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Asian Fund for Cancer Research Limited

AFCR–CityU Symposium on Precision and Digital Medicine at BIOHK2024: Highlights

ASIAN FUND FOR CANCER RESEARCH LIMITED

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I. Introduction

The AFCR–CityU Symposium on Precision and Digital Medicine was convened on 12–13 September 2024 as part of BIOHK2024 at the Hong Kong Convention and Exhibition Centre. The symposium was co-organized by the Asian Fund for Cancer Research (AFCR) and City University of Hong Kong, under the broader framework of the annual biotechnology convention hosted by the Hong Kong Biotechnology Organization.

This symposium was designed to provide a focused, high-level platform examining the convergence of precision medicine and digital innovation in oncology and biomedical science. As global healthcare systems increasingly integrate molecular diagnostics, artificial intelligence, and data-driven clinical tools, the need for interdisciplinary collaboration between scientists, clinicians, technologists, and industry leaders has become more urgent. The AFCR–CityU Symposium addressed this intersection directly by highlighting translational strategies that bridge laboratory discovery, computational medicine, and real-world clinical implementation.

Throughout the program, speakers explored how advances in genomics, biomarker discovery, digital pathology, AI-supported analytics, and computational modeling are reshaping cancer research and therapeutic development. Emphasis was placed on transforming scientific insight into scalable clinical solutions, strengthening translational pipelines, and fostering global partnerships across academia and industry.

In summary, the AFCR–CityU Symposium on Precision and Digital Medicine at BIOHK2024 underscored the accelerating integration of biological science and digital technology as a defining force in next-generation oncology. By convening international experts and promoting cross-sector collaboration, the symposium reinforced AFCR’s commitment to advancing innovative cancer research and supporting sustainable global progress in precision and digital health.

II. Government Keynotes and Strategic Vision

Professor Lo Chung-mau Highlights Regulatory Reform and Innovation at BIOHK2024 Keynote

At the keynote session of BIOHK2024, Lo Chung-mau, Secretary for Health of the Hong Kong Special Administrative Region, reaffirmed the government's strategic commitment to positioning Hong Kong as an international health and medical innovation hub. Addressing distinguished guests and international delegates, Professor Lo emphasized that biotechnology and biomedicine are central to Hong Kong's future economic and scientific development.

In his remarks, Professor Lo underscored that laboratory breakthroughs must be supported by rigorous clinical research, efficient regulatory pathways, and forward-looking policy reform to translate into real-world medical impact. He highlighted ongoing government initiatives aimed at strengthening Hong Kong's drug and medical device regulatory framework, including progress toward establishing a Centre for Medical Products Regulation and accelerating patient access to innovative therapies through streamlined approval mechanisms.

Professor Lo also referenced Hong Kong's accession as an observer to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), reinforcing the city's ambition to align with the highest international regulatory standards. Additionally, he outlined plans to enhance clinical research capacity through the development of the Greater Bay Area International Clinical Trial Institute, leveraging Hong Kong's healthcare infrastructure and its strategic integration within the Greater Bay Area.

Concluding his address, Professor Lo reaffirmed that reform and innovation remain ongoing commitments rather than finite milestones. With strong national support and continued policy evolution, he expressed confidence that Hong Kong will emerge as a leading regional and global destination for biomedical research, clinical trials, and health technology innovation.

Under Secretary Lillian Cheong Outlines Strategic Investment and Policy Roadmap for Life and Health Technology at BIOHK2024

At BIOHK2024, Lillian Cheong, Under Secretary for Innovation, Technology and Industry of the Hong Kong Special Administrative Region, delivered a comprehensive address detailing Hong Kong's strategic vision and policy commitments to advancing life and health technology.

Emphasizing that life and health technology is both a national priority and a sector of transformative global potential, Ms. Cheong highlighted Hong Kong's unique positioning within the international innovation landscape. She underscored the city's world-class universities, globally recognized clinical trial infrastructure, state key laboratories, and international research collaborations with leading institutions worldwide. Notably, Hong Kong remains one of the few jurisdictions whose clinical trial data are widely recognized by regulatory authorities including China's NMPA, the U.S. FDA, and the European Medicines Agency.

Ms. Cheong outlined a series of major funding initiatives designed to strengthen the full innovation pipeline - from upstream research to downstream commercialization. These include a HK$6 billion subsidy scheme to establish life and health research institutes, a HK$3 billion

Frontier Technology Research Support Scheme, and the HK$10 billion Research, Academic and Industry Sectors One-plus Scheme (RAISe+) to accelerate the transformation of university research into commercial applications through government matching investments.

