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From Cancer Dependency Maps to Antiviral Structures: Highlights of Recent Advances in Medicine and Biology

— A Research Brief on Frontier Progress, September 2026

Dan-Dan Wang[1]

1 Parkway Xintiandi Medical Center, Shanghai, 200001, People's Republic of China

**Correspondence to: Wang DD, Parkway Xintiandi Medical Center, 138 Middle Huaihai Rd., Shanghai, 200001, People's Republic of China, E-mail: drwangdandan@outlook.com*

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Abstract

The September 2026 issues of a leading international science journal present a rich harvest of biomedical research. This communication selects 34 original research articles with close relevance to medicine and the medical biosciences, and organizes them into six themes: cancer biology and translational oncology; neuroscience and brain disorders across the lifespan; neuroimmunology; metabolism, ageing and the microbiome; infection, haematology and global health; and broader biological advances that underpin future medicine. For each study we provide a concise summary and brief commentary, aiming to offer clinicians and researchers a panoramic view of current progress.

Keywords: cancer models; immunotherapy; neurodegeneration; multiple sclerosis; metabolism; antivirals

Editorial

Biomedical science in 2026 continues to accelerate at the interface of large-scale human genetics, single-cell and spatial omics, artificial intelligence and structural biology. The September issues surveyed here are emblematic of this convergence: patient-derived cancer models are being industrialized into publicly available dependency maps; single-nucleus atlases now span the entire human lifespan and hundreds of donors; engineered living therapeutics and AI-redesigned enzymes are leaving the proof-of-concept stage; and long-awaited structural blueprints of priority pathogens have finally yielded rational antiviral starting points. The thirty-four studies summarized below were selected from the original research articles published in the September 2026 issues (Nos. 8131-8133, Vol. 657) of a leading international science journal, with emphasis on work that is closest to clinical and translational relevance. Each entry offers a short summary of the findings followed by a brief commentary on significance and limitations.

1. Cancer Biology and Translational Oncology

1.1 GPC3-targeted, TGFβ-armoured CAR T cells show first-in-human activity in advanced liver cancer

Chimeric antigen receptor (CAR) T cell therapy has transformed haematological malignancies but remains disappointing in solid tumours such as hepatocellular carcinoma (HCC), where the immunosuppressive cytokine TGFβ dominates the microenvironment. Zhang and colleagues report a first-in-human trial (NCT05155189) of C-CAR031, GPC3-specific CAR T cells engineered with a dominant-negative TGFβ receptor II, in 36 patients with advanced, treatment-refractory HCC across four dose levels. Cytokine release syndrome occurred in 34 patients (two grade 3), and tumour regression was observed in 32 patients; the objective response rate was 44.4%, with median progression-free survival of 4.2 months and median overall survival of 14.2 months. Analyses of resistance pointed to GPC3 antigen loss and increased TGFβ levels.

Commentary: This trial provides the first clinical evidence that neutralizing TGFβ signalling can unlock CAR T activity in a solid tumour, with a manageable safety profile in heavily pretreated patients. The identified resistance mechanisms — antigen loss and residual TGFβ — directly instruct next-generation designs, such as dual-targeting and TGFβ-converting armour strategies.[1]

1.2 A diet–gut microbiome axis explains the obesity paradox of immunotherapy

High body-mass index is paradoxically associated with better outcomes from immune checkpoint inhibitors (ICIs), but the mechanism has been obscure. Using twelve mouse diet models that span diverse obesity biology, Desharnais and colleagues show that obesity-associated ICI responses correlate poorly with metabolic dysfunction and instead depend on the diet–gut microbial axis: obesogenic diets build a robust microbial ecosystem capable of restoring ICI sensitivity after a short-term diet switch or faecal microbiota transplantation (FMT). Mono-colonization with bacteria such as Lactobacillus johnsonii synergized with an obesogenic diet to promote tumour regression through microbiota-derived aromatic amino-acid metabolites, and FMT from donors with high BMI enhanced ICI efficacy in humanized models.

