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Collection 01 July 2020

Cancer at Nature Portfolio

The Nature Portfolio editors who handle cancer primary research, methods, protocols and reviews bring you the latest articles, covering all aspects from disease mechanisms to therapeutic approaches. Collected here you will also find specially curated content, such as collections, focus issues and animations, all ready to be used in presentations and educational materials. You can also find out about the editors handling cancer content, and the journals at Nature Portfolio that publish articles on this topic and how to submit to them.



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Research Articles

<u>Dysfunctional adipocytes promote tumor progression through YAP/TAZ-dependent cancer-associated</u> <u>adipocyte transformation</u>

The impact of obesity on cancer remains insufficiently explored. Here the authors show that in mouse models, dysfunctional adipocytes exhibit low levels of BECN1 which induce YAP/TAZ activity to promote breast and colorectal tumor progression.

Yaechan Song, Heeju Na ... Han-Woong Lee

Article Open Access 14 May 2024 Nature Communications

dsRNAi-mediated silencing of PIAS2beta specifically kills anaplastic carcinomas by mitotic catastrophe

Anaplastic thyroid cancer (ATC) is a particularly aggressive cancer type with limited effective therapeutic options. Here, the authors identify the SUMO E3 ligase PIAS2 as a potential therapeutic target in ATC and mechanistically investigate its role in mitotic spindle and centrosome assembly.

Joana S. Rodrigues, Miguel Chenlo ... Clara V. Alvarez

Article Open Access 14 May 2024 Nature Communications

<u>Trastuzumab deruxtecan in HER2-positive advanced gastric cancer: exploratory biomarker analysis of the</u> <u>randomized, phase 2 DESTINY-Gastric01 trial</u>

Exploratory analyses of the DESTINY-Gastric01 trial show that baseline HER2-associated biomarkers in circulating tumor DNA or tissue samples were associated with therapeutic response in patients with HER2-positive tumors, and these analyses identify potential drivers of resistance.

Kohei Shitara, Yung-Jue Bang ... Kensei Yamaguchi

Article Open Access 14 May 2024 Nature Medicine

<u>Phase separation-competent FBL promotes early pre-rRNA processing and translation in acute myeloid</u> <u>leukaemia</u>

Yang et al. report that the nucleolar protein fibrillarin (FBL) affects acute myeloid leukaemia (AML) cell function through biomolecular condensationdependent regulation of early pre-rRNA processing and translation.

Lin Yang, Zhaoru Zhang ... Pengxu Qian

Article 14 May 2024 Nature Cell Biology









Generation of allogeneic CAR-NKT cells from hematopoietic stem and progenitor cells using a clinically guided culture method

Off-the-shelf CAR-NKT cells for cancer immunotherapy are advanced toward clinical translation.

Yan-Ruide Li, Yang Zhou ... Lili Yang

Article Open Access 14 May 2024 Nature Biotechnology

<u>Targeting TGFβ-activated kinase-1 activation in microglia reduces CAR T immune effector cell-associated</u> neurotoxicity syndrome

Zeiser and colleagues show that CAR T cell therapy results in upregulation of the TGFβ-activated kinase-1 (TAK1)–NF-κB–p38 MAPK pathway in microglia, causing neurocognitive defects, and find that TAK1 inhibition can reduce immune effector cell-associated neurotoxicity syndrome.

Janaki Manoja Vinnakota, Francesca Biavasco ... Robert Zeiser

Article 13 May 2024 Nature Cancer

Mammographic density mediates the protective effect of early-life body size on breast cancer risk

Mammographic density is known to be linked to breast cancer risk. Here, the authors use Mendelian randomization to estimate the effects of childhood body size and age at menarche on density phenotypes and breast cancer risk.

Marina Vabistsevits, George Davey Smith ... Eleanor Sanderson

Article Open Access 13 May 2024 Nature Communications

Platelets favor the outgrowth of established metastases

It is unclear if platelets regulate the growth of established metastases. Using syngeneic mouse models of metastasis, the authors show that platelets support the outgrowth of established metastases via immune suppression, and that targeting the platelet-specific receptor GPVI, efficiently reduces established metastases, providing a promising therapeutic avenue for inhibiting cancer metastasis.

Maria J. Garcia-Leon, Cristina Liboni ... Jacky G. Goetz

Article Open Access 13 May 2024 Nature Communications

Association between pretreatment emotional distress and immune checkpoint inhibitor response in nonsmall-cell lung cancer

In a prospective observational study, symptoms of anxiety and/or depression were associated with worse response to first-line treatment with immunotherapy in patients with advanced non-small-cell lung cancer.

Yue Zeng, Chun-Hong Hu ... Fang Wu

Article Open Access 13 May 2024 Nature Medicine

Genome-wide association analyses of breast cancer in women of African ancestry identify new susceptibility loci and improve risk prediction

Genome-wide association analyses identify risk loci for breast cancer in women of African ancestry. Polygenic risk scores derived from these data improve ancestry-specific risk prediction.

