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AACR 2026 – General Overview

- ➔ • **Meeting Scope:** AACR 2026 is expected to cover the full cancer research spectrum, from early detection and biomarkers to therapy, resistance, and survivorship
- ➔ • **Immunology Focus:** The meeting is set to strongly feature cancer immunology, including CAR-T, CAR-NK, T-cell engagers, checkpoint strategies, and immune modulation
- ➔ • **Mechanistic Depth:** Presentations are expected to connect therapeutic response with lineage plasticity, clonal evolution, metabolic adaptation, and spatially defined resistance programs
- ➔ • **Translational Depth:** The conference is expected to connect biology with application through organoids, xenografts, mouse models, and other translational systems
- ➔ • **Broad Tumor Coverage:** Presentations are expected to span major solid tumors and hematologic cancers, reflecting broad scientific and clinical relevance
- ➔ • **Clinical Relevance:** The dataset suggests strong focus on treatment response, resistance, outcomes, and real-world relevance across oncology care



AACR 2026– Conference Themes



- **Precision Diagnostics:** Key data are expected to show blood-based and genomic platforms improving early detection, resistance tracking, and treatment selection across solid tumors
- **Immune Resistance:** A major theme should address immune evasion, stromal suppression, myeloid remodeling, and other drivers of immunotherapy resistance
- **Biomarkers and Detection:** Studies are expected to reinforce biomarker-led oncology through liquid biopsy, cfDNA, genomic scoring, and early detection platforms
- **Novel Modalities:** The meeting should feature ADCs, epigenetic therapies, targeted combinations, and RNA or nanoparticle-enabled approaches
- **Tumor Microenvironment:** Spatial and microenvironment studies are set to clarify how fibroblasts, B cells, and immune architecture shape treatment response
- **Real-World and Population Science:** AACR 2026 is expected to include real-world analyses, disparities research, and long-term outcome studies across diverse populations

Noteworthy Scientific presentations at AACR 2026





Key Topics From Notable Presentations (1/5)



- **Precision Oncology, Genomics, and Diagnostic Platforms:** AACR 2026 precision oncology is expected to move beyond static genotyping toward scalable, real-world, and population-aware platforms that improve early detection, resistance monitoring, and therapy matching
- **Liquid Biopsy and Blood-Based Detection:** Serial plasma CGP in 718 NSCLC patients (818 tests) is expected to refine resistance tracking, while rbcDNA screening in 1,251 participants is set to detect advanced adenomas and CRC at 85% and 95% sensitivity at 90% specificity
- **Biomarker Stratification and Equitable Genomics:** WES-based HRD scoring in 81 ovarian cancers is likely to outperform BRCA alone for PARPi selection, while KMT2C from 143,961 tumors and the 10,000-patient India–Germany platform are poised to expand biomarker precision and population relevance



Key Topics From Notable Presentations (2/5)



- **Immunotherapy and Cell Therapy:** Sessions are expected to show that immunotherapy efficacy will increasingly depend on pairing engineered immune effectors with precise microenvironment remodeling to improve persistence, infiltration, and durability in solid tumors
- **Engineered Cell Therapies and T-Cell Optimization:** AACR 2026 immunotherapy is expected to highlight next-generation cellular engineering, with LM-103 showing 75% disease control in acral melanoma, STK-012 achieving 55% ORR in first-line PD-L1–negative NSCLC, and CAR platforms advancing through GPC2, GPC3, and CRISPR-All/CACTUS2 optimization strategies
- **Microenvironment-Directed Immunotherapy:** The field is likely to emphasize overcoming stromal and immune suppression through localized or combinatorial approaches, including CBD-αCTLA4 extending survival by 140% in recurrent glioblastoma, IL-12 circRNA LNPs synergizing with anti-PD-L1, and FGFR1/CAF, bacterial, dietary fiber, and versikine strategies enhancing immune activation



Key Topics From Notable Presentations (3/5)



- **Targeted and Novel Therapies:** Experts will target therapy data are expected to show that deeper mechanistic stratification will drive the next wave of efficacy by pairing novel agents with resistance-informed combinations and biomarker-guided selection
- **ADCs and Next-Generation Targeted Platforms:** Sessions are expected to highlight therapeutic diversification, with T-DXd improving 5-year OS to 66.6% vs 62.1% in HER2-amplified mCRC, STRO-004 showing multiple CRs across solid tumors, and ASP2998 combining TROP2 targeting with STING agonism for cytotoxic and immune effects
- **Mechanism-Guided Combination and Resistance Targeting:** The meeting is likely to emphasize biologically informed combinations, including AURKA+KRAS co-inhibition in CRC, CBP/p300+PARP synergy in mCRPC, REM-422 activity in 8/10 T-ALL PDXs, and IM156 targeting chemotherapy-induced OxPhos dependence in PDAC



Key Topics From Notable Presentations (4/5)



- **Tumor Biology and Resistance:** Tumor biology data are expected to show that resistance will be best overcome by matching therapy to dynamic lineage states, spatial immune context, and microenvironment-dependent adaptive vulnerabilities
- **Microenvironment-Driven Resistance Biology:** AACR 2026 is expected to show that resistance will increasingly map to stromal and immune circuits, including 268 NeoTRIP TNBC samples linking B-cell niches to response, 80% complete regression with NAT10 inhibition in MSS CRC, and neutrophil-, fibroblast-, and CAF-mediated suppression across prostate, bladder, and lung tumors
- **Context-Specific Vulnerabilities and Models:** The conference will emphasise stage-, genotype-, and lineage-specific liabilities, including KDM5B-SOX9 in t-NEPC, KRAS G12C-AURKA cotargeting in 15 NSCLC lines, and 3D bioprinted HER2-positive models showing 3–10-fold higher IC50s than 2D cultures



Key Topics From Notable Presentations (5/5)



- **Epidemiology and Outcomes:** Epidemiology data are expected to show that cancer outcomes will be increasingly shaped by survivorship toxicity, inherited risk architecture, and population-specific factors that sharpen prevention and monitoring strategies
- **Survivorship Risks and Long-Term Outcomes:** Trials will show that survivorship burden will extend beyond recurrence, with 8,365 breast cancer patients linking endocrine adherence to higher cardiometabolic risk and 3,876 CRC patients showing higher BMR associated with improved 5-year, but not 10-year, survival
- **Population Risk Stratification and Diverse Epidemiology:** Advanced risk stratification is expected to be highlighted, with a multi-ancestry breast cancer GWAS uncovering 469 loci (including 249 novel), alongside large cohort analyses (365,735, 94,232, and 49,370 participants) identifying distinct high-risk population subsets



Notable Presentations And Late-breaking Sessions At AACR 2026

Notable Presentations At AACR 2026



Precision Oncology, Genomics, and Diagnostic Platforms (1/5)

Date	Title	Author	Summary
19 April 2026	Serial plasma comprehensive genomic profiling detects therapy resistance and guides management of metastatic non-small cell lung cancer	H. R. Robinson	• Introduction: Plasma CGP offers a minimally invasive alternative to tissue genotyping in NSCLC, but real-world clinical utility remains unclear. • Methodology: Retrospective analysis of 718 patients (818 tests) integrating clinical data with Guardant360/360CDx sequencing and ensemble variant annotation. • Results: pCGP informed management in 13%, notably when tissue was unavailable, and improved turnaround and mutation detection. Undetectable ctDNA correlated with significantly prolonged OS. Genotype-matched therapy improved survival. In EGFR-mutant NSCLC, pCGP identified actionable resistance (22%), with therapy-line-specific emergence of PIK3CA and RAS alterations. • Conclusions: Serial pCGP enables prognostication, resistance monitoring, and optimized targeted therapy selection in NSCLC.
19 April 2026	Genomic signatures in red blood cell DNA enable early non-invasive detection of colorectal neoplasia: A multicenter clinical study	Z. Shah	• Introduction: CRC mortality remains high, while current non-invasive screening underperforms for advanced adenomas. This study evaluates red blood cell DNA as a blood-based genomic instability marker for early colorectal neoplasia detection. • Methodology: Multicenter study of 1,251 colonoscopy-confirmed participants across CRC, advanced adenoma, and control groups. rbcDNA from 1–2 mL blood underwent low-coverage whole-genome sequencing, with model development in discovery/internal test sets and locked external validation in two cohorts. • Results: At 90% specificity, sensitivity reached 85% for advanced adenomas and 95% for CRC. External cohorts showed consistent neoplasia detection (78–80%), including fecal occult blood test-negative AA and early-stage CRC cases. • Conclusions: rbcDNA shows strong promise as a minimally invasive, high-sensitivity platform for early CRC interception, particularly for premalignant lesions.