Commentary: This study reframes the epidemiological "obesity paradox" as a diet–microbe–drug interaction, and points to concrete, testable adjuncts — defined bacterial consortia plus dietary modulation — for improving ICI response. Prospective clinical validation is now the key hurdle.[2]

1.3 A dual-function Rb protein limits CDK4/6 inhibitor efficacy in breast cancer

CDK4/6 inhibitors are a mainstay of hormone receptor-positive (HR+) breast cancer therapy, yet their benefits are heterogeneous. Watt and colleagues show that pharmacological activation of the retinoblastoma protein (Rb) redistributes it to promoters and enhancers, where — beyond repressing cell-cycle genes — it unexpectedly integrates into oestrogen receptor (ER)-rich transcriptional hubs and promotes expression of ER target genes, partly through KDM5A. This pro-proliferative Rb-driven programme is neutralized by anti-oestrogen therapy in endocrine-sensitive tumours, explaining therapeutic synergy, but persists in ESR1-mutant, endocrine-resistant disease, limiting CDK4/6 inhibitor efficacy.

Commentary: The work redefines Rb from a pure tumour suppressor to a context-dependent transcriptional regulator, and provides a mechanistic rationale for combining CDK4/6 inhibitors with agents that disable the ER programme in resistant disease. Biomarker-guided patient selection may follow.[3]

1.4 A tumour-derived organoid biobank maps cancer gene dependencies

Cancer cell lines inadequately capture tumour diversity and lack patient context. Herranz-Ors and colleagues derived and characterized 256 clinically annotated tumour organoids from colorectal, oesophageal, ovarian, pancreatic and gastric cancers as renewable, genetically stable models, integrating whole-genome and transcriptome sequencing with genome-wide CRISPR-Cas9 screens across 162 organoids. The analyses identified organoid-specific essential genes, genomic and clinical markers of dependency, targetable vulnerabilities revealed by paired pre- and post-treatment samples, and differential effects of KRAS variant alleles on the EGFR–RAS–MAPK axis.

Commentary: This publicly available resource bridges the gap between cell lines and clinical trials, and its paired-treatment design uniquely captures dependencies acquired during tumour evolution — a valuable compass for precision oncology trials.[4]

1.5 A global compendium of next-generation patient-derived cancer models

The Human Cancer Models Initiative generated 665 next-generation models from 2,780 donors spanning 25 cancer types, including 153 rare-cancer and 71 non-European-ancestry models. Analysis of 421 matched tumour–model pairs revealed high genetic (97.8%) and epigenetic (95%) concordance, defined correlates of discordance, and characterized preservation of extrachromosomal DNA and post-treatment mutational signatures, while single-nucleus RNA sequencing identified subsets of models in which culture conditions significantly reshape cell states.

Commentary: By systematically quantifying model fidelity and expanding representation of rare cancers and under-represented ancestries, this international resource

addresses two structural weaknesses of preclinical cancer research and is expected to become standard infrastructure for translational studies.[5]

1.6 The cancer dependency map expands into three-dimensional models

The Cancer Dependency Map (DepMap) has traditionally relied on two-dimensional cell lines. A companion study reports 147 genome-scale CRISPR screens and multi-omic characterizations of next-generation organoid and spheroid models across ten cancer types, extending DepMap to new genomic and molecular subtypes. The three-dimensional models preserve transcriptional programmes that are silenced in traditional cell lines and harbour specific gene dependencies associated with these programmes, while direct comparisons disentangle the effects of growth format and culture medium on gene essentiality.

Commentary: Together with the organoid biobank above, this work signals a migration of functional-genomics screening into physiologically richer models; vulnerabilities invisible in two dimensions are now entering the druggable space, with all data openly accessible through the DepMap portal.[6]

1.7 Chromosome-arm aneuploidy selects for driver genes in breast cancer

How chromosome-scale aneuploidy promotes tumorigenesis has been hard to test experimentally. Using CRISPR-KOALA, a high-throughput bidirectional screening platform in immunocompetent mouse models, the authors screened 3,752 mouse orthologues across the ten most frequent chromosome-arm alterations of basal-like breast cancer and identified 90 cancer driver genes, most previously unknown, converging on MAPK, HIPPO and WNT signalling. Manipulating these drivers overcame the need for copy-number alterations, and the 9p gene PLGRKT emerged as a potent oncogene linked to stress-resistant mitochondria and enhanced detoxification of reactive oxygen species.