Guochong Jia, Jie Ping ... Wei Zheng

Article 13 May 2024 Nature Genetics

Single-cell mtDNA dynamics in tumors is driven by coregulation of nuclear and mitochondrial genomes

Amplification-free single-cell whole-genome sequencing shows that genomic, evolutionary and biophysical factors collectively drive cell-to-cell variation in mitochondrial DNA copy number.

Minsoo Kim, Alexander N. Gorelick ... Ed Reznik

Article Open Access 13 May 2024 Nature Genetics

VOLTA: an enVironment-aware cOntrastive ceLl represenTation leArning for histopathology

While machine learning platforms can improve the assessment of Hematoxylin & Eosin (H&E) stained-tumour tissue images, current models typically require manual cell-type annotations in training. Here, the authors develop VOLTA, a self-supervised machine learning framework to improve cell representation learning in H&E images based on the cells environment

Ramin Nakhli, Katherine Rich ... Ali Bashashati

https://www.nature.com/collections/bpwtvhdwgf

Article Open Access 10 May 2024 Nature Communications







227 natients eligible for analysis	
	Excluded: 5 withdrew consent
232 patients receiving ICIs as first-line treatments enrolled	43 not receiving immunitherapy 5 other clinical trial recruitment 4 performance status access 2 3 currently receiving anti-depression/anti anxiety drug 2 no messurable lesion





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Pretreatment with IL-15 and IL-18 rescues natural killer cells from granzyme B-mediated apoptosis after cryopreservation Natural killer (NK) cells are assessed for various therapies, but sub-optimal cryopreservation dampens their clinical feasibility. Here the authors show

that pretreating human NK cells with IL-15/IL-18 prior to cryopreservation improves NK cell post-thaw viability and functions, potentially via antiapoptosis gene induction and granzyme B degranulation.

Abdulla Berjis, Deeksha Muthumani ... Neil C. Sheppard

Article Open Access 10 May 2024 Nature Communications

The STING agonist IMSA101 enhances chimeric antigen receptor T cell function by inducing IL-18 secretion

It has been previously suggested that STING agonists can improve response to CAR-T therapy. Here the authors report the characterization of the STING agonist IMSA101, showing that STING-induced IL18 secretion enhances CAR-T activity in preclinical cancer models.

Ugur Uslu, Lijun Sun ... Carl H. June

Reviewer recognition:

Article Open Access 10 May 2024 Nature Communications

Pervasive structural heterogeneity rewires glioblastoma chromosomes to sustain patient-specific transcriptional programs

By applying Hi-C to cells derived from the tumors of 24 GBM patients, the authors show pervasive structural variation in GBM chromosomal organization. How such patient-to-patient variation explains the characteristic gene expression patterns in each tumor is investigated.

Ting Xie, Adi Danieli-Mackay ... Argyris Papantonis

Article Open Access 9 May 2024 Nature Communications

Zhusheng Huang, Rong Gu ... Ahu Yuan Article Open Access 9 May 2024 Nature Communications

gadolinium nanowires with immune checkpoint blockade therapy to synergistically induce antitumor immunity.

Network-based elucidation of colon cancer drug resistance mechanisms by phosphoproteomic timeseries analysis

Aberrant signalling pathway activity is relevant for tumour growth and resistance to therapy, but remains hard to understand and target. Here, the authors develop VESPA, a phosphoproteomics-based machine learning algorithm that can elucidate response and adaptation to drug perturbations in cancer signalling pathways.

Radiation-induced tumor vaccination is insufficient to elicit robust antitumor immune response. Here they combine chiral vidarabine monophosphate

George Rosenberger, Wenxue Li ... Andrea Califano

Article Open Access 9 May 2024 Nature Communications

Mapping genotypes to chromatin accessibility profiles in single cells

The JAK2^{V617F} mutation leads to epigenetic rewiring in a cell-intrinsic and cell-type-specific manner, influencing inflammation states and differentiation trajectories in patients with myeloproliferative neoplasms.

Franco Izzo, Robert M. Myers ... Dan A. Landau

Article 8 May 2024 Nature

PD-1/CD80⁺ small extracellular vesicles from immunocytes induce cold tumours featured with enhanced adaptive immunosuppression

Immune checkpoint inhibition is a successful form of immune therapy; however response rates vary widely among individual patients. Here authors show that circulating small extracellular vesicles might contribute to poor response to anti-PD-1 treatment by carrying PD-1 and CD80 which results in higher level of vesicular PD-L1 expression in the circulation at the expense of expression on tumour cell membranes, causing immunosuppression.

Lin-Zhou Zhang, Jie-Gang Yang ... Gang Chen

Article Open Access 8 May 2024 Nature Communications

Targetable leukaemia dependency on noncanonical PI3Ky signalling

Using a multimodal approach across acute leukaemias, a targetable PI3Ky dependency in leukaemias is explored.