Notable Presentations At AACR 2026



Precision Oncology, Genomics, and Diagnostic Platforms (2/5)

Date	Title	Author	Summary
19 April 2026	Real-world analysis of NSCLC variant-level frequencies from liquid biopsy testing in diverse U.S. populations	Z. Liu	• Introduction: NSCLC is genomically heterogeneous, and community access to molecular profiling remains uneven, especially in rural and underrepresented populations. This study assessed real-world liquid biopsy data to define actionable variant frequencies across diverse U.S. groups. • Methodology: Analysis of >350,000 send-out liquid biopsy tests over 10 years using amplicon-based NGS and ddPCR across >20 ethnically diverse populations, covering SNV/INDELs, fusions, amplifications, and exon skipping events. • Results: ddPCR positivity was 1.5%, with KRAS G12C most frequent among positives. NGS showed 46% SNV/INDEL positivity, dominated by TP53; fusion positivity was 15%, led by EML4-ALK. African American patients and the Southeastern U.S. showed disproportionately high mutation burdens. • Conclusions: Centralized liquid biopsy expands molecular profiling access and reveals meaningful demographic and geographic disparities relevant to community treatment planning.
19 April 2026	Developing a real-world clinical genomic platform to deliver precision oncology in underrepresented populations	S. Karan	• Introduction: Precision oncology datasets remain heavily biased toward Caucasian populations, limiting biomarker validity and treatment transferability in high-burden, underrepresented regions. • Methodology: This India-Germany initiative built a real-world multi-omics platform linking oncology centers, structured source-data capture, clinician training, AI-enabled clinical integration, deep whole-genome sequencing, matched controls, transcriptomics, and tumor-board analytics. • Results: The program targets 10,000 diverse Indian patients. Early data show feasible cross-institutional harmonization and suggest population-specific differences in mutational signatures, copy-number changes, and immune states, with added actionable findings and missed diagnostic recovery. • Conclusions: This scalable platform could improve biomarker discovery, treatment matching, and global precision oncology equity.





Precision Oncology, Genomics, and Diagnostic Platforms (3/5)

Date	Title	Author	Summary
19 April 2026	A spatiotemporal proteome map of chemotherapy response in metastatic breast cancer	X. Zhao	• Introduction: Tumor-cell behavior depends on dynamic spatial and functional protein organization, which can be profoundly altered by chemotherapy. This study maps these treatment-driven changes in metastatic breast cancer cells. • Methodology: Multi-modal spatiotemporal proteomics combined immunofluorescence imaging, mass spectrometry, and single-cell CRISPR sequencing, with self-supervised contrastive learning used to fuse cross-modal protein embeddings while preserving treatment effects. • Results: Chemotherapy induced marked protein reorganization. HDAC8 shifted from a cytosolic assembly with TET1/SETDB2/PHF6/YWHAG in untreated cells to a nuclear, treatment-associated complex with PARP1, KAT6B, DNMT3A, HDAC9, HDAC2, and BRD4 after paclitaxel. • Conclusions: This framework enables high-resolution mapping of drug-driven cellular architecture and functional state transitions.
19 April 2026	NSCLC patient-derived organoids recapitulate tissue signalling and impairment of infiltrated immune cell activation predicting patients' response to therapy	A. Pasto	• Introduction: NSCLC has poor long-term outcomes, and immunotherapy benefits only a subset of patients. This study explored whether patient-derived organoids can model treatment response and immune susceptibility. • Methodology: Twelve chemotherapy-naïve high-risk NSCLC PDOs underwent cisplatin treatment, immune-cell co-culture, and multi-omics profiling including imaging, flow cytometry, transcriptomics, genomics, and extracellular-vesicle proteomics. • Results: Cisplatin IC50 distinguished clinical responders from non-responders. Non-responder PDOs showed greater post-cisplatin immune infiltration, but baseline infiltrating CD8+ cells were more exhausted and inflammatory signaling was higher, mirrored in matched tumors; EV cargo also differed. • Conclusions: PDOs recapitulate patient biology and may predict chemoresponse and immune resistance states.





Precision Oncology, Genomics, and Diagnostic Platforms (4/5)

Date	Title	Author	Summary
20 April 2026	Clinical validation of WES-based HRD scoring and its prognostic value for PARP inhibitor maintenance therapy in ovarian cancer	D. Kyung	• Introduction: HRD is a key determinant of PARP inhibitor sensitivity in ovarian cancer, but scalable assays that jointly assess HRD and BRCA status require stronger clinical validation. • Methodology: This retrospective study analyzed 81 epithelial ovarian cancers using matched tumor-blood WES, deriving scarHRD-based scores and concurrent germline/somatic BRCA profiling, with prognostic assessment in PARPi-treated patients. • Results: HRD ≥ 50 outperformed ≥ 42, correlated more strongly with germline BRCA, and consistently predicted longer PFS, especially in non-neoadjuvant and recurrent settings. BRCA predicted benefit more narrowly and mainly in first-line NAC-treated disease. • Conclusions: WES-based HRD scoring appears more robust than BRCA alone for PARPi stratification.
20 April 2026	Sequential cell free DNA analysis reveals genetic heterogeneity in patients with relapsed neuroblastoma enrolled in the SIOPEX-ITCC BEACON study	G. Schleiermacher	• Introduction: Relapsed high-risk neuroblastoma has poor outcomes, and deeper understanding of evolving resistance biology is needed to improve combination treatment strategies. • Methodology: Molecular profiling was performed on BEACON trial tumor samples and serial plasma using lcWGS, WES, or targeted sequencing with paired germline analysis to assess genomic alterations and clonal evolution. • Results: MYCN amplification, ALK mutations, and RAS/MAPK/p53 alterations were recurrent. Baseline cfDNA quantity correlated with outcome, not disease burden. Plasma captured 53% of tumor SNVs and revealed additional plasma-specific variants, with dynamic emergence of resistance-associated mutations during progression. • Conclusions: Serial cfDNA is a powerful tool for monitoring heterogeneity, evolution, and resistance in refractory neuroblastoma.





Precision Oncology, Genomics, and Diagnostic Platforms (5/5)

Date	Title	Author	Summary
20 April 2026	Real-world evidence of KMT2C mutation as a biomarker of sensitivity to platinum-based therapy in solid cancers	B. Bockorny	• Introduction: KMT2C loss disrupts epigenetic regulation and homologous recombination repair, providing a rationale that KMT2C-mutant tumors may show enhanced platinum sensitivity. This study tested that hypothesis in real-world solid tumor datasets. • Methodology: A Tempus multimodal cohort of 143,961 solid tumors with DNA profiling was analyzed for survival after platinum chemotherapy, with adjusted rwOS/rwPFS comparisons and external validation in AACR GENIE. • Results: KMT2C mutations occurred in 5.3%, enriched in cervical, endometrial, urinary tract, and breast cancers. Mutations predicted longer platinum-associated survival, strongest in GI cancers, especially CRC, and not with irinotecan. • Conclusions: KMT2C appears to be a promising predictive biomarker for platinum benefit, particularly in colorectal cancer.

Notable Presentations At AACR 2026

Immunotherapy and Cell Therapy (1/8)



Date	Title	Author	Summary
19 April 2026	Circulating tumor cell (CTC) informed pipeline for rapid personalization of synergistic cytokine-armed CAR-NK cell therapy in PDAC	E. K. Longshore	• Introduction: PDAC remains highly lethal because of marked tumor heterogeneity and an immunosuppressive microenvironment that limits durable immunotherapy. This study developed a personalized CTC-guided, cytokine-armed CAR-NK strategy. • Methodology: Label-free CTC isolation with multi-omics profiling identified patient-specific antigens, followed by generation of anti-MUC4 and anti-MSLN CAR-NK cells with IL-12 and/or IL-15 cytokine arming, assessed in cytotoxicity and serial killing assays. • Results: MSLN+ CTCs were detected in 92% and metastatic-restricted MUC4+ CTCs in 67%. Dual cytokine arming produced the strongest sustained IFN-γ response and preserved cytotoxicity through six rounds. • Conclusions: CTC-informed, IL-12/IL-15-armed CAR-NK cells provide a compelling adaptive precision immunotherapy framework for PDAC.
19 April 2026	Tumor-specific antibodies elicited by engineered bacteria promote bladder cancer immunotherapy	K. L. Swancutt	• Introduction: The intratumoral microbiome can modulate tumor progression and therapeutic response, creating opportunities to engineer bacteria as immune-remodeling agents. This study tested whether CXCL13-expressing probiotic E. coli Nissle could enhance antitumor immunity in bladder cancer. • Methodology: Synthetic biology was used to engineer E. coli Nissle 1917 to express human CXCL13, followed by intravesical delivery in orthotopic bladder cancer models with assessment alone and with PD-1 blockade. • Results: Engineered bacteria colonized tumors, induced germinal center responses in draining lymph nodes, amplified antitumor antibody responses, and improved long-term survival and rechallenge protection with PD-1 blockade. • Conclusions: CXCL13-engineered intratumoral bacteria may potentiate checkpoint inhibition by strengthening tumor-specific humoral immunity.