Commentary: This study converts correlative copy-number biology into a catalogue of actionable driver genes and nominates PLGRKT as a new therapeutic target, while illustrating how arm-level aneuploidy sculpts — rather than merely accompanies — tumour heterogeneity.[7]

1.8 Chemotherapy leaves a genomic footprint in relapsed childhood cancers

The mutagenic cost of curative-intent therapy in children has been difficult to quantify. Using whole-genome sequencing of tumours from a multi-institutional cohort with uniformly collected treatment-exposure data, the authors show that chemotherapy and radiotherapy were the only exogenous mutagens in relapsed childhood tumours and often the dominant source of DNA alteration: post-therapy cancers carried nearly three times more private

mutational signatures and twice the somatic mutation burden of treatment-naive tumours. Platinum-based agents were the most mutagenic, and more than one-third of platinum-treated tumours displayed detectable platinum signatures within one year.

Commentary: These data provide genomic-level evidence to guide treatment de-escalation in low-risk childhood cancers and open the door to tracking therapy-induced resistant clones before clinical relapse — a step toward prevention, not just rescue.[8]

1.9 ZFP36L2 is a molecular switch of stress-adaptive plasticity in regeneration and cancer

Phenotypic plasticity underlies both intestinal regeneration and metastasis. ZFP36L2, an RNA-binding protein mutated in 5-10% of colorectal cancers, was shown to orchestrate dynamic dedifferentiation of intestinal cells into a stem-cell state: its ablation impairs regeneration in mice, while in human colorectal cancer its loss abolishes metastatic seeding of LGR5-positive metastases yet promotes non-canonical lineage plasticity. Mechanistically, ZFP36L2 binds AU-rich 3-prime untranslated regions of stress-associated mRNAs and forms dynamic biomolecular condensates that terminate the stress response.

Commentary: The work identifies a druggable stress-sensing switch coupling plasticity to metastasis, but also issues a caution: suppressing plasticity may simply reroute tumours toward heterogeneous, clinically worse states, underscoring the need to target the switch itself rather than its output.[9]

2. Neuroscience and Brain Disorders Across the Lifespan

2.1 Amygdala astrocyte primary cilia govern stress-related behaviours

Stress remodels the amygdala, but the glial dimension of this remodelling has been underappreciated. The authors show that amygdala astrocytes undergo molecular alterations during stress, with shortened primary cilia and reduced expression of cilium-related molecules. Chemogenetic and pharmacological targeting of astrocyte sphingosine-1-phosphate receptor 1 (S1PR1) restored cilium length, corrected molecular alterations and improved stress-related behaviours in mice; cilium-related genes were abundantly expressed in human amygdala astrocytes and disrupted in stress-related brain disorders.

Commentary: By placing the astrocyte primary cilium at the centre of stress pathophysiology, this study opens a tractable, druggable glial target for stress-related disorders — and intriguingly, S1PR1 is already modulated clinically, raising near-term repurposing possibilities.[10]

2.2 Human brain organoids record the passage of time over years

Human brain organoids have largely recapitulated only early development. By optimizing long-term culture, the authors maintained organoids for five years — the longest to date — and showed that they transcriptionally age with cell-type specificity, tracking endogenous maturation programmes; whole-genome methylation profiling revealed that predicted epigenomic age correlates precisely with time in vitro. In chimeric organoids mixing progenitors of different ages, older progenitors retained a memory of culture time and skipped earlier neuronal fates.

Commentary: Long-lived organoids finally make the protracted, species-specific phase of human postnatal brain development experimentally accessible, providing a platform for studying late-onset neuropsychiatric and neurodegenerative disease ex vivo.[11]

2.3 Brain stimulation reshapes gene-linked cell assemblies in human cortex

How neuromodulation works in the human brain remains largely unknown. The authors developed an ex vivo platform integrating microelectrode-array stimulation with simultaneous recording and single-nucleus genomics on resected temporal cortex from neurosurgical patients, finding that stimulation strengthens cell assemblies and linking this effect to cell-type-specific gene regulatory networks; common expression signatures were also identified after in vivo stimulation.