Additional measures include the HK$10 billion New Industrialisation Acceleration Scheme to support smart production facilities, the development of the InnoLife Healthtech Hub at the Hong Kong–Shenzhen Innovation and Technology Park (the LOOP), and expanded regulatory and clinical trial infrastructure. The address also highlighted Hong Kong's strong capital market environment, with 65 pre-revenue biotech companies listed under Chapter 18A of the Hong Kong Exchanges and Clearing Limited framework, reinforcing the city's role as a leading biotech fundraising hub in Asia.

Concluding her remarks, Ms. Cheong reaffirmed the government's unwavering commitment to policy innovation, regulatory reform, and ecosystem development. She called for sustained collaboration among government, academia, and industry to accelerate Hong Kong's transformation into an international innovation and technology center, with life and health technology as a central pillar of growth.

III. Public Health and Hepatology

Professor Wang Yu Calls for Coordinated Mainland–Hong Kong Action to Eliminate Hepatitis-Related Liver Cancer

At the AFCR-CityU Symposium on Precision and Digital Medicine during BIOHK2024, Wang Yu, Chairman of the China Foundation for Hepatitis Prevention and Control and former Director-General of the Chinese CDC, delivered a compelling address on the persistent burden of hepatitis B and hepatocellular carcinoma (HCC) in Mainland China and Hong Kong.

Professor Wang presented the latest national survey data (completed in 2020), showing that approximately 5.86% of the general population in Mainland China are hepatitis B virus (HBV) carriers, with continued transmission occurring despite widespread vaccination and access to antiviral therapy. He emphasized that HBV remains a dominant driver of liver cirrhosis and HCC in China, accounting for a significant proportion of global liver cancer cases and mortality. Alarmingly, over the past five decades, liver cancer mortality trends have remained largely unchanged, even in economically developed regions such as Beijing and Shanghai, underscoring that economic growth alone does not reduce disease burden.

Drawing comparisons with Hong Kong, where liver cancer incidence has also remained relatively stable over two decades (approximately 1,400 new cases annually among 7 million residents), Professor Wang highlighted a shared and persistent public health challenge. Despite the availability of effective vaccines, affordable antiviral drugs, and improved diagnostics, early detection rates remain low and five-year survival for HCC remains around 15%.

Referencing the World Health Organization's 2030 hepatitis elimination targets, Professor Wang outlined a structured three-step strategy being implemented across Mainland China:

Large-scale adult screening to identify undiagnosed HBV carriers.

Expansion of antiviral treatment to reduce progression to cirrhosis and cancer.

Routine surveillance for high-risk populations, including biannual ultrasound and blood-based biomarker testing to detect early-stage (≤3 cm) liver cancers amenable to curative intervention.

He emphasized that hepatocellular carcinoma must be addressed as a public health issue rather than solely a clinical oncology problem. Unlike HIV and tuberculosis, which are managed through structured public health targets (e.g., 90-90-90 strategies), hepatitis control has not yet achieved comparable systematic implementation levels.

Professor Wang highlighted successful provincial initiatives in Hainan and Guangdong, including government-funded adult HBV screening programs and structured surveillance protocols at township and community hospital levels. However, he acknowledged the absence of a unified national policy framework and called for stronger inter-regional collaboration.

Concluding his remarks, Professor Wang proposed establishing a formal Guangdong–Hong Kong–Macau cooperation mechanism to facilitate data sharing, coordinated screening strategies, and harmonized intervention models. He affirmed the commitment of the China Foundation for Hepatitis Prevention and Control to support sustained cross-border collaboration aimed at

achieving measurable reductions in hepatitis-related morbidity and mortality across the Greater Bay Area.

Digital Chinese Medicine: Integrating Wave Physics, AI, and Policy to Modernize Traditional Healing

An overview of the research and industrial development of digital Chinese medicine within the context of China's recent national policy plan to build a comprehensive digital Chinese medicine system within three to five years. Framing digitalization as a global healthcare trend, the presentation compares China's strategy with digital health initiatives in Germany, Canada, Israel, and the UK, emphasizing that digital transformation is becoming central to medical innovation worldwide.

Digital Chinese medicine is described as having evolved through four generations from traditional mechanical tools to smart, integrated diagnostic and therapeutic systems. Current applications include AI-assisted diagnostic devices, full-body red-white spectrum analysis, voice signal recognition, robotic acupuncture systems, and waveform-based treatment technologies. The speaker categorizes these innovations into two major groups: digital diagnostic devices and digital therapeutic devices.