Qingyu Luo, Evangeline G. Raulston ... Andrew A. Lane Article 8 May 2024 Nature



















Cancer at Nature Portfolio

Chiral coordination polymer nanowires boost radiation-induced in situ tumor vaccination

Tumor-repopulating cells evade ferroptosis via PCK2-dependent phospholipid remodeling

Phosphorylation of ACSL4 by mitochondria-located metabolic kinase PCK2 is critical to regulating ferroptosis-associated phospholipid remodeling in tumor-repopulating cells that are resistant to chemotherapy and radiotherapy.

Cancer at Nature Portfolio

Zhe Li, Zhi-min Xu ... Zhuo-wei Liu

Article Open Access 8 May 2024 Nature Chemical Biology

<u>TLR agonists polarize interferon responses in conjunction with dendritic cell vaccination in malignant</u> <u>glioma: a randomized phase II Trial</u>

Autologous tumor lysate (ATL) dendritic cell (DC) vaccination can induce local and systemic anti-tumor immune responses in malignant glioma patients. In this randomized phase II clinical trial, the authors evaluate the effectiveness of adding the TLR agonists, poly-ICLC or resignimod, to ATL-DC vaccination in patients with newly-diagnosed or recurrent WHO Grade III-IV malignant gliomas.

Richard G. Everson, Willy Hugo ... Robert M. Prins

Article Open Access 8 May 2024 Nature Communications

Plasma proteome profiling reveals dynamic of cholesterol marker after dual blocker therapy

Dual blockade therapy is currently being trialled for multiple tumour types, but efficacy is variable. Here, the authors use longitudinal proteomics profiling of 22 patients to develop a predictive model of therapy response.

Jiacheng Lyu, Lin Bai ... Chen Ding

Article Open Access 8 May 2024 Nature Communications

Reviews

Cancer therapy with antibodies

In this Review, Paul et al. provide an overview of therapeutic antibodies as an important modality in cancer therapy today. They summarize the different approaches used by antibodies to target cancer cells including those of immune checkpoint inhibitors, bispecific antibodies and antibody–drug conjugates, as well as describing current strategies aimed at improving their efficacy and reducing toxicities.

Suman Paul, Maximilian F. Konig ... Shibin Zhou

Review Article 13 May 2024 Nature Reviews Cancer

Mitochondrial function and gastrointestinal diseases

Mitochondria of the intestinal epithelium are vital in intestinal health and disease. This Review provides a comprehensive overview of intestinal epithelial cell mitochondrial dysfunction in inflammatory bowel diseases and colorectal cancer and discusses mitochondrial-targeted therapeutics for these diseases.

Parsa S. Haque, Neeraj Kapur ... Arianne L. Theiss

Review Article 13 May 2024 Nature Reviews Gastroenterology & Hepatology

Centralization of care for rare genetic syndromes associated with cancer: improving outcomes and advancing research on VHL disease

In this Perspective, Larcher et al. describe a dedicated treatment programme for Von Hippel–Lindau disease established at San Raffaele Hospital, which encompasses diagnosis, surveillance, treatment, research and outreach. The authors then discuss the benefits of care centralization for Von Hippel–Lindau disease and other rare diseases.

Alessandro Larcher, Federico Belladelli ... Andrea Salonia

Perspective 8 May 2024 Nature Reviews Urology

Targeted protein degradation: from mechanisms to clinic

This article reviews the current landscape of targeted protein degradation approaches and how they have parallels in biological processes. The authors also outline the ongoing clinical exploration of novel degraders and provide some perspectives on the directions the field might take.

Jonathan M. Tsai, Radosław P. Nowak ... Eric S. Fischer Review Article 29 Apr 2024 Nature Reviews Molecular Cell Biology













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From biology to the clinic - exploring liver metastasis in prostate cancer

In this Review, the authors provide a comprehensive overview of the epidemiological characteristics, prognosis, biological mechanisms, detection methods and treatment options for liver metastasis in prostate cancer. Guidance for future research directions in the field is also provided.

Xudong Ni, Yu Wei ... Yao Zhu

Review Article 26 Apr 2024 Nature Reviews Urology

Engineering immune-evasive allogeneic cellular immunotherapies

Genome editing approaches can be used to confer immune-evasive properties to allogeneic cellular immunotherapies, with the aim of achieving persistent responses and efficiencies that are comparable to those of autologous chimeric antigen receptor T cell therapies. This Perspective discusses how current knowledge about viral or tumour immune evasion could be incorporated into the design of off-the-shelf tumour-specific T and NK cells for the production of cost-effective and scalable cancer immunotherapies.

Karen E. Martin, Quirin Hammer ... Karl-Johan Malmberg

Perspective 24 Apr 2024 Nature Reviews Immunology

Circadian regulation of cancer stem cells and the tumor microenvironment during metastasis

Barker and colleagues discuss the interplay between circadian rhythm, the tumor microenvironment and stem cells and how these are linked to metastasis as well as how these interactions could be clinically relevant.

Yu Wang, Rajesh Narasimamurthy ... Nick Barker

Perspective 23 Apr 2024 Nature Cancer

<u>Unlocking ferroptosis in prostate cancer — the road to novel therapies and imaging markers</u>

Ferroptosis induction is a promising new therapeutic strategy for advanced prostate cancer. In this Perspective, the authors discuss the interplay between ferroptosis and metabolism. Current efforts to target ferroptosis and combination therapies in prostate cancer, as well as emerging methods to monitor this process in patients, are also discussed.