Notable Presentations At AACR 2026

Immunotherapy and Cell Therapy (2/8)



Date	Title	Author	Summary
19 April 2026	DPP-4: A CD8+ T cell metabolic checkpoint and cancer immunotherapy target	Daniela A. Garcia	• Introduction: CD8+ T-cell exhaustion in tumors is tightly linked to metabolic failure, limiting effective antitumor immunity. This study identifies DPP-4 as a metabolic immune checkpoint in exhausted brain tumor-infiltrating T cells. • Methodology: Investigators combined expression profiling, pharmacologic DPP-4 inhibition with sitagliptin, functional assays, mechanistic GAD1 inhibition, preclinical glioblastoma models, and retrospective clinical outcome analysis. • Results: DPP-4 increased with terminal exhaustion. Sitagliptin restored activation programs, mitochondrial reserve, proliferation, cytotoxicity, and CAR-T function; these effects were GAD1-dependent. In vivo, DPP-4 inhibition prolonged survival in a CD8-dependent manner, with supportive retrospective patient signals. • Conclusions: DPP-4 inhibition is a compelling metabolic immunotherapy repurposing strategy for glioblastoma.
19 April 2026	On-demand GLUT3 expression augments CAR-T cell metabolic fitness and antitumor efficacy while preventing toxicity in glioblastoma models	M. Orr	• Introduction: CAR-T therapy in glioblastoma is constrained by the glucose-depleted tumor microenvironment, which drives metabolic insufficiency and functional failure. • Methodology: The study evaluated GBM-associated glucose deprivation and compared CAR-T cells with constitutive versus NFAT-inducible, antigen-triggered GLUT3 expression in functional and intracranial xenograft models, including toxicity assessments. • Results: Stable GLUT3 restored killing and cytokine output but caused overactivation, apoptosis, exhaustion, adverse events, and death. In contrast, on-demand GLUT3 enhanced metabolic fitness, sustained tumor control, and avoided cognitive or histologic neurotoxicity. • Conclusions: Temporally controlled metabolic rewiring, rather than continuous enhancement, may be critical for safe and effective CAR-T therapy in solid tumors.



Notable Presentations At AACR 2026

Immunotherapy and Cell Therapy (3/8)



Date	Title	Author	Summary
19 April 2026	Dual remodeling of RCC-associated fibroblasts via miR-196b antagomir and COUP-TFII inhibitor ultrasmall lactoferrin-lipid nano-assemblies augments immunotherapy	A. Ziada	• Introduction: RCC often resists checkpoint blockade, partly due to immunosuppressive CAFs. This study targeted CAF plasticity using a dual nanotherapy designed to reverse fibroblast activation and remodel the tumor microenvironment. • Methodology: Patient-derived RCC CAFs were profiled for oncomiRs, then treated with ultrasmall recombinant lactoferrin-stabilized lipid nano-assemblies co-delivering anti-miR-196b and a COUP-TFII inhibitor; functional, secretory, and in vivo biodistribution effects were assessed. • Results: Nanoparticles were efficiently internalized, suppressed CAF activation/ECM markers, increased p27, reduced IL-6/IL-8/MCP1, and indirectly decreased cancer-cell migration, stemness, EMT, and proliferation; kidney tumor accumulation was favorable in vivo. • Conclusions: Dual CAF-reprogramming nanotherapy is a promising RCC microenvironment-directed strategy.
20 April 2026	The cellular architecture of the infused T cell predicts efficacy of autologous tumor-infiltrating lymphocyte therapy (LM-103) in acral melanoma	Chao Zhang	• Introduction: Acral melanoma responds poorly to checkpoint blockade, creating strong rationale for alternative cell therapies and biomarkers of durable response. • Methodology: This investigator-initiated study analyzed LM-103 TIL therapy in four advanced cases using integrated scRNA-seq, TCR-seq, pseudotime, cell-cell communication, and longitudinal peripheral blood tracking. • Results: Disease control reached 75%, including one durable complete response. Responders were enriched for Tfh and intermediate exhausted CD8+ T cells, showed stronger costimulatory signaling and higher clonality, while non-response aligned with terminal exhaustion and suppressive TGFβ/MIF networks. Persistent TEX_int-derived progenitor-like clones supported long-term immunity. • Conclusions: Coordinated Tfh-TEX_int ecosystems, not infusion size, appear central to durable TIL efficacy.



Notable Presentations At AACR 2026

Immunotherapy and Cell Therapy (4/8)



Date	Title	Author	Summary
20 April 2026	Decoding the medulloblastoma surfaceome prioritizes the oncofetal antigen GPC2 for potent CAR-T cell therapy	S. Heitzeneder	• Introduction: Medulloblastoma has poor outcomes at relapse and lacks robust CAR-T targets. This study sought clinically actionable surface antigens, emphasizing antigen density and normal-tissue sparing. • Methodology: Investigators integrated tumor/normal-tissue surfaceome analyses with quantitative flow-cytometric antigen-density mapping across 24 biopsies, then tested GPC2-CAR-T constructs with or without cJUN overexpression in orthotopic xenograft models. • Results: GPC2 emerged as the leading oncofetal target, with broad but variable density. Both CARs controlled intermediate-density tumors, whereas repeated dosing or cJUN improved persistence in high-density disease and only cJUN-enabled CAR-T retained efficacy in low-density tumors. • Conclusions: GPC2 density is a key determinant of CAR-T activity, and cJUN tuning may expand therapeutic reach in medulloblastoma.
20 April 2026	Universal T cell therapy screening library in preclinical models of CAR T cell therapy	A. Eapen	• Introduction: Durable remission after current T-cell therapies remains limited, creating need for systematic discovery of genetic programs that improve engineered T-cell fitness and persistence. • Methodology: The study developed CRISPR-All, a combinatorial perturbation platform enabling simultaneous overexpression, knockout, knockdown, and synthetic sequence insertion, then built the CACTUS2 meta-library and screened edited CD19-28Z CAR-T cells under chronic repetitive tumor stimulation. • Results: Across leukemia and lymphoma co-culture models, top-performing hits were predominantly synthetic chimeras of overexpressed genes, highlighting multi-feature engineering strategies that enhance CAR-T fitness under prolonged stress. • Conclusions: CRISPR-All/CACTUS2 provides a scalable framework for rational next-generation CAR-T design.



Notable Presentations At AACR 2026

Immunotherapy and Cell Therapy (5/8)



Date	Title	Author	Summary
20 April 2026	Triple disruption of CCDC6, CBLB, and ASB2 promotes the therapeutic efficacy of Glypican 3 targeted T cells	Azlann Arnett	• Introduction: Rare viral CAR-cassette integrations can drive clonal expansion, offering a natural experiment to identify genetic regulators of CAR-T proliferation and efficacy in solid tumors. • Methodology: Investigators analyzed clonal dynamics from single-cell VDJ/RNA sequencing in 12 GPC3 CAR-T trial patients, performed whole-genome integration mapping, validated integrations by single-cell DNA sequencing, and functionally tested candidate genes in HCC models. • Results: One IL15-CAR-T-treated HCC patient developed massive clonal expansion with marked tumor regression. Expanded clones harbored integrations disrupting CBLB, CCDC6, and ASB2, generating chimeric transcripts and proliferation-associated transcriptional states. Combinatorial knockout enhanced expansion and antitumor activity. • Conclusions: Integration-linked disruption of specific regulators can potentiate CAR-T persistence and tumor control.
20 April 2026	Tumor-tailored ionizable lipid nanoparticles facilitate IL-12 circular RNA delivery for enhanced lung cancer immunotherapy	Y. Xu	• Introduction: mRNA immunotherapies, particularly IL-12, are limited by transient expression and systemic toxicity. This study developed a lung-targeted circRNA platform to enable safer, sustained cytokine delivery. • Methodology: A combinatorial lipid screen identified H1L1A1B3, an ionizable LNP delivering IL-12 circRNA with enhanced transfection and intrinsic NF-κB/IRF activation; efficacy was tested in subcutaneous and orthotopic lung cancer models. • Results: The platform prolonged IL-12 expression, delayed tumor growth, synergized with anti-PD-L1, increased leukocyte and T-cell infiltration, improved CD8/Treg balance, and suppressed orthotopic lung tumors without liver toxicity. • Conclusions: Dual-function LNP-circRNA delivery offers a potent, localized, and safer IL-12 immunotherapy strategy for lung cancer.



Notable Presentations At AACR 2026

Immunotherapy and Cell Therapy (6/8)



Date	Title	Author	Summary
20 April 2026	Collagen binding enhances anti-CTLA4 therapy in recurrent glioblastoma	L. Barr	• Introduction: Recurrent glioblastoma remains rapidly fatal, partly because CTLA4-directed therapy fails to adequately penetrate its collagen-remodeled, highly immunosuppressive microenvironment. • Methodology: Investigators engineered a collagen-binding αCTLA4 fusion targeting COL I/III, then evaluated biodistribution, single-cell transcriptomics, survival, humanized antibody translation, and human GBM slice/PBMC-humanized mouse models. • Results: CBD-αCTLA4 showed superior tumor accumulation, reduced Treg and exhausted T cells, recruited cDC1s, and prolonged survival by 140% with complete responses, unlike conventional αCTLA4. Humanized CBD-ipilimumab also reduced Tregs and improved survival. • Conclusions: Collagen-targeted CTLA4 blockade is a compelling strategy to overcome delivery failure and immunosuppression in recurrent glioblastoma.
20 April 2026	A novel DLL3 trispecific T cell engager antibody integrating the CD2/CD58 co-stimulatory pathway demonstrates superior antitumor efficacy and balanced safety profile	Yu Liang	• Introduction: Solid-tumor T-cell engagers are constrained by poor T-cell infiltration, suppressive microenvironments, and toxicity from existing co-stimulatory designs. This study developed DLL3$\times$CD3$\times$CD2 trispecific antibodies to improve activity and safety. • Methodology: Novel trispecific TCEs incorporating a CD2 co-stimulatory arm were tested in vitro for killing, proliferation, cytokine release, and antigen dependence, then evaluated for pharmacokinetics and efficacy in PBMC-reconstituted xenograft models. • Results: Compared with parental DLL3$\times$CD3 and tarlatamab, trispecifics showed stronger killing and T-cell proliferation, particularly at low effector-to-target ratios, with more balanced cytokines and minimal antigen-independent activation. In vivo activity and PK were favorable. • Conclusions: CD2 co-stimulation may meaningfully widen the therapeutic window of DLL3-targeted TCEs in solid tumors.