A core argument of the talk is that the foundation of digital Chinese medicine lies in physics - particularly electromagnetic and mechanical waves - rather than purely biochemical testing. Technologies such as signal processing and Fourier analysis are used to interpret health states through frequency patterns, linking modern waveform analysis to traditional theories such as the Five Elements and meridian systems. The speaker emphasizes that waves and frequency analysis provide a scientific bridge between traditional diagnostic methods (observation, listening, questioning, pulse-taking) and contemporary digital measurement tools.

The presentation also highlights the development of large-scale data platforms and AI models for Chinese medicine, with participation from major universities and technology companies. Emerging wearable devices, VR integration, and home-based monitoring systems suggest future applications beyond hospitals, particularly in remote care and emergency contexts.

A featured research example demonstrates how brainwave frequency patterns, collected through non-invasive forehead sensors, may correlate with body structure indicators such as BMI. The findings suggest that holistic signal integration-rather than isolating single "effective components" - may better reflect physiological states, reinforcing parallels with traditional multi-component herbal formulations.

In conclusion, the speaker argues that digital Chinese medicine represents not merely technological modernization, but a paradigm shift that integrates physics, big data, artificial intelligence, and traditional medical theory. By aligning with national policy and advancing interdisciplinary research, digital Chinese medicine aims to transform diagnosis, treatment, and industry development while remaining grounded in the foundational principles of traditional Chinese medicine.

Dr. Jiali Li on Advancing Hepatology: Innovation, Data Integrity, and the Future of Liver Cancer Care

Dr. Jiali Li highlights the urgent need to modernize hepatology in response to the growing burden of liver disease and hepatocellular carcinoma (HCC), particularly across the Asia-Pacific region. Despite major advances in antiviral therapies for hepatitis B and C, liver cancer incidence and mortality remain high, underscoring persistent gaps between scientific progress and real-world public health implementation.

Dr. Li emphasizes the importance of high-quality clinical trials, rigorous data integrity, and region-specific research to generate evidence tailored to Asian populations rather than relying solely on Western guidelines. She advocates for stronger integration between laboratory innovation, translational medicine, and patient-centered care.

A central theme of her vision is the application of artificial intelligence in hepatology-from genomics and digital pathology to predictive analytics and precision oncology. AI-driven tools, she notes, can support earlier diagnosis, personalized treatment strategies, improved response prediction, and more efficient drug development.

Ultimately, Dr. Li calls for a new generation of hepatology leaders equipped with interdisciplinary skills, ethical grounding, and technological fluency to reshape liver disease management, reduce mortality, and strengthen Asia-Pacific’s role in global medical innovation.

IV. Cell Therapy and Translational Oncology

Prof. Toh Han Chong: Building Asia's Cell Therapy Ecosystem Through Innovation and Access

Professor Toh Han Chong is a leading Singaporean medical oncologist and a pioneer in advancing cancer immunotherapy and cell therapy in Asia. He serves as Deputy Medical Director at the National Cancer Centre Singapore and plays a key leadership role in the SingHealth Duke-NUS Cell Therapy Centre, where he oversees clinical translation of advanced cellular therapies.

Trained at Harvard Medical School and affiliated institutions, Prof. Toh has been instrumental in bringing CAR-T cell therapy from experimental platforms into real-world clinical practice in Singapore. Under his leadership, Singapore became one of the first countries in Southeast Asia to implement commercially approved CAR-T therapies, expanding access to patients with relapsed and refractory hematologic malignancies.

His work extends beyond clinical implementation. Prof. Toh is deeply involved in developing regional manufacturing capabilities, regulatory frameworks, and sustainable financing models to reduce dependence on imported therapies, which can cost upwards of USD 500,000 per treatment. He has championed efforts to shorten vein-to-vein time, strengthen quality control, and build multidisciplinary teams capable of safely delivering these complex therapies.

V. AFCR Leadership and Symposium Opening

Dr. Sujuan Ba: Advancing Precision Medicine and Building Hong Kong's Life Sciences Future

Dr. Sujuan Ba, Founder and President of the Asian Fund for Cancer Research (AFCR), reaffirmed her commitment to strengthening Hong Kong's role as a global hub for biomedical innovation during the AFCR symposium hosted in partnership with Hong Kong Biotechnology Organization (HKBIO).

Expressing gratitude to HKBIO and Professor Aubrey Young for providing a platform over the past three years, Ba highlighted the growing collaboration between AFCR and CityU, established at last year's symposium. Under the leadership of Professor Michael Yang, the partnership has focused on accelerating biomedical innovation and entrepreneurship in Hong Kong through cross-sector collaboration.

Reflecting on more than a decade of collaborative work, Dr. Ba emphasized that sustained partnerships among research institutions, clinical networks, and translational platforms are essential to transforming scientific discovery into real-world patient impact. She described herself as privileged to stand "at the center of this exciting change," helping convene leaders committed to positioning Hong Kong as the next major life sciences hub.

