Integrate fragmented health R&I efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs*", whereas the aim of this Accelerator Challenge Call is to support individual SMEs.

- **Objectives**: The IHI Calls focus on image-guided and multi mode therapeutic approaches, whereas this Challenge Call aims to support first clinical stage evidence of new liquid or other type of biomarker-based guided cancer treatment

Relevant Innovative Health Initiative Calls

- Next generation imaging and image-guided diagnosis and therapy for cancer
- Personalised oncology: Innovative people-centred, multi-modal therapies against cancer

Relevance to EU health cluster policies in cancer

EIC Accelerator Call is complementary to Cancer Mission

- The present EIC Accelerator Call: ***Novel biomarker-based assays to guide personalised cancer treatment*** is complementary to the Cancer Mission, and in particular to its third specific objective: *"To ensure that more patients have access to the latest, minimally invasive treatments adapted to their conditions, and with minimal secondary effects"*. [The Cancer Mission has four specific objectives aimed at benefitting cancer patients: (1) understanding, (2) prevention, including screening and early detection, (3) optimize diagnosis and treatment, and (4) quality of life]

- Cancer Mission's Scientific Officer Jan Van de Loo contributed to the preparation of this EIC Accelerator Challenge-based Call

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Q&A, Discussion

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Join at **Sli.do**

With the event code
#Challenges

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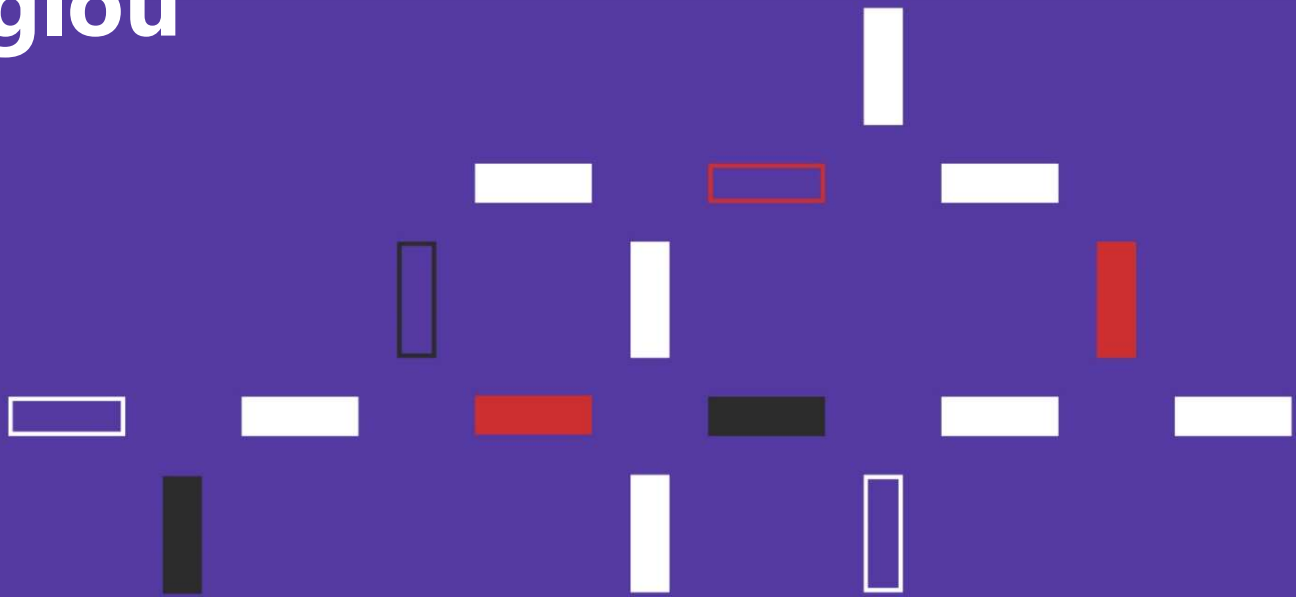
Q&A

Iordanis Arzimanoglou
Vilma Radvilaite



Useful links to the EIC Work Programme 2023:

EIC Work Programme 2023:
(the legal basis)

Recording of EIC Info-day 13 December:
(not repeated today)

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Questions: contact your National Contact Point

National Contact Points for Horizon Europe:
(NCP Portal)

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