Notable Presentations At AACR 2026

Immunotherapy and Cell Therapy (7/8)



Date	Title	Author	Summary
20 April 2026	FGFR1+ cancer-associated fibroblasts contribute to the failure of CAR-T cell therapy in B-cell lymphoma through the secretion of TGFβ	N. Di Siervi	• Introduction: Durable remission after lymphoma CAR-T remains limited, partly due to CAF-driven, TGFβ-rich immunosuppressive microenvironments that promote T-cell dysfunction and treatment resistance. • Methodology: The study examined FGFR1 regulation of CAF-derived TGFβ using genetic and pharmacologic inhibition, then tested FGFR1 blockade with CD19- or BAFFR-CAR-T cells in a refractory patient-derived lymphoma xenograft model. • Results: FGFR1 inhibition reduced CAF TGFβ production, lowered circulating tumor burden, increased CAR-T expansion and intratumoral infiltration, decreased PD1+LAG3+ exhausted CD4+/CD8+ cells, and improved survival with both CAR platforms. • Conclusions: FGFR1 inhibition appears to reprogram the lymphoma microenvironment and meaningfully enhance CAR-T efficacy.
21 April 2026	Selective immune activation of antigen activated T cells with STK-012, an a/b IL-2 receptor biased partial agonist, with pembrolizumab and chemotherapy in 1L PD-L1 negative non-squamous NSCLC	S. Punekar	• Introduction: PD-L1-negative nonsquamous NSCLC has poor outcomes with pembrolizumab plus chemotherapy, especially in immune-cold subsets. STK-012 was designed to selectively expand antigen-activated CD25+ T cells while avoiding classic IL-2 toxicities. • Methodology: In this phase 1a/b cohort, 22 efficacy-evaluable first-line patients received subcutaneous STK-012 plus pembrolizumab/chemotherapy, with serial cytokine, flow cytometry, and TCR clonality analyses. • Results: ORR was 55% overall, including 50% in PD-L1<1%, 55% in loss-of-function tumor suppressor cases, and 80% in mucinous tumors. Treatment drove sustained activated/exhausted CD8+ T-cell proliferation, TCR repertoire remodeling, and durable IFNγ/IL-18/IP-10 induction with limited TNFα/IL-6. • Conclusions: STK-012 shows promise for overcoming immune resistance in cold NSCLC.



Notable Presentations At AACR 2026

Immunotherapy and Cell Therapy (8/8)



Date	Title	Author	Summary
21 April 2026	Peripheral immune profiling from the DIET trial - A randomized double blinded dietary intervention study in melanoma patients receiving immunotherapy	Carrie R. Daniel	• Introduction: Dietary fiber may improve melanoma response to immune checkpoint blockade, potentially through microbiome-mediated systemic immune modulation. This analysis examined peripheral immune effects of a high-fiber intervention versus control diet. • Methodology: In a randomized phase II trial, paired PBMCs underwent NanoString and CyTOF profiling; complementary fecal microbiota transfer studies tested causality in anti-PD-L1-treated melanoma-bearing mice. • Results: High fiber reduced circulating monocytes/macrophages/neutrophils and increased effector-memory CD4+/CD8+ T cells, with stronger effects in nivolumab/ipilimumab-treated patients. FMT from post-intervention stool improved murine ICB response and lowered monocyte/dendritic-cell frequencies. • Conclusions: High fiber appears to favorably reprogram peripheral immunity through microbiome-dependent mechanisms that may enhance immunotherapy efficacy.
21 April 2026	Biomarker-driven restoration of tumor provisional matrix signaling network reverses resistance to checkpoint inhibition immunotherapy	D. J. Lagal	• Introduction: Stromal immune niches at the tumor-stroma interface are crucial for immunotherapy response, and defective versican proteolysis may underlie immune exclusion and checkpoint resistance. • Methodology: Using biomarker-stratified tumor models mimicking VCAN proteolysis-weak phenotypes, investigators tested versikine delivered as LNP-mRNA or recombinant protein, alone and with checkpoint-based combinations, while interrogating immune-cell dependencies. • Results: Versikine induced Tfh-like CD4+ cells, dendritic cell-CD8 "immune triads," and activated cytolytic CD8+ expansion. It showed monotherapy activity in VPW-VCAN^{lo} tumors and synergized with immunotherapy in both VPW-VCAN^{lo} and immune-excluded VPW-VCAN^{hi} settings. • Conclusions: Versikine supports a biomarker-guided stromal reprogramming strategy to overcome checkpoint resistance.



Notable Presentations At AACR 2026

Epidemiology and Outcomes (1/4)



Date	Title	Author	Summary
19 April 2026	Asymmetric emergence of cardiovascular disease in hematologic malignancy survivors: A national real-world analysis	Y. Song	• Introduction: Hematologic malignancies and cardiovascular disease are bidirectionally linked, but the relative magnitude and timing of risk remain poorly defined in large real-world populations. • Methodology: EHR data from All of Us identified survivors of hematologic cancers without prior CVD and, conversely, CVD patients without prior blood cancer; cumulative incidence, time-to-event, and adjusted risk ratios were compared. • Results: New-onset CVD was frequent, early, and far more common than subsequent blood cancer after CVD. Risk was highest in MDS and multiple myeloma, with arrhythmias and heart failure predominant. Younger age and female sex were protective. • Conclusions: Hematologic cancer survivorship confers a marked, front-loaded cardiovascular hazard, supporting intensive early cardio-oncology surveillance.
19 April 2026	Endocrine therapy adherence and 10-year risk of cardiometabolic outcomes among women with hormone receptor-positive breast cancer	J. R. Ledesma	• Introduction: Adjuvant endocrine therapy lowers recurrence in hormone receptor-positive breast cancer but may worsen long-term cardiometabolic health, an increasingly important survivorship issue. • Methodology: This prospective cohort included 8,365 postmenopausal women with stage I–III disease; annual adherence over five years was linked to 10-year cardiometabolic outcomes using sequentially doubly robust competing-risk models, stratified by aromatase inhibitor versus tamoxifen. • Results: Longer adherence increased hypertension, dyslipidemia, and diabetes risk, most clearly with aromatase inhibitors; tamoxifen mainly increased hypertension. Risks rose progressively with each additional adherent year. • Conclusions: Extended aromatase inhibitor exposure carries meaningful cardiometabolic trade-offs, supporting closer risk-adapted monitoring during survivorship.



Notable Presentations At AACR 2026

Epidemiology and Outcomes (2/4)



Date	Title	Author	Summary
19 April 2026	Cardiorespiratory multimorbidity and lung cancer risk: A population-based cohort study	K. Chen	• Introduction: Cardiorespiratory multimorbidity may define a particularly high-risk phenotype for lung cancer, but its effect on risk magnitude and disease progression has been insufficiently characterized. • Methodology: This prospective UK Biobank analysis followed 365,735 initially cancer-, respiratory-, and cardiovascular-disease-free participants using time-varying Cox, accelerated failure time, and multi-state trajectory models. • Results: CRM conferred the highest lung cancer risk and fastest onset versus isolated respiratory or cardiovascular disease. Multi-state analyses showed greater progression from respiratory disease to CRM and the strongest transition probability, intensity, and shortest time from CRM to lung cancer. • Conclusions: CRM appears to be a clinically important accelerated-risk state for lung cancer prevention.
19 April 2026	Generational immigration status and gastric cancer incidence among Japanese descendants: An analysis of the Multiethnic Cohort study	H. In	• Introduction: Gastric cancer disproportionately affects racial and ethnic minorities, but the contribution of immigration history to persistent risk among Japanese descendants remains insufficiently defined. • Methodology: This population-based cohort analysis evaluated 94,232 Japanese descendants and non-Hispanic Whites using adjusted Cox models to assess gastric cancer risk by immigration generation and anatomic subtype. • Results: Gastric cancer risk declined stepwise across generations but remained elevated versus non-Hispanic Whites in every generation, with the strongest associations in first-generation and non-cardia disease. Elevated risk persisted in both men and women. • Conclusions: Immigration generation modifies, but does not eliminate, excess gastric cancer risk, supporting generation-aware surveillance in Japanese-descendant populations.