The symposium brought together leading experts in precision medicine and digital health from the United States and Asia to exchange best practices across cancer, cardiovascular disease, and other major health challenges. Dr. Ba underscored that such dialogue is not merely academic—it represents a critical inflection point for advancing innovative therapies and overcoming systemic barriers in drug development.

As founder of AFCR, she reiterated her belief that meaningful progress in cancer research requires synergy across basic science, translational research, and clinical application. By aligning stakeholders across sectors and geographies, she argued, Asia can play a transformative role in delivering breakthrough medicines to the world.

Ba concluded by inviting participants to deepen collaboration, expand partnerships, and collectively work toward a shared vision: establishing Hong Kong as a leading global center for life sciences and accelerating medical breakthroughs from Asia to the global stage.

Mengsu (Michael) Yang: Uniting Academia, Industry, and Genomics to Advance Precision Medicine

Professor Mengsu (Michael) Yang opened the Precision Medicine and Digital Medicine Symposium at BIOHK 2024 by reaffirming Hong Kong's ambition to become a global leader in translational biomedical innovation. Representing City University of Hong Kong, he highlighted the university's collaboration with the Asian Fund for Cancer Research and the Hong Kong Biotechnology Organization in convening world-leading scientists, clinicians, and entrepreneurs.

Yang emphasized that the symposium reflects a broader interdisciplinary strategy -integrating basic science, translational research, clinical application, and entrepreneurship - to accelerate

progress in precision oncology and digital health. Beyond academic exchange, the initiative also supports startup incubation and commercialization, strengthening Hong Kong's innovation ecosystem.

Introducing keynote speaker Raju Kucherlapati of Harvard Medical School, Yang underscored the transformative impact of genomics on drug development. Kucherlapati traced the origins of precision medicine to the Human Genome Project, launched in 1990, which initially required billions of dollars and a decade to sequence a single genome. Today, genome sequencing costs have fallen below $300, enabling large-scale clinical integration.

The presentation illustrated how genomic insights have revolutionized treatment across rare genetic disorders, hemoglobinopathies, and cancer. From pathway-based therapies in RAS/MAPK-related syndromes to CRISPR-enabled treatments for sickle cell disease, precision medicine now directly informs therapeutic innovation.

In oncology, large-scale initiatives such as The Cancer Genome Atlas have redefined cancer classification. Rather than viewing tumors as single diseases, genomic profiling reveals distinct molecular subtypes, each with actionable targets. In non-small cell lung cancer alone, nearly 100 targeted therapies are now available -transforming survival prospects and enabling personalized treatment strategies.

Yang concluded that the next frontier lies in data integration: combining genomic, clinical, pathological, and therapeutic information into large-scale databases capable of guiding real-time clinical decisions. Such systems would allow physicians to match new patients with evidence derived from thousands of similar cases - ushering in a truly data-driven era of medicine.

VI. Precision Oncology and Molecular Medicine

Hai Yan: From IDH Discovery to Transforming Glioma Diagnosis and Targeted Therapy

At the Precision Medicine Symposium, Professor Hai Yan of A*STAR delivered a compelling presentation on how a single genetic discovery reshaped the classification and treatment of glioma - and what it teaches us about the future of precision oncology in Asia.

A former Chair Professor at Duke University School of Medicine, Yan is internationally recognized for discovering mutations in **IDH1 and IDH2**, now considered defining molecular events in glioma biology. His work not only transformed scientific understanding of brain tumors but also rewrote diagnostic standards globally.

A Devastating Disease — and a Breakthrough Discovery

Glioblastoma (GBM) remains one of the most aggressive cancers, with limited survival despite surgery, radiation, and chemotherapy. Two decades ago, large-scale sequencing efforts such as The Cancer Genome Atlas began mapping its genetic landscape.

During early sequencing studies, Yan's team identified recurrent hotspot mutations in **IDH1**, later discovering complementary mutations in **IDH2**. These mutations were found predominantly in younger patients with secondary glioblastoma — a pivotal insight that revealed glioma is not one disease but a group of biologically distinct entities.

The mutations produce an abnormal metabolite, **2-hydroxyglutarate**, which reprograms cellular metabolism and causes widespread DNA and histone hypermethylation. This single-point mutation alters thousands of genes, effectively locking cells in a stem-like state and driving tumor formation.

From Genetic Insight to Targeted Therapy

The path from discovery to drug approval was long - nearly 16 years. IDH inhibitors were first approved for acute myeloid leukemia, and in 2023–2024 received FDA approval for **IDH-mutant grade 2 gliomas**.