Commentary: This work connects the physiology of stimulation to its molecular machinery at single-cell resolution, establishing a foundation for identifying targetable genetic signatures that could make neuromodulation therapies such as DBS and focused ultrasound rational rather than empirical.[12]

2.4 A population-scale single-cell atlas of transcriptomic vulnerability across brain disorders

The PsychAD consortium generated a single-cell transcriptomic atlas of the human dorsolateral prefrontal cortex from 1,494 donors and more than 6.3 million nuclei, spanning eight neurodegenerative and neuropsychiatric disorders alongside controls. The analyses reveal universal cross-disease signatures enriched in basic cellular functions, closer concordance among Alzheimer's disease, diffuse Lewy body disease, vascular dementia and Parkinson's disease, and disease-specific architecture: severe Alzheimer's disease shows reduced neuronal abundance with expanded immune and vascular populations, deep-layer excitatory neurons are associated with neuropsychiatric symptoms, and transcriptomic trajectories implicate cell-type-specific responses at early and late stages of Alzheimer's progression.

Commentary: This population-scale reference distinguishes normative ageing from disease biology and supplies the statistical power needed to link symptoms — not just diagnoses — to cellular mechanisms, a template for precision neuropathology.[13]

2.5 A lifespan single-cell atlas of the human prefrontal cortex

Complementing the disease atlas, a lifespan-resolved single-nucleus transcriptomic atlas of the dorsolateral prefrontal cortex reveals non-linear, cell-type-specific trajectories: dynamic remodelling during development, relative stability in midlife, and selective molecular reactivation in late adulthood, including glial programmes of immune activation, stress response and circadian reorganization organized across cortical layers and grey–white matter domains.

Commentary: By defining when and in which cells the ageing cortex shifts from resilience to vulnerability, this normative lifespan baseline is essential infrastructure for interpreting disease atlases and for timing interventions in age-related cognitive decline.[14]

2.6 Single-nucleus transcriptome-wide association studies sharpen genetic signals for brain disorders

Most genetic risk loci for brain disorders lie in non-coding regions and act in specific cell types invisible to bulk-tissue analysis. Using single-nucleus expression profiles from the multi-ancestry PsychAD cohort, the authors built cell-type-resolved transcriptomic imputation models for the prefrontal cortex, revealing thousands of gene–trait associations undetectable in bulk data and resolving them to discrete neuronal, glial and immune populations; cross-ancestry analyses in the Million Veteran Program confirmed the associations and demonstrated conserved, pleiotropic effects.

Commentary: This ancestry-aware, cell-type-resolved framework directly addresses the Euro-centric bias of brain genetic studies and converts association signals into prioritized, testable therapeutic targets for complex brain disorders.[15]

3. Neuroimmunology

3.1 Antigen presentation by CD40+MHC-II+ astrocytes promotes CNS autoimmunity

Whether astrocytes directly interact with CD4+ T cells in multiple sclerosis (MS) has been unclear. Combining rabies-barcode interaction detection, single-cell RNA sequencing, SorTagging of intercellular contacts and in vivo CRISPR perturbation, the authors establish that CD40+MHC-II+ astrocytes promote CNS autoimmunity: direct astrocyte–CD4+ contacts enhance pathogenic T helper 17 responses, and CD40 ligation induces PLIN4-positive lipid

droplets that supply acetyl-CoA for p65-acetylation-dependent NF-κB activation and antigen presentation. CD40+MHC-II+ lipid-droplet-positive astrocytes were detected in MS patient tissue.

Commentary: This study defines astrocytes as bona fide, lipid-fuelled antigen-presenting cells in CNS autoimmunity, linking metabolic state to immune function and nominating the CD40–NF-κB axis and astrocyte lipid handling as new therapeutic entry points in MS.[16]

4. Metabolism, Ageing and the Microbiome

4.1 Late-life semaglutide treatment slows ageing and extends lifespan in female mice

GLP-1 receptor agonists show pleiotropic benefits beyond glycaemic control, but their mechanistic basis is debated. Treating 20-month-old female mice with semaglutide for three months improved physiological function, attenuated hallmarks of ageing, modulated nutrient-sensing and conserved longevity regulators, and extended lifespan. In longitudinal comparison with matched calorie restriction, semaglutide preserved baseline function, recapitulated many caloric-restriction benefits, and exceeded them in exploratory drive, spatial memory and glucose control.