Pham Hong Anh Cao, Abishai Dominic ... Elavarasan Subramani

Perspective 16 Apr 2024 Nature Reviews Urology

Combinatorial strategies to target RAS-driven cancers

In this Review, Cichowski and colleagues provide an overview of combinatorial strategies designed to treat RAS-driven cancers that are based on four concepts that include vertical pathway inhibition, co-targeting RAS and adaptive survival pathways, co-targeting downstream or converging pathways and capitalizing on other cancer-associated vulnerabilities.

Naiara Perurena, Lisa Situ & Karen Cichowski

Review Article 16 Apr 2024 Nature Reviews Cancer

Lymphatic vessels in the age of cancer immunotherapy

Tumour-associated lymphatic growth and remodelling were once viewed as a passive means by which cancer cells could regionally spread to lymph nodes. However, recent data point to an active and contrasting role for lymphatic vessels and their transport in antitumour immune surveillance. In this Review, Karakousi et al. provide a working framework to define this role for the lymphatic system in tumour progression and present avenues for its therapeutic manipulation to improve cancer immunotherapy.

Triantafyllia Karakousi, Tenny Mudianto & Amanda W. Lund

Review Article 11 Apr 2024 Nature Reviews Cancer

Antiangiogenic-immune-checkpoint inhibitor combinations: lessons from phase III clinical trials

The benefit of combining antiangiogenic agents with immune-checkpoint inhibitors has been demonstrated in pivotal phase III trials across different cancer types, some with practice-changing results; however, other phase III trials have had negative results. The authors of this Perspective discuss the variable outcomes of these trials, considering factors that account for these differences and suggesting future initiatives for improving the outcomes in patients receiving these combinations.

Hung-Yang Kuo, Kabir A. Khan & Robert S. Kerbel

Perspective 10 Apr 2024 Nature Reviews Clinical Oncology

Nucleic acid-based drugs for patients with solid tumours

Nucleic acid-based therapies offer an alternative to traditional cancer treatment modalities, with promising data beginning to emerge. In this Review, the authors describe the design and development of nucleic acid-based therapies administered virally and non-virally, including discussions of the advantages and disadvantage of each approach, as well as the role of patient-specific factors such as the tumour microenvironment, and consider the most promising future research directions.

Sebastian G. Huayamares, David Loughrey ... Eric J. Sorscher

Review Article 8 Apr 2024 Nature Reviews Clinical Oncology

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Hallmarks of sex bias in immuno-oncology: mechanisms and therapeutic implications

Sex differences impact various non-reproductive organ cancers, often leading to higher cancer incidence and poorer outcomes in male individuals. In this Perspective article, Xiao, Lee et al. outline the biological factors contributing to sex bias in immuno-oncology, emphasizing the need for future research to offer a fuller understanding of sex disparities in cancer.

Cancer at Nature Portfolio

Tong Xiao, Juyeun Lee ... Zihai Li

Perspective 8 Apr 2024 Nature Reviews Cancer

The pleiotropic functions of reactive oxygen species in cancer

Papagiannakopoulos and colleagues discuss the roles of reactive oxygen species in cancer and the ways in which redox mechanisms may be exploited for cancer therapy.

Katherine Wu, Ahmed Ezat El Zowalaty ... Thales Papagiannakopoulos

Review Article 22 Mar 2024 Nature Cancer

Bone marrow inflammation in haematological malignancies

Haematological malignancies are associated with inflammation in the bone marrow. In this Review, the authors discuss how tumour-associated inflammation affects the normal functions of the bone marrow and supports the outgrowth and survival of malignant cells. Moreover, they describe how the inflammatory changes in the bone marrow differ in myeloid and lymphoid malignancies.

Madelon M. E. de Jong, Lanpeng Chen ... Tom Cupedo

Review Article 15 Mar 2024 Nature Reviews Immunology

Future direction of total neoadjuvant therapy for locally advanced rectal cancer

In this article, the authors discuss the use of total neoadjuvant therapy for locally advanced rectal cancer. They highlight ongoing trials and discuss future treatment options, including the potential use of multi-omics and artificial intelligence to facilitate treatment selection and prediction of response.

Yoshinori Kagawa, J. Joshua Smith ... Takayuki Yoshino

Perspective 14 Mar 2024 Nature Reviews Gastroenterology & Hepatology

Targeting cuproplasia and cuproptosis in cancer

Copper is an essential trace element with inherent redox properties and fundamental roles in a diverse range of biological processes; therefore, maintaining copper homeostasis is crucial. In this Review, the authors discuss new insights into the mechanisms by which disrupted copper homeostasis contributes to tumour initiation and development, including the recently defined concepts of cuproplasia (copper-dependent cell growth and proliferation) and cuproptosis (a mitochondrial pathway of cell death triggered by excessive copper exposure). They also discuss potential strategies to exploit cuproplasia and cuproptosis for the treatment of cancer.