Clinical data showed remarkable results:

- Progression-free survival extended from 11 months to 28 months
- Significant delay in need for further intervention
- Favorable safety profile with minimal toxicity

Notably, these inhibitors work well in lower-grade tumors but not in high-grade gliomas — highlighting the complexity of tumor evolution and microenvironmental change.

Redefining Brain Tumor Classification

Yan's work contributed directly to revisions in the World Health Organization classification of central nervous system tumors. Molecular markers such as:

- **IDH mutations**
- **1p/19q codeletion**
- **ATRX mutation**
- **TERT promoter mutation**

are now essential for diagnosis and treatment planning.

Glioma surgery increasingly relies on rapid molecular diagnostics. Surgeons must distinguish tumor subtypes intraoperatively to determine surgical aggressiveness. However, conventional next-generation sequencing (NGS) is slow and costly.

Yizhou Jiang: Redefining Triple-Negative Breast Cancer Through Molecular Subtyping and Precision Therapy

Professor Yizhou Jiang from Fudan University Shanghai Cancer Center presented a decade-long effort to transform the treatment paradigm of triple-negative breast cancer (TNBC) through molecular subtyping and subtype-guided precision therapy.

The Challenge of Triple-Negative Breast Cancer

Breast cancer remains the most common malignancy among women globally. In China alone, there are approximately 2.5 million patients, with over 120,000 deaths annually.

Among breast cancers, **triple-negative breast cancer (TNBC)** lacks:

- Estrogen receptor (ER)
- Progesterone receptor (PR)
- HER2 expression

Because TNBC does not respond to endocrine therapy or HER2-targeted therapy, chemotherapy has traditionally been the "one-size-fits-all" standard — with limited success and poor prognosis.

Professor Jiang emphasized a central lesson:
TNBC is not one disease, but multiple biologically distinct entities.

A Four-Subtype Molecular Classification

In a landmark 2019 publication in *Cancer Cell*, Jiang's team analyzed 465 TNBC cases and established a four-subtype classification based on transcriptomic profiling:

Basal-like Immunosuppressed (BLIS)

High genomic instability

Sensitive to platinum agents and PARP inhibitors

Immunomodulatory (IM)

Immune "hot" tumors

Responsive to anti–PD-1 immunotherapy

Luminal Androgen Receptor (LAR)

High androgen receptor expression

Potential sensitivity to anti-HER2 ADCs and CDK4/6 inhibitors

Mesenchymal-like (MES)

Enriched in angiogenesis and STAT3 signaling

Candidates for anti-angiogenic therapy or STAT3 inhibitors

This framework replaced uniform chemotherapy with **subtype-based precision treatment**.

Beyond Single Mutations: Genetic Interactions

The team further investigated co-occurring mutations and functional genetic interactions:

BRCA mutations + MYC amplification → increased DNA damage sensitivity

TP53 mutation + MYC amplification → impaired immune response and immunotherapy resistance

These findings were incorporated into Fudan's multi-gene panel reports, adding genetic interaction analysis to guide therapeutic decisions.

Remodeling the Tumor Microenvironment

Recognizing that certain subtypes (especially BLIS and LAR) are immune "cold," Jiang's group explored strategies to sensitize tumors to immunotherapy:

BLIS Subtype:

- Identified a metabolite (GDP balance) that induces BRCA2 ubiquitination
- Leads to homologous recombination deficiency
- Activates cGAS-STING pathway

Proposed triple combination:

- PARP inhibitor
- Immune checkpoint inhibitor

- Metabolic modulation

LAR Subtype:

- Discovered hypersensitivity to ferroptosis
- Targeted GPX4 inhibition to induce ferroptosis
- Observed immune microenvironment remodeling
- Combination with immunotherapy showed promising preclinical results

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Making Subtyping Clinically Practical

To translate molecular subtyping into routine care, the team developed:

1. IHC-Based Clinical Subtyping

Using four biomarkers:

FOXC1

CD8

AR

ZNF703

Over 6,000 TNBC cases in China have already been classified using this method.

2. AI-Based Rapid Subtyping

MRI radiomics models

Digital pathology (whole-slide imaging)

Machine learning algorithms for non-invasive molecular prediction

Ability to predict actionable mutations such as PIK3CA

This enables faster, more accessible precision classification.

Clinical Trial Validation: The FUTURE Trials

The **FUTURE trial (umbrella design)** enrolled heavily pretreated metastatic TNBC patients:

Subtype-guided therapy arms

Objective Response Rate (ORR): ~30%
(vs. 5–10% in historical chemotherapy controls)

The **FUTURE-SUPER randomized trial** advanced the model to first-line therapy:

Subtype-based precision treatment vs. Chemotherapy

- Median PFS: 11.3 months vs. 5.8 months
- Hazard ratio: 0.38
- ORR reached ~80% in certain subtypes

These findings were published in *Nature Medicine* (fast-track publication).