Commentary: Positioning GLP-1 receptor activation as a late-life-initiated caloric-restriction mimetic reframes these drugs within geroscience; however, mouse data — in females only — warrant caution before extrapolating lifespan claims to humans, even as cardiometabolic benefit evidence accumulates.[17]

4.2 Glucose-responsive probiotic living drugs for glycaemic control

Engineered living therapeutics promise closed-loop metabolic control without transplantation. The authors built an orally deliverable probiotic carrying a synthetic glucose-sensing circuit based on the transcriptional regulator HexR; the cells reside temporarily in the intestine and express therapeutic transgenes only when glucose exceeds threshold. The platform achieved glycaemic control in multiple diabetic mouse and non-human-primate models, improved lipid profiles during long-term administration, and attenuated diabetic complications.

Commentary: A programmable, sense-and-respond oral living drug that works in non-human primates is a genuine step toward translation; the remaining hurdles are containment, ecological safety and durability of the engineered circuit in humans.[18]

4.3 FNIP1 variants are associated with favourable metabolism in one million humans

In an exome-sequencing analysis of 1,032,116 people, rare protein-truncating variants in FNIP1 — encoding a suppressor of energy expenditure — were associated with a lower triglyceride-to-HDL ratio, lower liver fat, lower glycaemia, favourable fat distribution and about 60% lower odds of cardiometabolic disease. Across 59 significant genes, 39% encode approved or clinical-stage drug targets. FNIP1 knockdown in human hepatocytes induced lipid breakdown, and hepatic knockdown of Fnip1/Fnip2 or its interactor Flcn protected mice from high-fat-diet-induced weight gain and insulin resistance.

Commentary: Human knockout genetics here provides both target validation and a preliminary human safety readout for inhibiting the FNIP1 pathway — a textbook example of how population exomics can de-risk cardiometabolic drug development.[19]

5. Infection, Haematology and Global Health

5.1 Structures and inhibition of the Crimean–Congo haemorrhagic fever virus polymerase

Crimean–Congo haemorrhagic fever virus (CCHFV) is a tick-borne WHO priority pathogen with no licensed vaccines or drugs. The authors defined the cofactors required for in vitro RNA synthesis by the viral L polymerase and determined structures of the elongating L–RNA complex, revealing a markedly enlarged polymerase whose peripheral domains order during RNA synthesis. They further resolved the inhibition mechanisms of the baloxavir-derived experimental drug WXSH0208 (endonuclease inhibition) and of the nucleoside analogue 2-prime-deoxy-2-prime-fluorocytidine (post-translocation chain termination), which has nanomolar cellular potency.

Commentary: These first elongation-complex structures of one of the largest viral polymerases provide the structural blueprint needed to optimize nucleotide analogues and cap-endonuclease inhibitors against a pathogen of high epidemic concern.[20]

5.2 RNA synthesis and substrate-analogue inhibition in the CCHFV polymerase

A companion study determined structures of full-length CCHFV L, including a 3.0-angstrom elongation complex capturing early and late elongation. Large insertions extend RNA-binding paths around the polymerase active site and create interaction networks essential for replication; nucleotide analogues carrying the ribose-2-prime modifications found in sofosbuvir specifically inhibited the RdRP through immediate chain termination.

Commentary: Together, the two studies converge on immediately actionable chemistry: sofosbuvir-like nucleotide analogues, validated against the structurally characterized polymerase, offer a repurposing-ready route to CCHFV antivirals while novel scaffolds are optimized.[21]

5.3 A century of data resolves the climate–malaria link in African children

Whether climate change has altered childhood malaria burden in sub-Saharan Africa has been debated for decades. Leveraging more than a century of clinical data, the authors estimate that rising temperatures probably increased malaria in East and southern Africa while averting a comparable number of cases in West Africa, for a near-neutral continental net effect to date; looking forward, climate change could marginally accelerate elimination in West and central Africa, whereas holding warming under 2°C rather than 3°C could prevent about five excess cases per 1,000 children by 2100 in high-elevation East Africa and southern Africa.