Notable Presentations At AACR 2026

Epidemiology and Outcomes (3/4)



Date	Title	Author	Summary
19 April 2026	Age-related differences in predicted basal metabolic rate and survival outcomes after colorectal cancer in the ColoCare Study	S. Hardikar	• Introduction: Basal metabolic rate reflects systemic metabolism and may influence colorectal cancer outcomes, but its prognostic relevance after diagnosis has not been defined. • Methodology: This multicenter ColoCare analysis included 3,876 stage I–IV CRC patients, estimating baseline BMR by Schofield equation and examining 5- and 10-year overall and CRC-specific survival using adjusted Cox models stratified by age and BMI. • Results: Higher BMR correlated with male sex, younger age, and obesity. It was associated with improved 5-year survival, most notably in younger men, independent of BMI, but showed no significant 10-year survival association. • Conclusions: Higher BMR may serve as a short-term prognostic metabolic marker in CRC.
19 April 2026	The Confluence Project: Largest multi-ancestry genome-wide association study of breast cancer identifies 469 susceptibility loci in over two million participants	T.-. National Cancer Institute	• Introduction: Breast cancer heritability remains partly unexplained, and prior GWAS were heavily Eurocentric, limiting discovery and polygenic risk prediction across diverse populations. • Methodology: This multi-ancestry GWAS analyzed ~47.8 million variants across Confluence and external biobanks, combining harmonized genotyping, TOPMed imputation, array-specific REGENIE analyses, and fixed-effect meta-analysis. • Results: The study identified 469 independent significant loci, including 249 novel signals, and replicated 92% of previously reported loci. Newly discovered loci substantially increased explained genetic variance, especially across non-European ancestry groups. • Conclusions: This landmark diverse GWAS materially expands breast cancer susceptibility architecture and strengthens foundations for equitable risk modeling.



Notable Presentations At AACR 2026

Epidemiology and Outcomes (4/4)



Date	Title	Author	Summary
20 April 2026	Therapy-associated clonal hematopoiesis and risk of hematologic malignancy after primary cancer treatment	K. M. Barnao	• Introduction: Cancer therapy can select clonal hematopoiesis, but its role in promoting mosaic chromosomal alterations and later hematologic malignancy risk remains insufficiently defined. • Methodology: Using UK Biobank genomic data, investigators compared CHIP and autosomal mCAs in therapy-exposed versus unexposed participants and assessed associations with subsequent hematologic malignancy using adjusted logistic regression. • Results: Therapy exposure was associated with higher CHIP and mCA prevalence. Among exposed individuals who later developed hematologic malignancies, both alterations were markedly enriched, including high-risk lesions such as chr9pCNLOH, chr14qCNLOH, and chr13q loss. • Conclusions: Detectable CHIP and mCAs may serve as early biomarkers of therapy-related hematologic malignancy risk.
21 April 2026	Adult height and prostate cancer in the Health Professionals Follow-Up Study: Integrating epidemiologic, genetic, and transcriptomic evidence	A. Wang	• Introduction: Taller adult height has been linked to fatal prostate cancer, but the relative contributions of inherited growth biology, early-life diet, and tumor-level mechanisms remain unclear. • Methodology: In 49,370 men followed prospectively, height associations were modeled for total and fatal prostate cancer, with decomposition into genetic and teenage-dairy residual components plus transcriptomic profiling of tumor, normal, and stromal tissues. • Results: Taller height associated with higher fatal, but not total, prostate cancer risk. The attenuation after genetic adjustment suggests shared inherited determinants, while dietary effects were minimal. Height also correlated with distinct tumor/stromal transcriptional programs. • Conclusions: Height appears to mark genetically driven susceptibility to lethal prostate cancer.



Notable Presentations At AACR 2026

Targeted and Novel Therapies (1/6)



Date	Title	Author	Summary
19 April 2026	Real-world overall survival with trastuzumab deruxtecan versus standard chemotherapy in HER2-amplified MSS metastatic colorectal cancer	P. M. Schürch	• Introduction: HER2-amplified, MSS mCRC is a rare, aggressive subset with limited benefit from standard chemotherapy. T-DXd showed prior trial activity, but its second-line real-world effectiveness remained uncertain. • Methodology: TriNetX data (2010–2025) identified adults receiving second-line T-DXd or chemotherapy. Anti-EGFR-treated patients were excluded. Propensity score matching balanced baseline factors; OS was assessed by Kaplan-Meier and Cox models. • Results: After matching (1,870/group), 1-year OS differed minimally, but 5-year OS favored T-DXd (66.6% vs 62.1%). Standard chemotherapy carried higher mortality risk (HR 1.14; p=0.0024). • Conclusions: T-DXd demonstrated a modest but meaningful long-term survival advantage in second-line HER2-amplified mCRC.
19 April 2026	Targeting Aurora kinase A for potentiating colorectal cancer to KRAS targeted therapy	G. Hernandez	• Introduction: KRAS mutations drive nearly half of CRC cases, yet KRAS-targeted agents show limited efficacy in CRC because intrinsic resistance blunts apoptosis induction • Methodology: The study evaluated apoptotic sensitization strategies in KRAS-mutant CRC using in vitro and in vivo models, interrogating AURKA co-inhibition with KRAS blockade and defining downstream effects on signaling and apoptotic regulators • Results: AURKA emerged as a key apoptosis suppressor under KRAS inhibition. Dual AURKA/KRAS targeting produced strong antitumor activity, reduced rebound KRAS-pathway signaling, promoted GSK3β-mediated Mcl-1 degradation, and enhanced apoptosis. Additional Mcl-1 inhibition further increased sensitivity. • Conclusions: AURKA inhibition is a mechanistically rational combination strategy to overcome intrinsic CRC resistance to KRAS-directed therapy.



Notable Presentations At AACR 2026

Targeted and Novel Therapies (2/6)



Date	Title	Author	Summary
19 April 2026	STRO-004, an exatecan-based next-generation tissue factor (TF)-targeted ADC, demonstrates superior efficacy across TF-expressing solid tumors in a comprehensive single-mouse PDX trial	J. A. Kuleape	• Introduction: TF is widely expressed across solid tumors and linked to poor prognosis, but earlier TF-directed ADCs have been constrained by off-tumor toxicity and premature payload release. • Methodology: This preclinical study tested STRO-004, a site-specific DAR8 β-glucuronidase-exatecan ADC, in single-mouse PDX models across HNSCC, NSCLC, PDAC, and CRC, with benchmarking against approved TF ADCs at 5 mg/kg, alongside biomarker, in vitro safety, and NHP tolerability analyses. • Results: STRO-004 showed broader, deeper, and more durable tumor regressions, including multiple CRs, activity across TF-expression ranges, reduced epithelial cytotoxicity, and markedly improved NHP exposure without ocular or hematologic toxicity. • Conclusions: STRO-004 demonstrates best-in-class potential with a substantially improved therapeutic index.
19 April 2026	Targeting the ubiquitin reading function of DNMT1 as a next-generation approach for epigenetic cancer therapy	E. Klacking	• Introduction: DNMT1 sustains aberrant methylation in cancer, driving tumor suppressor silencing and immune escape, while current DNMT inhibitors remain constrained by pharmacokinetic and resistance liabilities. • Methodology: Using genetic complementation in two colon cancer cell lines, the study compared wild-type DNMT1 with catalytic-dead and UIM-deficient mutants, alongside benchmark nucleoside and non-nucleoside DNMT inhibitors. Functional, methylomic, transcriptional, and xenograft effects were assessed, plus a pilot chemical screen. • Results: UIM disruption phenocopied DNMT1 loss or catalytic blockade, causing broad hypomethylation, re-expression of silenced tumor suppressors and transposable elements, reduced proliferation/colony formation, and impaired xenograft growth. Four compounds disrupted DNMT1-ubiquitinated nucleosome binding. • Conclusions: DNMT1 ubiquitin-reading UIMs define a tractable allosteric vulnerability and credible route to next-generation epigenetic therapeutics.