Charles Hu Chairs Session on Precision Oncology for Rare and High-Risk Cancers presented by Dr. Daniel Johnson

Charles Hu, Vice President of the conference, chaired this session of the Precision Medicine and Digital Medicine Symposium at BioHongKong 2024, emphasizing how deeply cancer affects families and why precision medicine remains one of the most urgent frontiers in oncology. He reflected on the strong scientific momentum from earlier talks and introduced the next group of experts addressing head and neck cancer, gliomas, and cardiovascular disease.

The first speaker of the session was Professor Daniel Johnson from the University of California, San Francisco, who presented an innovative precision medicine strategy for an extremely rare and highly lethal cancer: head and neck squamous cell carcinoma associated with Fanconi anemia.

Precision Oncology for a Rare Genetic Disease

Fanconi anemia is a rare inherited DNA repair disorder caused by mutations in over 20 FANC genes, including BRCA2. While hematopoietic stem cell transplantation now allows many patients to survive childhood, they face a dramatically increased lifetime risk (500–800-fold higher than the general population) of developing head and neck squamous cell carcinoma.

Treatment is especially challenging because these patients are hypersensitive to DNA-damaging therapies such as radiation and cisplatin — standard treatments for head and neck cancer. As a result, surgery is often the only viable option, and once surgery is no longer possible, therapeutic choices become extremely limited.

Developing Patient "Avatars" to Guide Therapy

To overcome the rarity of the disease and the limited patient population, Johnson's team - in collaboration with Rockefeller University and Oregon Health and Science University - developed the first patient-derived xenograft (PDX) models of Fanconi anemia–associated head and neck cancer.

These models allowed for:

Whole-exome sequencing

Proteomic profiling using digital spatial analysis

Functional drug testing

Prioritization of targeted therapies

The PDX tumors successfully replicated the hypersensitivity to DNA-damaging agents seen in patients, validating them as reliable preclinical models.

Key Molecular Findings and Targeted Strategies

EGFR Amplification

One model demonstrated strong EGFR amplification and activation. Treatment with cetuximab (FDA-approved for head and neck cancer) led to significant tumor regression — even at lower-than-standard doses.

A broader HER-family inhibitor, dacomitinib, also showed potent activity in this model.

PI3K Pathway Activation

Another model carried an activating PIK3CA mutation with elevated PI3K-AKT signaling. Treatment with a PI3K inhibitor suppressed tumor growth, and combining it with EGFR inhibition further enhanced response.

BCL2-Driven Resistance

A third, highly resistant model showed elevated expression of anti-apoptotic BCL2 family proteins. Treatment with venetoclax, an FDA-approved BCL2 inhibitor, produced strong tumor inhibition - identifying a therapeutic vulnerability in otherwise refractory disease.

Min Li Highlights ZIP4-Driven Precision Strategies and Cachexia Research in Pancreatic Cancer

Following the previous presentation, the session-chaired by Charles Hu - continued with Professor Min Li, a leading expert in pancreatic cancer research and precision oncology.

Professor Min Li serves as the George Lynn Cross Research Professor and Virginia Kerley Cade Endowed Chair in Cancer Treatment at the University of Oklahoma Health Sciences Center. He is also Associate Director of Global Oncology at the NCI-designated Stephenson Cancer Center. Over the past decade, he has played a pivotal role in securing and renewing the center’s National Cancer Institute designation, advancing its mission to translate laboratory discoveries into clinical and community impact.

Focus: Precision Medicine in Pancreatic Cancer

Professor Li's presentation centered on one of the most lethal malignancies: pancreatic cancer. With only 15–20% of patients eligible for surgical resection and limited success from immunotherapy or chemotherapy alone, he emphasized the urgent need for:

- Early diagnostic biomarkers
- Novel molecular targets
- Rational combination therapies

ZIP4: A Diagnostic and Therapeutic Target

A major focus of his research over the past two decades has been the zinc transporter ZIP4 (SLC39A4), which his team identified as significantly overexpressed in pancreatic cancer across multiple international cohorts.

Key Findings:

ZIP4 overexpression promotes tumor growth and metastasis

Silencing ZIP4 via shRNA significantly suppresses tumor progression

Targeting ZIP4 improves overall survival in multiple mouse models

ZIP4 contributes to chemotherapy resistance

These findings position ZIP4 as both a diagnostic marker and a therapeutic target in pancreatic cancer.