Daolin Tang, Guido Kroemer & Rui Kang

Review Article 14 Mar 2024 Nature Reviews Clinical Oncology

Immunogenic cell death in cancer: targeting necroptosis to induce antitumour immunity

In this Review, Meier et al. discuss the molecular mechanisms of necroptosis, delineate how this form of immunogenic cell death activates antitumour immune responses and explore the opportunities and limitations of targeting necroptosis for anticancer therapy.

Pascal Meier, Arnaud J. Legrand ... John Silke

Review Article 7 Mar 2024 Nature Reviews Cancer

The present and future of bispecific antibodies for cancer therapy

Bispecific antibodies (bsAbs) can mediate therapeutic effects beyond those of natural monospecific antibodies. This Review provides an overview of recent developments in the field of bsAbs for cancer therapy and an outlook into next-generation bsAbs in earlier stages of development.

Christian Klein, Ulrich Brinkmann ... Roland E. Kontermann

Review Article 6 Mar 2024 Nature Reviews Drug Discovery

In this Viewpoint article, we asked three scientists working on the cancer mycobiome to provide their opinions on advancements and challenges and what the future holds for this exciting field of cancer research.

Jessica Galloway-Peña, Iliyan D. Iliev & Florencia McAllister Viewpoint | 12 Feb 2024 | <u>Nature Reviews Cancer</u>

Cancer burden in low-income and middle-income countries













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Cancer at Nature Portfolio

In this Viewpoint, we asked four experts to discuss the increasing burden of cancer in low- and middle-income countries; they explore the changes that are necessary to improve cancer diagnosis, prevention and treatment within these nations.

Sharmila Anandasabapathy, Chite Asirwa ... Chemtai Mungo

Viewpoint 8 Feb 2024 Nature Reviews Cancer

The mechanisms of nanoparticle delivery to solid tumours

The mechanisms of nanoparticle delivery to solid tumours guide the engineering of nanoparticles for cancer applications. This Review discusses two contrasting nanoparticle delivery mechanisms, the enhanced permeability and retention effect and the active transport and retention principle, and their implications for the design of cancer nanomedicines.

Luan N. M. Nguyen, Wayne Ngo ... Warren C. W. Chan

Review Article 8 Feb 2024 Nature Reviews Bioengineering

Dendritic cells as orchestrators of anticancer immunity and immunotherapy

Dendritic cells (DCs) are antigen-presenting cells that function at the interface between innate and adaptive immunity, thereby acting as key mediators of antitumour immune responses and immunotherapy efficacy. In this Review, the authors outline the emerging complexity of intratumoural DC states that is being revealed through single-cell analyses as well as the contributions of different DC subsets to anticancer immunity and the activity of immune-checkpoint inhibitors. The authors also discuss advances in the development of DC-based cancer therapies and considerations for their potential combination with other anticancer therapies.

Ignacio Heras-Murillo, Irene Adán-Barrientos ... David Sancho

Review Article 7 Feb 2024 Nature Reviews Clinical Oncology

Molecular profile of bladder cancer progression to clinically aggressive subtypes

In this Review, the authors describe the molecular profile of bladder cancer progression associated with the subtypes of this disease and comment on their potential diagnostic, prognostic and therapeutic importance.

Charles C. Guo, Sangkyou Lee ... Bogdan Czerniak

Review Article 6 Feb 2024 Nature Reviews Urology

Multiplex protein imaging in tumour biology

In this Review, de Souza et al. discuss how advances in the ability to image protein markers at high-plex, at single-cell and even subcellular resolution, are expanding our understanding of tumour biology and clinical outcomes, and outline the future promise of combining such multiplex protein imaging methods with other forms of spatial omics.

Natalie de Souza, Shan Zhao & Bernd Bodenmiller

Review Article 5 Feb 2024 Nature Reviews Cancer

The yin and yang of chromosomal instability in prostate cancer

Chromosomal instability is a hallmark of advanced prostate cancer. In this Review, the authors discuss the biological causes and paradoxical consequences of chromosomal instability, its potential clinical role in the stratification of prostate cancer aggressiveness and the development of novel treatment strategies.

Marc Carceles-Cordon, Jacob J. Orme ... Veronica Rodriguez-Bravo

Review Article 2 Feb 2024 Nature Reviews Urology

Management of patients with muscle-invasive bladder cancer with clinical evidence of pelvic lymph node metastases

Muscle-invasive bladder cancer with clinically positive pelvic lymph nodes is a particular situation at the interface between localized and metastatic disease. In this Review, the authors discuss the advances and challenges of currently available strategies for the diagnosis and treatment of patients with muscle-invasive bladder cancer with clinically positive pelvic lymph nodes.

Elisabeth Grobet-Jeandin, Louis Lenfant ... Thomas Seisen

Review Article 31 Jan 2024 Nature Reviews Urology

News & Commentary

CAR T cells offer hope in glioblastoma

Novel CAR T cells delivered directly to the CNS could have therapeutic effects in recurrent glioblastoma, according to two early-stage trials.