Notable Presentations At AACR 2026

Targeted and Novel Therapies (3/6)



Date	Title	Author	Summary
19 April 2026	<u>ASP2998, a TROP2-targeted immunostimulatory antibody drug conjugate (iADC) with dual payloads, demonstrates potent efficacy and a favorable safety profile in nonclinical models</u>	M. Orr	• Introduction: TROP2 overexpression drives tumor progression. ASP2998 is a dual-payload iADC combining cytotoxic (topo I inhibitor) and immunostimulatory (STING agonist) mechanisms. • Methodology: Nonclinical studies included PBMC co-cultures, MC38-hTROP2 mouse models (TME, efficacy, rechallenge), and 4-week GLP toxicity in cynomolgus monkeys • Results: ASP2998 induced potent cytotoxicity, broad immune activation, increased NK/CD8⁺ infiltration, superior tumor control, enhanced rechallenge protection, and acceptable safety with minimal free payload exposure • Conclusions: ASP2998 demonstrates strong efficacy and immune engagement, supporting clinical translation.
20 April 2026	<u>Targeting MYB with REM-422 for the treatment of pediatric T-cell acute lymphoblastic leukemia - A report from the Pediatric Preclinical Testing Consortium (PIVOT)</u>	R. B. Lock	• Introduction: Relapsed/refractory pediatric T-ALL remains a high-unmet-need setting. REM-422 is an oral MYB mRNA degrader in early clinical testing. • Methodology: MYB expression was profiled across pediatric PDXs; REM-422 was tested ex vivo and in NSG mice at 5 mg/kg daily for 3 weeks across 28 ALL PDXs using EFS and objective response measures. • Results: REM-422 nearly abolished MYB protein, was well tolerated, prolonged EFS, and showed strongest activity in T-ALL, with responses in 8/10 T-lineage versus 2/18 B-lineage models. • Conclusions: REM-422 shows marked single-agent promise in pediatric T-ALL



Notable Presentations At AACR 2026

Targeted and Novel Therapies (4/6)

Date	Title	Author	Summary
20 April 2026	CBP/p300 and PARP inhibitor combination treatment synergistically enhances anti-tumor efficacy in models of advanced prostate cancer	O. I. Richter	• Introduction: mCRPC remains lethal and resistant to single agents. CBP/p300, androgen receptor coactivators linked to poor outcomes, also regulate homologous recombination, providing a rationale for combining CBP/p300 and PARP inhibition. • Methodology: The study used 2D/3D prostate cancer models and racially diverse patient-derived explants, integrating proliferation assays, clinically relevant PARPi screening, whole-exome sequencing, and planned spatial transcriptomics. • Results: Dual CBP/p300-PARP inhibition outperformed monotherapy, showing broad synergy, reduced growth, and lower Ki67. Genomic profiling identified variants associated with responder versus non-responder subsets. • Conclusions: This combination is a promising biomarker-guided strategy for mCRPC
20 April 2026	Lymphotoxin alpha induces myeloid differentiation and programmed cell death in myeloid leukemic stem cells resulting in deep and sustained remission in vivo	P. J. Jost	• Introduction: AML relapse is driven by therapy-resistant leukemic stem/progenitor cells. This study explored whether cytokine-induced differentiation could selectively eliminate LSCs while sparing normal hematopoiesis. • Methodology: The authors dissected TNF-family cytokine effects across AML models, using mechanistic studies, co-cultures of malignant and healthy progenitors, genetic mouse models, and patient-derived xenografts. • Results: LTa3 triggered TNFR1/TNFR2-dependent TRAF2 depletion, impaired pro-survival signaling, and induced RIPK3-mediated inflammatory death of LSCs. It suppressed AML, promoted healthy progenitors, and produced deep sustained PDX remissions. • Conclusions: LTa3 represents a selective, hematopoiesis-sparing therapeutic strategy in AML.

Notable Presentations At AACR 2026

Targeted and Novel Therapies (5/6)



Date	Title	Author	Summary
21 April 2026	Antitumor activity of datopotamab deruxtecan in a co-clinical trial with patient derived xenografts	Dhruv Chachad	• Introduction: Dato-DXd is an approved TROP2-directed ADC, but response determinants and optimal combinations across tumors remain unclear. • Methodology: A co-clinical study generated 23 multi-tumor PDXs, mostly from biopsies obtained immediately before patient Dato-DXd treatment, and compared PDX drug response with matched clinical outcomes. PDAC models also tested Dato-DXd plus gemcitabine. • Results: Dato-DXd showed activity across tumors, with 77% concordance between PDXs and matched patients. In resistant PDAC, Dato-DXd plus gemcitabine was synergistic and outperformed both monotherapies. • Conclusions: Dato-DXd has broad translational activity, and rational combinations may overcome resistance.
21 April 2026	Targeting mitochondrial complex I overcomes adaptive response to chemotherapy in advanced pancreatic cancer	S. Attanasio	• Introduction: Chemotherapy resistance drives relapse and poor survival in advanced PDAC, creating need for biomarkers and strategies targeting resistant clones. • Methodology: High-complexity barcoding identified chemo-sensitive versus non-sensitive PDAC clonal lineages in vivo. Transcriptomic profiling generated the chemo-type signature, validated across 301 patients and applied to 36 PDAC PDX models to define vulnerabilities. • Results: Chemo-type stratified survival and predicted chemotherapy response. A subset showed adaptive OxPhos dependence after chemotherapy. Adding the complex I inhibitor IM156 eradicated resistant clones, suppressed relapse, and prolonged survival. • Conclusions: Chemo-type enables prognostic and therapeutic stratification in PDAC.

Notable Presentations At AACR 2026

Targeted and Novel Therapies (6/6)



Date	Title	Author	Summary
21 April 2026	Estrogen therapy alleviates cancer-associated cachexia in mouse models of both sexes	V. T. Pham	• Introduction: Cancer-associated cachexia lacks approved therapies and is more severe in males, suggesting sex-specific protective mechanisms. • Methodology: Using B16F10 melanoma and KPL lung cancer CAC mouse models, the study compared males versus females, tested gonadectomy effects, and evaluated 17β-estradiol (E2) supplementation before tumor challenge. • Results: Females showed less severe cachexia. Ovariectomy worsened wasting, whereas castration had no effect. E2 preserved skeletal muscle and subcutaneous fat, but did not meaningfully improve visceral fat loss or anemia. • Conclusions: Ovarian E2 signaling is a mechanistically credible therapeutic avenue for CAC.



Notable Presentations At AACR 2026

Tumor Biology and Resistance (1/5)

Date	Title	Author	Summary
19 April 2026	The essential role of KDM5B/SOX9 signaling Axis in the development and progression of therapy-induced neuroendocrine prostate cancer	T. Mohan	• Introduction: t-NEPC is a lethal, ADT-resistant prostate cancer subtype with poorly defined biology. This study examined whether the epigenetic regulator KDM5B drives t-NEPC through SOX9. • Methodology: The authors used human PCa/NEPC cell models, CRISPR knockout and add-back systems, promoter-binding analyses, and castrated Pten/Trp53 genetically engineered mice with or without Kdm5b. • Results: KDM5B and SOX9 were elevated in t-NEPC. KDM5B loss reduced SOX9 and neuroendocrine markers, while re-expression restored them. Kdm5b deficiency blocked t-NEPC progression in vivo; SOX9 loss reduced proliferation. • Conclusions: KDM5B-SOX9 is a key t-NEPC driver and therapeutic target.
19 April 2026	Evaluation of kinase inhibitor efficacy and cancer-associated fibroblast-organoid crosstalk in a CRISPR-edited mouse model of bladder cancer	T. Haque	• Introduction: PI3K/AKT/mTOR alterations are common in BCa, but effective targeting remains limited, especially within a CAF-dependent microenvironment. • Methodology: CRISPR-engineered murine urothelial organoids with Trp53/Rb1 or 9p21 loss plus PIK3CA H1047R were tested in immune-competent/incompetent models, with kinase inhibitor studies, CAF co-engraftment, cytokine profiling, and GM-CSF knockout experiments. • Results: Triple-mutant organoids were PI3K inhibitor-sensitive and tumorigenic only with CAF support in immunocompetent hosts. Organoid-derived GM-CSF induced CAF IL-6, defining a reciprocal pro-tumor cytokine loop • Conclusions: BCa may require dual targeting of genotype-specific kinase dependencies and CAF-mediated GM-CSF/IL-6 signaling.



Notable Presentations At AACR 2026

Tumor Biology and Resistance (2/5)



Date	Title	Author	Summary
20 April 2026	3D bioprinted cancer models for drug screening versus 2D and in vivo models: A comparison study	Aurélie Cadiou	• Introduction: 3D bioprinted tumor models may better replicate in vivo biology than standard 2D cultures for preclinical HER2-positive cancer drug testing. • Methodology: BT-474 and SK-OV-3 were compared across 2D culture, 3D bioprinted matrices, and mouse xenografts using RNA-seq, drug sensitivity assays, paclitaxel pharmacology, and stromal co-culture systems. • Results: 3D models showed 3–10-fold higher IC50s, sustained proliferation, stromal-mediated drug resistance, and transcriptomic profiles closer to in vivo tumors, especially for adhesion/ECM programs. • Conclusions: 3D bioprinted models better predict in vivo therapeutic response than 2D systems.
20 April 2026	Dissecting myeloid-driven mechanisms of immunotherapy resistance in prostate cancer bone metastases	A. Lyu	• Introduction: mCRPC bone metastases are highly resistant to ICIs, and neutrophil-driven immunosuppression may underlie this resistance. • Methodology: The study used human single-cell profiling across tumor sites and disease stages, tumor-free bone controls, plus murine intraosseous CRPC models with multi-omic, functional, and mechanistic analyses. • Results: IL1Bhi mature neutrophils were enriched in human bone metastases, suppressed CD8+ T cells, and drove ICI resistance in mice. CXCR1/2 or IL-1R inhibition reduced suppression and improved ICI response. • Conclusions: IL1Bhi neutrophils represent a compelling therapeutic target in mCRPC bone metastases.