Commentary: This rigorous attribution study replaces speculation with region-specific estimates and, crucially, reframes mitigation itself as a health intervention — while warning that local heterogeneity demands locally tailored surveillance rather than continental generalizations.[22]

5.4 An ancient mitochondrial program tunes translation to haem availability

How cells sense haem — essential yet toxic — has been obscure. The authors uncover an OMA1–DELE1 axis in which haem deficiency triggers mitochondrial release of DELE1, which in the cytosol releases inhibitory haem from the eIF2α kinase HRI, reshaping translation during erythroid differentiation. The sensor–actuator system operates across human tissues including erythroid progenitors, is conserved down to bloodless invertebrates, and — critically — can be manipulated pharmacologically to enhance fetal globin expression, a central therapeutic objective in haemoglobinopathies.

Commentary: Beyond solving a fundamental cell-biology puzzle, this primordial haem-sentinel system offers a new, druggable lever for fetal haemoglobin induction in sickle cell disease and thalassaemia, where raising HbF ameliorates disease severity.[23]

6. Broader Biological Advances Underpinning Medicine

Several additional studies, though more basic in orientation, supply concepts and technologies likely to seed future medical applications; we summarize them briefly here.

6.1 AI-redesigned proteins evolve better than natural ones

Applying ProteinMPNN to redesign botulinum neurotoxin proteases, the authors show that AI-redesigned enzymes are more mutationally robust and serve as superior starting points for directed evolution; across campaigns, redesigned starting points consistently yielded higher-activity proteases, and evolution toward ataxin-2 cleavage achieved more than 79-fold greater specificity than the best variant evolved from wild type — a therapeutically relevant target protein.

Commentary: Pairing generative protein design with continuous evolution compresses the path to bespoke proteases, with applications from therapeutics to industrial biocatalysis.[24]

6.2 Subnuclear compartmentalization controls bivalent chromatin in human neurogenesis

Mapping genome interactions with the nuclear lamina and speckles in mid-gestational human cortex, the authors show that hundreds of bivalent neurodevelopmental genes relocate from lamina to speckles during cortical neurogenesis; relocation resolves bivalent chromatin to active H3K4me3 states and raises transcription more than eightfold, demonstrating that spatial location — not H3K27me3 alone — maintains the poised state.

Commentary: Establishing that the three-dimensional address of a gene instructs its epigenetic regulation reframes neurodevelopmental gene control and may explain context-specific effects of regulatory variants.[25]

6.3 Structural logic of the glycosphingolipid gatekeeper UGCG

Cryo-electron microscopy structures of full-length human UDP-glucose ceramide glucosyltransferase (UGCG) in eight functional states reveal a previously unrecognized triple-pass transmembrane architecture, a metal-independent arginine-network catalytic mechanism, and a primate-specific steric element that tunes lipid affinity; structures with clinically used inhibitors explain their potency and selectivity.

Commentary: As the single committed step controlling entry into glycosphingolipid metabolism, druggable UGCG sits at the junction of membrane biology, lysosomal storage disorders and neurobiology; these structures enable precision modulation.[26]

6.4 Watching a virus-like particle assemble, molecule by molecule

Combining mass photometry with single-molecule trapping, the authors monitored real-time self-assembly of individual virus-like particles, showing that weak, reversible multivalent interactions guide stochastic selection of on-pathway intermediates, with

symmetry-encoded first-passage times creating a nucleation-and-growth mechanism that achieves high-fidelity assembly despite thousands of possible intermediates.

Commentary: A quantitative, molecule-level framework for multimeric assembly will inform vaccine nanoparticle design and the engineering of self-assembling delivery vehicles.[27]

6.5 Bacterial pattern-recognition receptors sense the core phage proteome

Systematic phylogenetics identified at least 90 STAND NTPase families involved in antiviral defence. Structural and genetic work showed that these receptors recognize conserved phage proteins — the major capsid protein, portal, tail components and replication machinery — establishing structure-based pattern recognition as a fundamental bacterial immunity strategy, with host elongation factor Tu repurposed as a defence component.