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A milestone method to make natural killer T cells

Research Highlight | 14 May 2024 | Nature Reviews Neurology

A differentiation protocol to produce off-the-shelf natural killer T cells may enable clinical application.

Leonid S. Metelitsa

News & Views 14 May 2024 Nature Biotechnology

Refining neoadjuvant immunotherapy for resectable lung cancer

In an era of expanding perioperative approaches for resectable non-small-cell lung cancer, new data demonstrate that dual neoadjuvant immunotherapy targeting PD-1 and LAG-3 is feasible; future analyses may enhance patient selection by identifying immune signatures predictive of response.

Misty D. Shields & Christine M. Lovly

News & Views 13 May 2024 Nature Medicine

Overcoming barriers in cancer care for gender minorities

As the population of gender minorities grows in the setting of rising incidence of cancers globally, health-care professionals and institutions must be prepared to provide inclusive care. Individual-level training as well as institutional-level efforts on gender identity data collection and creation of inclusive clinical spaces could help mitigate health-care disparities.

David J. Benjamin, Omid Yazdanpanah & Arash Rezazadeh Kalebasty

Comment 13 May 2024 Nature Reviews Urology

Right ON target: a new RAS-GTP inhibitor

Two studies published concurrently in *Nature* report the development and preclinical activity of RMC-7977, a multi-selective inhibitor targeting the active, GTP-bound form of RAS.

Daniela Senft

Research Highlight 10 May 2024 Nature Reviews Cancer

New route to target RAS

M. Teresa Villanueva

Research Highlight 10 May 2024 Nature Reviews Drug Discovery

Studying paired patient tissue and blood enables insights into immunotherapy toxicity

Using single-cell RNA and T cell receptor sequencing along with microscopy, we identified the cell types and genes associated with immune checkpoint inhibitor therapy-related colitis. Our study will help to identify targets for early diagnosis and lays the groundwork for the development of safer immunotherapy regimens.

Research Briefing 9 May 2024 Nature Medicine

AACR 2024

The annual American Association for Cancer Research (AACR) meeting provides a platform for scientists, clinicians and other stakeholders to share the latest advances in cancer science and medicine. Here, we outline some highlights of the 2024 meeting.

Gabrielle Brewer

Research Highlight 8 May 2024 Nature Reviews Cancer

Dodging death

Ferroptosis, a cell death mechanism induced by lipid peroxidation, is pivotal in tumor suppression. A recent study shows that tumor repopulating cells evade ferroptosis and develop resistance to therapy via subverting a lipid metabolism enzyme.

Yuelong Yan & Boyi Gan

News & Views 8 May 2024 Nature Chemical Biology

https://www.nature.com/collections/bpwtvhdwgf

Adjuvant pembrolizumab improves overall survival in patients with RCC

Peter Sidaway











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8/12

PRMT9 inhibition sparks immune responses in AML

Research Highlight 29 Apr 2024 Nature Reviews Clinical Oncology

Arginine methylation is crucial for tumor maintenance. PRMT9 levels are elevated in acute myeloid leukemia, and its inhibition eradicates leukemia by diminishing arginine methylation of proteins involved in DNA damage response and RNA translation. This activates the cGAS-STING pathway, which triggers immune responses directed against leukemia. Epigenetic targeting of DNA-damage-response mechanisms may bolster anti-tumor immunity

Antonella Santoro & Raffaella Di Micco

News & Views 29 Apr 2024 Nature Cancer

Experimental evolution of cancer chromosomal changes

Experimental genome evolution of normal human cells reveals an intrinsic propensity to develop cancer-associated chromosomal alterations.

Molly A. Guscott & Sarah E. McClelland

News & Views 29 Apr 2024 Nature Genetics

Sarcoma ecotypes determine immunotherapy benefit

Sarcomas are heterogeneous connective tissue tumors that occur at various anatomic sites and are generally difficult to treat. Cell states in sarcoma ecosystems are now shown to be conserved across multiple subtypes and associated with response to immunotherapy and patient outcome.

Johanna Wagner & Stefan Fröhling

News & Views 29 Apr 2024 Nature Cancer

Adjuvant alectinib improves outcomes in ALK-mutant NSCLC

Diana Romero

Research Highlight 25 Apr 2024 Nature Reviews Clinical Oncology

NALIRIFOX for metastatic pancreatic adenocarcinoma: hope or hype?

The FDA has approved nanoliposomal irinotecan, 5-fluorouracil, leucovorin and oxaliplatin (NALIRIFOX) for patients with metastatic pancreatic adenocarcinoma on the basis of results from the NAPOLI 3 trial, in which this four-drug regimen improved overall survival relative to a doublet regimen. Here we discuss how, in the context of prior results from the PRODIGE 4 trial testing 5-fluorouracil, leucovorin, irinotecan and oxaliplatin (modified FOLFIRINOX), NALIRIFOX does not seem to raise the bar, but rather exposes patients and health-care systems to financial toxicities.