Zinc Homeostasis and Cancer Progression

Professor Li explained the broader biological framework: zinc is an essential trace element required for enzyme function and transcriptional regulation. Two major transporter families regulate intracellular zinc balance:

ZnT family (reduces intracellular zinc)

ZIP family (increases intracellular zinc)

Disruption of this balance—particularly via overexpression of ZIP4—activates oncogenic pathways, including CREB-mediated transcription and downstream tumor-promoting signaling cascades.

Cancer Cachexia: An Understudied Crisis

A significant portion of the talk addressed cancer cachexia, a severe muscle-wasting syndrome highly prevalent in pancreatic cancer patients.

Professor Li's team demonstrated that:

ZIP4 overexpression promotes tumor-driven muscle wasting

Exosomal heat shock proteins (HSP70/90) mediate tumor–muscle crosstalk

Activation of signaling pathways such as p38 MAPK and UBR2 contributes to skeletal muscle degradation

Targeting ZIP4 not only slows tumor growth but rescues muscle mass and improves survival

This work highlights pancreatic cancer as not just a tumor-centric disease, but a systemic metabolic disorder involving tumor–host interactions.

Combination Therapy and Translational Impact

Professor Li emphasized that monotherapy is insufficient. His team has explored:

ZIP4 inhibition combined with surgery

Zinc-modified dietary interventions

Nanoparticle-delivered RNA therapies

Immunotherapy and phototherapy combinations

Cancer vaccines and stem-cell–based approaches

These integrated strategies significantly extended survival in preclinical models—demonstrating translational potential.

Jinguang Wang Showcases AI-Driven Models to Predict Cancer Evolution and Improve Precision Treatment

Professor Jinguang Wang, founder of the Wang Genomics Laboratory at the Hong Kong University of Science and Technology, presented groundbreaking research on cancer evolution and precision medicine. With a background in applied mathematics and computational biology, Wang focuses on building in silico models to predict how tumors evolve, particularly in glioma patients.

Challenging the assumption that recurrent tumors mirror primary tumors, Wang's longitudinal genomic studies revealed critical evolutionary changes that drive treatment resistance. His team identified key alterations—such as MET amplification and CDKN2A deletion - that can predict recurrence risk and treatment response. Their work contributed to the development of a MET-

targeted drug (PLB-1001), now approved in China, while also uncovering mechanisms of resistance involving additional mutations like PIK3CA.

By analyzing sequencing data from 544 patients, Wang's team developed a machine learning framework capable of forecasting tumor progression and patient prognosis. They further advanced the field by integrating AI-based RNA-to-protein prediction models, enabling more refined subclassification of IDH-mutant gliomas into seven clinically distinct subgroups.

Wang's research demonstrates that although cancer evolution contains stochastic elements, certain patterns are predictable. Through combining genomics, proteomics, and artificial intelligence, his work moves precision oncology closer to truly personalized, evolution-informed treatment strategies.

Leslie Leinwand Highlights Breakthrough Myosin-Targeted Therapy That Reverses Hypertrophic Cardiomyopathy

Professor Leslie Leinwand of the University of Colorado Boulder presented a compelling story of how decades of fundamental muscle biology research led to the first FDA-approved therapy for hypertrophic cardiomyopathy (HCM), a common inherited heart disease.

Focusing on cardiac myosin—the motor protein responsible for heart muscle contraction - Leinwand explained how mutations in the beta-myosin gene (MYH7) cause hypercontractility, a hallmark of HCM. These mutations increase force production and energy consumption in heart muscle cells, contributing to thickened heart walls and elevating the risk of sudden cardiac death, particularly in young athletes.

Through biochemical assays measuring myosin motility and single-molecule force production, her team demonstrated that many HCM mutations are gain-of-function. This insight guided the development of a small-molecule myosin inhibitor designed to "put the brakes" on excessive contractile activity without affecting other muscle types.

Leinwand co-founded MyoKardia to translate this discovery into therapy. The company was later acquired by Bristol-Myers Squibb, and in 2022 the FDA approved the myosin inhibitor (mavacamten) for obstructive HCM following highly successful Phase III clinical trials. Remarkably, the treatment not only slowed disease progression but demonstrated the ability to reverse aspects of cardiac dysfunction—an unprecedented achievement in HCM care.

In addition to therapeutic development, Leinwand shared emerging research on sarcomere protein turnover using advanced isotope-labeling and imaging mass spectrometry techniques. Her lab is uncovering how heart muscle maintains protein homeostasis over a lifetime and how these processes may open new therapeutic avenues for autosomal dominant inherited cardiomyopathies.

Her work exemplifies how sustained basic science, when paired with translational vision, can lead to transformative therapies for genetic heart disease.