Commentary: The convergence of bacterial and mammalian innate immunity on pattern recognition illuminates the deep evolutionary roots of self–non-self discrimination, with implications for phage therapy and synthetic immunity.[28]

6.6 Structural basis of RNA editing in trypanosome mitochondria

Cryo-electron microscopy structures of the approximately one-megadalton RNA-editing catalytic complexes RECC1 and RECC2 reveal dragonfly-shaped machines that integrate guide-RNA-directed substrate recognition, mRNA cleavage, uridine deletion or insertion and ligation within a single, spatially adaptable reaction chamber.

Commentary: By defining how information is rewritten at the RNA level, this architecture completes a decades-old structural quest and highlights kinetoplastid-specific machinery as a potential target in neglected tropical diseases.[29]

6.7 Pre-meiotic gene conversion revealed by long-read sperm sequencing

Analysing 2,382 candidate gene-conversion events in long-read-sequenced sperm from 13 donors, the authors identified a consistent recombination component distinct from PRDM9-induced meiotic exchange, associated with genomic fragile sites and detectable in blood — indicating that a substantial fraction of sperm non-crossover gene conversion arises before meiosis.

Commentary: This finding revises the textbook picture of meiotic recombination and bears on how new mutations and rearrangements arise in gametes, with relevance to infertility and de-novo genetic disease.[30]

6.8 Genetic background sets the trajectory of cancer evolution

Re-running early tumour evolution hundreds of times in divergent inbred mouse strains under controlled conditions, the authors show that epistatic interactions between germline background and acquired somatic mutations determine driver choice, whole-genome duplication and subclonal dynamics — divergence comparable to that across human ancestry groups substantially alters evolutionary trajectories.

Commentary: This controlled-evolution framework explains why genetically diverse populations experience cancer differently and argues for ancestry-aware models in both cancer biology and clinical trial design.[31]

6.9 A glutathione-activated molecular glue degrader expands targeted protein degradation

Through unbiased chemical screening, the authors identified M12, a molecular glue that reprogrammes the E3 ligase DCAF11 to degrade DDX18. M12 functions as a prodrug activated by glutathione S-transferase-mediated glutathionylation; the glutathione moiety engages a conserved binding site on DCAF11 while the exposed M12 moiety recruits neo-substrates, a mechanism readily generalizable to other proteins.

Commentary: Metabolically activated glues harness endogenous redox chemistry for conditional protein degradation, adding a new modality to the targeted-degradation arsenal against previously undruggable targets.[32]

6.10 Raygun: miniaturizing and modifying natural proteins with generative AI

Raygun encodes proteins as probability distributions in fixed dimensions, enabling length-agnostic design controlled by two parameters: it can shrink proteins by 10-25% (occasionally more than half) or expand them while preserving structure and function, as demonstrated by miniaturized fluorescent proteins and TurboID and by EGF variants with higher receptor affinity than wild type.

Commentary: Function-preserving protein miniaturization could yield compact biologics and enzymes with better tissue penetration and lower immunogenicity — a broadly useful complement to antibody engineering.[33]

6.11 In situ structures of plant photosystem supercomplexes

In situ cryo-electron microscopy of rice chloroplasts resolved photosystem II–light-harvesting supercomplexes in their native membrane, including antenna trimers lost during purification, and revealed higher-order assemblies that form a trans-lumenal and trans-stromal skeleton shaping thylakoid architecture, alongside high-resolution PSI–LHCI–LHCII structures.

Commentary: The first molecular framework of native photosynthetic architecture not only deepens fundamental understanding but also provides engineering targets for improving photosynthetic efficiency in crops.[34]

Concluding Remarks

Viewed together, the thirty-four studies above trace the contour of contemporary biomedicine: cancer research is being reorganized around patient-derived models and functional dependency maps; neuroscience is acquiring lifespan-resolved, ancestry-aware cellular references; metabolism and ageing are converging on druggable human-genetics targets; and structural biology is delivering antiviral starting points against priority pathogens. The common thread is convergence — of AI with experiment, of omics with mechanism, and of basic discovery with clinical need. For the practising clinician and the translational researcher alike, the pace at which such findings move from journal page to bedside will define the coming decade of medicine.

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