Christopher Nevala-Plagemann & Ignacio Garrido-Laguna

News & Views 25 Apr 2024 Nature Reviews Clinical Oncology

From AACR 2024

Diana Romero

Research Highlight 25 Apr 2024 Nature Reviews Clinical Oncology

Mini-colon and brain 'organoids' shed light on cancer and other diseases

Tiny 3D structures made from human stem cells sometimes offer insights that animal models cannot.

Sara Reardon

News 24 Apr 2024 Nature

Tonic-ing emissions and compatibility to turbocharge CAR-T

Optimization of energy and carbon-nitrogen allocation maximizes the proliferation and functionality of chimeric antigen receptor (CAR)-T cells. Lakhani et al. report that tonic signalling elements (scFvs) affect CAR-T cell metabolic fitness in an antigen-independent manner. A modest carbonnitrogen emission (overflow) and resilient metabolic phenotype (compatibility) are associated with effective CAR-T cell therapy.

Haopeng Wang, Yuwei Huang & Ruoning Wang

News & Views 24 Apr 2024 Nature Metabolism

Bioengineered 'mini-colons' shed light on cancer progression

Cells grown on a 3D scaffold have generated a 'mini-colon' that mimics key features of the organ. Controlled expression of cancer-associated genes in the system offers a way to examine tumour formation over space and time.

Nicolò Riggi & Felipe de Sousa e Melo













News & Views 24 Apr 2024 Nature

Tumours form without genetic mutations

Researchers find that brief and reversible inhibition of a gene-silencing mechanism leads to irreversible tumour formation in fruit flies, challenging the idea that cancer is caused only by permanent changes to DNA.

Anne-Kathrin Classen

News & Views 24 Apr 2024 Nature

<u>Lighting the torch: intratumoural T cell-to-stroma enrichment score as a predictor of immunotherapy</u> <u>response in urothelial carcinoma</u>

T cell infiltration in the tumour microenvironment (TME) is a prerequisite for sustained antitumour immune responses. However, identifying predictive biomarkers that quantify T cell infiltration and the presence of proinflammatory TMEs associated with immune-checkpoint inhibitor (ICI) response for clinical implementation has proved challenging. Here, we highlight a study that validates a T cell-to-stroma enrichment score generated from RNA sequencing data as a novel biomarker for ICI response in patients with urothelial carcinoma.

David H. Aggen & Jonathan E. Rosenberg

News & Views 15 Apr 2024 Nature Reviews Clinical Oncology

A CAF subpopulation promotes LVI in early-stage bladder cancer

Maria Chiara Masone

Research Highlight 15 Apr 2024 Nature Reviews Urology

The case for centralization of care in penile cancer - respecting geographical needs

Centralization of care for penile cancer has been underscored in the 2023 updated EAU–ASCO guidelines. Expertise consolidation enhances patient care, addressing penile cancer complexities from diagnosis to treatment. Centralization initiatives, like the European Reference Networks, and dedicated scientific societies have crucial roles in guiding centralized care pathways to ultimately improve patient outcomes.

Giuseppe Basile, Andrea Necchi ... Peter A. S. Johnstone

Comment 15 Apr 2024 Nature Reviews Urology

Targeting immunogenic cell stress and death for cancer therapy

Immunogenic cell death (ICD) is crucial for the elicitation of anticancer immune responses by therapy, but the successful development of ICDinducing treatments is hindered by various obstacles. This Review provides an overview of the core mechanisms of ICD, discusses obstacles to the development of novel ICD modulators and assesses established and innovative therapeutic approaches for ICD induction.

Lorenzo Galluzzi, Emma Guilbaud ... Francesco M. Marincola

Review Article | 15 Apr 2024 | Nature Reviews Drug Discovery

Programming immune escape

In a recent study published in *Nature*, Goto et al. explore mechanisms of immune evasion in early colorectal cancers and adenomas and identify SOX17 to be crucial for immune escape through suppression of interferon-γ signalling.

Daniela Senft

Research Highlight 12 Apr 2024 Nature Reviews Cancer

NET-working under stress

In this recent study, He et al. establish that chronic stress promotes metastasis through stress-induced formation of neutrophil extracellular traps (NETs).

Gabrielle Brewer
Research Highlight | 12 Apr 2024 | Nature Reviews Cancer

Biological age surges in survivors of childhood cancer

People who survived paediatric cancers age faster and are at higher risk of early death.

Research Highlight 11 Apr 2024 Nature



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Methods & Protocols

Engineering megabase-sized genomic deletions with MACHETE (Molecular Alteration of Chromosomes with Engineered Tandem Elements)

The authors introduce MACHETE (molecular alteration of chromosomes with engineered tandem elements), a clustered regularly interspaced short palindromic repeats directed Cas9-based system for the efficient deletion of megabase-sized genomic regions.

Francisco M. Barriga & Scott W. Lowe

Protocol 7 Feb 2024 Nature Protocols

CONIPHER: a computational framework for scalable phylogenetic reconstruction with error correction

CONIPHER is a computational framework for accurately inferring subclonal structure and the phylogenetic tree from multisample tumor sequencing, accounting for both copy number alterations and mutation errors.