Notable Presentations At AACR 2026

Tumor Biology and Resistance (3/5)

Date	Title	Author	Summary
21 April 2026	Mapping the spatial organisation of B cells and immune signalling in TNBC to characterise response to immunotherapy	L. Ahmad	• Introduction: B cells and TLS predict immunotherapy benefit, but their spatial organization and signaling context in TNBC remain poorly defined. • Methodology: Using imaging mass cytometry with simultaneous in situ protein/RNA detection, the study profiled 268 NeoTRIP TNBC samples at baseline, on-treatment, and post-treatment from patients receiving chemotherapy with or without atezolizumab. • Results: Germinal-center B, B-cell, plasma-cell, and B-activated niche densities predicted response on-treatment. Responders showed enriched B/plasma-TME interactions, expansion of B-cell populations, and spatially coordinated cytokine-rich niches. • Conclusions: Spatial B-cell architecture and signaling are strong on-treatment immunotherapy biomarkers in TNBC.
21 April 2026	NAT10-MYC loop induces MHC-I loss through autophagy to promote immune evasion and immunotherapy resistance in colorectal cancer	J. Weng	• Introduction: MSS CRC remains largely resistant to ICIs, requiring new strategies to reverse immune escape. This study examined NAT10-mediated ac4C RNA modification as a driver of immunotherapy resistance. • Methodology: The authors analyzed NAT10/MYC regulation, ac4C-dependent transcript stabilization, autophagy, MHC-I expression, immune infiltration, and anti-PD-1 response using genetic knockout and Remodelin inhibition. • Results: NAT10 was enriched in MSS CRC, promoted autophagy-gene stability, reduced MHC-I, and fostered immune-cold tumors. NAT10 inhibition restored T-cell infiltration and sensitized tumors to anti-PD-1, with 80% complete regression. • Conclusions: NAT10 is a druggable epitranscriptomic-autophagy checkpoint in CRC.





Notable Presentations At AACR 2026

Tumor Biology and Resistance (4/5)

Date	Title	Author	Summary
21 April 2026	Targeted therapy-induced chromosomal instability dictates mitotic dependency on Aurora kinase A	C. Li	• Introduction: KRAS G12C inhibitors improve NSCLC treatment but show limited durability; whether sublethal KRAS inhibition induces DNA damage/CIN-linked liabilities remained unclear. • Methodology: Fifteen KRAS G12C-mutant NSCLC lines were profiled after LY3499446 exposure for DNA damage, CIN, and combination sensitivity, with single-cell imaging, DNA barcoding, and mechanistic signaling analyses. • Results: G12Ci induced heterogeneous DNA damage/CIN. CIN most strongly predicted synergy with AURKA inhibition. Mechanistically, G12Ci activated ATR/ATM, stabilized Cyclin B1, prolonged mitotic arrest, and with AURKA blockade drove catastrophic mitotic death. • Conclusions: G12Ci-induced CIN is a predictive vulnerability and supports KRAS G12C-AURKA cotargeting.
21 April 2026	Targeting non-enzymatic HDAC-mediated repression reveals a selective stress-adaptive mechanism for cancer therapy	O. Debnath	• Introduction: Conventional HDAC inhibitors are limited by poor selectivity and systemic toxicity. This study evaluated E6R, a first-in-class non-enzymatic SIN3-HDAC modulator, as a potentially safer anti-cancer strategy. • Methodology: E6R was tested in yeast, neuroblastoma cells, and mouse xenografts using RNA-seq, SIN3A ChIP-seq, invasion/viability assays, and in vivo benchmarking against TSA or Vorinostat. • Results: E6R matched anti-tumor efficacy, altered ~14-fold fewer genes than TSA, reduced SIN3A binding at ISR loci, activated stress/senescence programs, and suppressed invasion and xenograft growth • Conclusions: E6R offers selective, mechanistically distinct HDAC-pathway modulation with strong therapeutic promise.





Notable Presentations At AACR 2026

Tumor Biology and Resistance (5/5)

Date	Title	Author	Summary
21 April 2026	Spatial single-cell analysis reveals stage-dependent mechanisms of anti-IL-1β therapy in lung adenocarcinoma	B. Zhu	• Introduction: IL-1β-driven inflammation promotes LUAD progression, but therapeutic blockade shows stage-dependent efficacy. • Methodology: The study used spatial single-cell profiling across human and mouse LUAD stages, integrated with scRNA-seq, plus early- versus late-stage anti-IL-1β treatment in Kras- and urethane-driven mouse models. • Results: IL-1β signaling primarily linked myeloid cells with fibroblasts, epithelial, and endothelial cells. Anti-IL-1β was effective only early, enhancing antitumor immunity and reducing IL1R1+ fibroblast/epithelial interactions; late-stage tumors showed minimal response. • Conclusions: Fibroblast and epithelial remodeling are key determinants of stage-specific anti-IL-1β efficacy in LUAD.
21 April 2026	Age-related clonal hematopoiesis drives immune remodeling that promotes lung cancer and alters neoadjuvant chemo-immunotherapy outcomes	J. Woo	• Introduction: TET2-mutant clonal hematopoiesis (CH) is common with aging and may influence NSCLC progression and immunotherapy outcomes through systemic immune remodeling. • Methodology: The study integrated orthotopic KP lung tumor models in young/aged Tet2-deficient mice, PBMC scRNA-seq from NSCLC patients, ligand-receptor analyses, and outcome data from the neoadjuvant real-NADIM cohort. • Results: Tet2-deficient aging accelerated tumor growth and immunosuppression. In patients, TET2-mutant CH associated with myeloid/Treg enrichment, NK-cell loss, and broad immune rewiring. CH-positive patients had similar response rates but better survival with immunotherapy. • Conclusions: TET2-mutant CH creates reversible, immunotherapy-responsive immune dysfunction.





Noteworthy AI / ML presentations at AACR 2026





Themes from key AI / ML presentations at AACR 2026 (1/2)

- **AACR 2026 AI/ML data are expected to show that multimodal, interpretable models using pathology, imaging, genomics, and spatial data will move closer to clinical decision-making by improving prediction, stratification, and treatment selection beyond conventional biomarkers**
- Check out the key AI / ML themes at AACR 2026 below:
- **Multimodal histology-to-biomarker modeling:**
 - AACR 2026 is expected to show H&E evolving into a biomarker engine, with CRC virtual genomics trained on 45,155 cases and externally validated in TCGA n=422, predicting 379 internal and 254 external mutations
- **LLMs entering clinical classification:**
 - AI/ML work is likely to move beyond captioning into decision support, led by CUPAI-2, where a three-LLM architecture plus XGBoost meta-learning achieved 76.93% Top-1 and 92.82% Top-3 accuracy across 20,483 tumors



Themes from key AI / ML presentations at AACR 2026 (2/2)

- **Digital twins for treatment optimization:**
 - Predictive modeling is poised to become more action-oriented through OncoTwin-2D and OncoTwin-3D in ALK-positive NSCLC, where multimodal inputs and BrightStar simulations suggested improved risk stratification and potential LCT-associated PFS gain
- **AI pathology for immunotherapy selection:**
 - Immuno-oncology AI is set to emphasize interpretable tissue features over single markers, exemplified by the NEPTUNE analysis, where 15 H&E-derived features from 426 patients matched or outperformed PD-L1, bTMB, and ECOG
- **Longitudinal imaging risk models maturing:**
 - Thoracic AI is expected to shift from single-scan prediction toward temporal learning, as six Sybil-based LDCT architectures showed near-perfect Year-1 discrimination, durable Year-6 accuracy, and external robustness after Moffitt fine-tuning
- **Spatial and foundation-model oncology expanding:**
 - AACR 2026 is likely to highlight integrated spatial AI, where GBM recurrence modeling combined Xenium, radiomics, and foundation embeddings, while AF3+ESM2 achieved AUC 0.782–0.810 for peptide–MHC II prediction



Noteworthy AI / ML presentations at AACR 2026

Notable Presentations At AACR 2026

AI / ML (1/6)



Date	Title	Author	Summary
19 April 2026	A multimodal AI framework integrating spatial omics and radiomics for recurrence prediction in glioblastoma	J. Louw	• Introduction: GBM recurrence timing varies despite uniformly poor prognosis; this study examined multimodal spatial determinants of early versus delayed recurrence. • Methodology: Primary GBMs underwent Xenium spatial transcriptomics with Seurat-based niche annotation; H&E, planned CODEX proteomics, MRI radiomics, and foundation-model embeddings supported interpretable survival modeling. • Results: Short-recurrence tumors showed diffuse malignant infiltration, AC-like dominance, and inflammatory/microglial activation. Longer-recurrence tumors retained vascular-immune compartmentalization, greater malignant-state heterogeneity, and angiogenic/extracellular-matrix programs. • Conclusions: Recurrence timing appears strongly linked to preserved tumor-immune-vascular spatial architecture.
19 April 2026	Structure-sequence integration for peptide:MHC class II binding prediction using AI foundation models (AlphaFold 3 and ESM2)	K. Lahouel	• Introduction: CD4 epitope prediction remains difficult because of MHC II polymorphism and antigen-presentation complexity; this study tests a low-data AI framework for peptide:MHC II binding. • Methodology: AF3 generated 3D peptide-MHC II structures; residue graphs incorporated spatial features plus ESM2 sequence embeddings and were trained on MHCII-PepSeq assay data. • Results: The AF3+ESM2 GNN achieved AUC 0.782, matching NetMHCIIpan 4.3 despite far smaller training data; ensemble performance improved to 0.810, while AF3-only reached 0.775 • Conclusions: Integrating structural and sequence foundation models enables accurate, data-efficient, interpretable antigen-presentation prediction