Kristiana Grigoriadis, Ariana Huebner ... Nicholas McGranahan

Protocol 28 Nov 2023 Nature Protocols

Robust scoring of selective drug responses for patient-tailored therapy selection

This protocol presents a computational approach to scoring drug sensitivity that integrates multiple dose-response parameters into a single response metric and identifies differences in drug-response patterns between cancer cells and healthy control cells.

Yingjia Chen, Liye He ... Tero Aittokallio

Protocol 23 Nov 2023 Nature Protocols

INVADEseq to identify cell-adherent or invasive bacteria and the associated host transcriptome at singlecell-level resolution

Invasion-adhesion-directed expression sequencing adapts the 10x Genomics 5' single-cell RNA sequencing protocol to enable generation of bacterial and eukaryotic DNA libraries to identify adherent or invasive bacteria and the associated host transcriptome at a single-cell level.

Jorge Luis Galeano Niño, Hanrui Wu ... Susan Bullman

Protocol 3 Oct 2023 Nature Protocols

Genome-wide pooled CRISPR screening in neurospheres

The authors present a protocol for genome-wide clustered regularly interspaced short palindromic repeat screening of three-dimensional neurospheres.

Tanaz Abid, Amy B. Goodale ... David E. Root

Protocol 7 Jun 2023 <u>Nature Protocols</u>

Newly diagnosed AML: quizartinib improves OS

David Killock
Research Highlight | 30 May 2023 | Nature Reviews Clinical Oncology

Promising results for antisense RNA therapy in mouse models of diffuse midline glioma

Caroline Barranco

Research Highlight 30 May 2023 Nature Reviews Neurology

Serum tumour markers for testicular cancer recurrence

The current serum tumour markers α-fetoprotein, human chorionic gonadotrophin, and lactate dehydrogenase show limited value for testicular cancer relapse detection. A recent study highlights that false-positive elevations in follow-up monitoring are common and, conversely, many patients do not have elevations despite proven relapse. These findings highlight the potential for circulating microRNAs to be used as improved biomarkers for relapse detection.

Matthew J. Murray, Cinzia G. Scarpini & Nicholas Coleman

News & Views 30 May 2023 Nature Reviews Urology

Cancer at Nature Portfolio





	Drug/selection sensitivity (4–7 d) Library titration (5 d) 🖈
5	Expansion
þ	Large-scale infection, Stage 2: CRISPR screening, Steps 2-33



https://www.nature.com/collections/bpwtvhdwgf

Stress response in tumor-infiltrating T cells is linked to immunotherapy resistance

A newly composed single-cell transcriptomic atlas of tumor-infiltrating T cells across 16 cancer types revealed previously undescribed T cell states and heterogeneity. A unique T cell stress response state, T_{STR}, was linked to immunotherapy resistance. Our high-resolution T cell reference maps, web portal, and annotation tool can assist efforts to develop T cell therapies.

Research Briefing 30 May 2023 Nature Medicine

CD4⁺ CAR T cells — more than helpers

Therapeutic products containing CD8⁺ and CD4⁺ T cells expressing CARs are effective at inducing remission in patients with cancer. How CD4⁺ CAR T cells contribute to the anti-tumor response has not been well established. A study uses syngeneic models and in vivo imaging to glean mechanistic insights into how CD4⁺ T cells target tumors.

M. Eric Kohler & Terry J. Fry

News & Views 29 May 2023 Nature Cancer

Venetoclax-obinutuzumab combinations are effective in fit patients with CLL

Diana Romero

Research Highlight 26 May 2023 Nature Reviews Clinical Oncology

Taking the temperature of lung cancer antigens

Antigen presentation is fundamental to anti-tumor immunity, but our understanding of the physiological and molecular inputs to the process in different contexts remains limited. Two new studies explore the contribution of cell-intrinsic proteolytic mechanisms and cell-extrinsic hot and cold tumor microenvironments in shaping the antigenic landscape in lung cancer.

Paul A. Stewart & Alex M. Jaeger

News & Views 26 May 2023 Nature Cancer

A skull bone marrow niche for antitumour neutrophils in glioblastoma

A preprint by Lad et al. shows that tumour-associated neutrophils in glioblastoma originate from skull bone marrow and acquire an antigen-presenting cell phenotype intratumorally in the presence of local T cells.

Austeja Baleviciute & Lily Keane

Journal Club 26 May 2023 Nature Reviews Immunology

Impaired RNA clearance

In this study, Insco et al. find patient-specific CDK13 mutations to impede RNA surveillance, leading to the accumulation and translation of prematurely terminated RNAs that drive malignancy in melanoma models.

Gabrielle Brewer

Research Highlight 25 May 2023 Nature Reviews Cancer

Peptide-mediated CRISPR engineering of cells

An article in Nature Biomedical Engineering reports a simple and hardware-independent peptide-mediated delivery method for the CRISPR-mediated engineering of T cells.

Nesma El-Saved Ibrahim

Research Highlight 25 May 2023 Nature Reviews Bioengineering

Nature.com