Notable Presentations At AACR 2026

AI / ML (2/6)



Date	Title	Author	Summary
19 April 2026	Pan-cancer landscape of alternative lengthening of telomeres revealed by machine learning analysis of clinical sequencing data	D. S. Chen	• Introduction: ALT drives telomere maintenance in 10–15% of cancers, but its genetic basis remains incompletely defined beyond ATRX/DAXX alterations. • Methodology: Using MSK-IMPACT off-target telomeric reads and 700 C-circle-assayed tumors, investigators trained calibrated ensemble Random Forest models on 300 high-confidence samples • Results: The model predicted ALT with strong accuracy (ROC-AUC 0.84; PRC-AUC 0.76) and scaled inference to 78,704 tumors, confirming enrichment in sarcomas, gliomas, and neuroendocrine tumors, including some ATRX/DAXX-wild-type cases • Conclusions: Routine clinical sequencing can enable scalable ALT detection and broader discovery of ALT-associated biology
20 April 2026	A large-scale, multi-target deep learning model for virtual genomic profiling in colorectal cancer	E. N. Bergstrom	• Introduction: Virtual genomics from H&E could complement molecular profiling in CRC, but prior studies lacked scale, breadth, and generalizability. • Methodology: A transformer-based multiple-instance learning framework using H-optimus-0 embeddings was trained on 45,155 matched CRC cases and externally validated in TCGA (n=422). • Results: Single-task models predicted 379 mutated genes internally and 254 externally at AUROC>0.7; multitask learning improved 85% of targets. MSI, BRAF, KRAS, and POLE/POLD1 were predicted strongly. • Conclusions: Large-scale histology-based virtual genomics enables clinically relevant, pathway-informed CRC stratification

Notable Presentations At AACR 2026

AI / ML (3/6)



Date	Title	Author	Summary
20 April 2026	Precision diagnostics for early melanoma detection using spatial biology and AI guided image analysis	Y.-C. Kao	• Introduction: Melanoma diagnosis is difficult because malignant lesions can mimic benign naevi, and morphology alone may miss invasive transcriptional states. • Methodology: The study combined Visium spatial transcriptomics across 75 progression samples, scRNA-seq for spot deconvolution, Xenium/Orion validation, 361-gene profiling, and deep learning on H&E slides. • Results: Distinct melanocyte state shifts emerged across progression, with spatially resolved benign- and malignant-specific signatures revealing occult malignant potential and tumor-immune microenvironment features. • Conclusions: Integrated spatial multiomics plus AI improved molecular discrimination of benign versus malignant melanocytic lesions.
21 April 2026	Multisite analysis of a deep learning model for prediction of palbociclib response in patients with ER+ HER2- advanced breast cancer	A. Singhal	• Introduction: Deep learning can predict treatment response in oncology, but clinical translation depends on robust validation in real-world patient populations. • Methodology: Two real-world ER+/HER2- advanced breast cancer cohorts treated with palbociclib were analyzed retrospectively: UCSD (n=139) and MSK (n=459), evaluating a published interpretable response model. • Results: The model significantly stratified PFS in both cohorts and OS with borderline-to-significant performance, while interpretation linked resistance to 18 pathways including RTK, DNA damage response, and cell cycle regulation. • Conclusions: Real-world validation supports clinically meaningful, interpretable prediction of palbociclib benefit.

Notable Presentations At AACR 2026

AI / ML (4/6)



Date	Title	Author	Summary
21 April 2026	A translational deep learning platform predicts metabolic pathway activity from routine H&E slides to enable patient stratification	Pahini Pandya	• Introduction: Cancer metabolism is clinically important but difficult to measure; this study tested whether routine H&E slides can infer pathway-specific metabolic states across cancers. • Methodology: A multi-omics framework combined TCGA transcriptomics, genome-scale metabolic modeling, and deep learning on WSIs to derive and predict 32 binary metabolic biomarkers across 21 tumor types • Results: Strongest predictions included nucleotide metabolism in testicular and pancreatic cancers, nuclear transport in colon, melanoma, and lung squamous tumors, and fatty acid beta-oxidation across multiple solid tumors • Conclusions: Routine histology can yield scalable digital biomarkers of functional metabolic dependencies for precision oncology
21 April 2026	CUPAI-2: A collaborative multi-agent large language model framework for diagnosis of cancer of unknown primary	Kai Wang	• Introduction: CUP has high mortality because unidentified primary sites limit targeted treatment and trial eligibility; this study evaluated an LAG/LLM-based genomic prediction framework. • Methodology: CUPAI-2 used three fine-tuned specialist LLMs on genomic alterations, an XGBoost meta-learner for stacked integration, and a final oversight agent for adjudication across 20,483 tumors. • Results: CUPAI-2 achieved Top1/Top3 accuracy of 76.93%/92.82%, outperforming oncologists, traditional machine learning, and standalone LLMs. • Conclusions: A coordinated multi-agent LLM architecture improved CUP origin inference with strong accuracy, calibration, and interpretability.

Notable Presentations At AACR 2026

AI / ML (5/6)



Date	Title	Author	Summary
21 April 2026	OncoTwin: A multimodal digital twin framework for predicting treatment response and guiding trial design in ALK-rearranged non-small-cell lung cancer	H. Xu	• Introduction: Outcomes in ALK-rearranged NSCLC remain heterogeneous under next-generation TKIs, and predictive biomarkers for individualized treatment selection are lacking. • Methodology: Real-world and trial datasets were integrated to develop OncoTwin-2D and OncoTwin-3D using serial tumor measurements, CT-derived volumetrics, blood tests, and demographics. • Results: Second-generation TKIs improved PFS versus first-generation therapy. OncoTwin-2D stratified risk robustly, while multimodal OncoTwin-3D achieved stronger prognostic accuracy and simulated substantial PFS benefit from adding LCT in BrightStar. • Conclusions: Multimodal digital twins can personalize outcome prediction and estimate escalation benefit in precision oncology.
21 April 2026	AI-derived H&E biomarkers predict differential survival under immunotherapy vs chemotherapy in phase-3 metastatic NSCLC study NEPTUNE	C. Parmar	• Introduction: Immunotherapy benefit in metastatic NSCLC remains heterogeneous, and standard biomarkers such as PD-L1 and bTMB incompletely capture response. • Methodology: In 426 NEPTUNE patients, AI-Pathology extracted 15 interpretable stromal and tumor-region H&E features from externally trained models, with OS assessed using Cox regression and treatment-marker interactions. • Results: Higher stromal fibroblast density was prognostic for worse OS in both arms, while higher stromal immune density specifically predicted improved durvalumab+tremelimumab benefit, outperforming or matching PD-L1, bTMB, and ECOG stratification. • Conclusions: AI-derived H&E microenvironment features may enable assay-free immunotherapy selection and stratification.

Notable Presentations At AACR 2026

AI / ML (6/6)



Date	Title	Author	Summary
21 April 2026	Enhancing lung cancer risk prediction with longitudinal fusion of LDCT data	H. Ajami	• Introduction: Single-scan LDCT models predict lung cancer risk, but annual screening generates longitudinal imaging data that may better capture evolving malignant patterns. • Methodology: Six longitudinal deep learning architectures extending Sybil were trained on NLST scans and evaluated using time-dependent AUC and C-index, with external testing on Moffitt data • Results: Hybrid models performed best, achieving near-perfect Year-1 discrimination internally, sustained Year-6 accuracy, and strong external generalizability after hazard-head fine-tuning; Tri-Fusion and Bi-Fusion showed weaker external robustness. • Conclusions: Longitudinal LDCT fusion substantially improved long-term risk prediction and translational generalizability.
21 April 2026	Predicting gastric cancer response to anti-PD-1 first-line treatment based on multi-modal data: A multi-center study	J. Wang	• Introduction: Predictive biomarkers for first-line immunotherapy in gastric cancer remain limited beyond PD-L1, motivating multimodal AI approaches. • Methodology: This multicenter retrospective study integrated clinical metastatic features, CT-based radiomics/deep embeddings, and WSI-derived pathomics/pathology embeddings using a cross-modal Transformer • Results: The CRP model showed strong discrimination (validation AUC 0.857; test AUC 0.917), predicted PFS and OS effectively, remained independently prognostic, and outperformed radiology-only, pathology-only, and PD-L1 CPS models. • Conclusions: Multimodal deep learning improved prediction of immunotherapy benefit and may better identify gastric cancer patients most likely to respond.

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