Richard Gibbs Urges Renewed Focus on Single-Gene Discovery to Unlock the Promise of Clinical Genomics

At the CityU-AFCR Symposium, Richard Gibbs of Baylor College of Medicine delivered a compelling call to refocus genomic research on single-gene (Mendelian) diseases to accelerate meaningful clinical translation. A founding leader of the Human Genome Sequencing Center and a key contributor to the Human Genome Project, Gibbs reflected on the extraordinary technological advances that have made large-scale genome sequencing routine and affordable.

Despite the accumulation of millions of genome sequences through major programs such as UK Biobank, All of Us Research Program, and others, Gibbs acknowledged that genomics has yet to deliver consistent, high-impact utility in everyday clinical practice. Polygenic risk scores, while promising, have not achieved broad clinical effectiveness.

He argued that single-gene disease discovery remains one of the most powerful engines for biological insight and medical progress. Using his team's work on AHDC1-related neurodevelopmental disorder as an example, Gibbs demonstrated how focused investigation of one gene can reveal functional mechanisms, genotype–phenotype relationships, and broader biological principles.

To overcome what he described as the "catch-22" of translational genomics - where limited clinical use restricts discovery, and limited discovery restricts clinical use - Gibbs outlined new pilot programs integrating genomic screening into adult cardiovascular care. In a study of ambulatory cardiac patients, his team identified actionable high-penetrance variants in approximately 10% of participants, far higher than rates seen in the general population, suggesting that targeted clinical integration can drive both patient benefit and new discovery.

Looking ahead, Gibbs emphasized the need for deeper clinical phenotyping, expanded routine genomic testing in healthcare settings, long-read sequencing to uncover structural variation, and systematic investigation of somatic mutations across tissues.

His central message was clear: advancing precision medicine requires renewed commitment to Mendelian gene discovery, tighter integration of genomics into frontline clinical care, and sustained effort to translate genetic insight into real-world health impact.

Precision Genomics Rescues Failed Drugs in Cancer and Depression Through Biomarker-Driven Strategy

Drawing on decades of experience spanning the Human Genome era to modern biotech, Wen Luo from Denova Biopharma presented a precision medicine strategy aimed at rescuing failed drugs by identifying genetic biomarkers that predict patient response.

Reflecting on the early genomic revolution and its promise, he described how large-scale genome discovery initially fueled expectations of rapid cancer cures. While that optimism proved premature, genomic tools have since become powerful assets in drug development - particularly in identifying responder subgroups that can transform unsuccessful clinical trials into targeted successes.

Using the example of IRESSA, developed by AstraZeneca, he illustrated how a failed Phase III lung cancer trial was later salvaged after researchers identified EGFR mutations as predictive biomarkers. This discovery launched the era of mutation-guided targeted therapy in oncology.

Building on this concept, his company developed a platform that retrospectively analyzes DNA from failed clinical trials to uncover germline genetic biomarkers that distinguish responders from non-responders. Rather than discarding drugs that narrowly miss statistical endpoints, the approach seeks to stratify patients and relaunch trials in biomarker-selected populations.

In oncology, this strategy was applied to a gene therapy for recurrent glioblastoma (DB107), originally unsuccessful in Phase III. Through genomic analysis, the team identified a predictive SNP biomarker (DGM7). When patients were stratified accordingly, biomarker-positive individuals demonstrated markedly improved survival - extending median survival from roughly 11–12 months to 18 months, with a hazard ratio of 0.5. New biomarker-guided trials are now underway.

The same precision framework was extended beyond cancer into central nervous system disorders. In treatment-resistant depression (TRD), a triple reuptake inhibitor (DB104) previously abandoned after multiple failed trials was reanalyzed using genomic stratification. Identification of a specific SNP (DGM4) revealed that approximately 20% of patients experienced significant clinical improvement, achieving robust efficacy in a prospective biomarker-selected study with strong statistical significance and favorable safety.

The talk emphasized that precision medicine should not be limited to oncology. By leveraging germline genomics and large-scale clinical data, the platform aims to revive high-potential compounds across therapeutic areas, reduce drug development failure rates, and deliver more personalized therapies for complex diseases.

Overall, the presentation highlighted a paradigm shift: failed drugs may not truly fail -they may simply need the right patients.

VII. Entrepreneurship and Innovation

Zongli Zheng Advances Liquid Biopsy Strategy for Early Liver Cancer Detection Using Circulating DNA Signatures

Professor Zongli Zheng of City University of Hong Kong presented a novel liquid biopsy framework aimed at detecting liver cancer at its earliest stages by analyzing circulating tumor-derived DNA in blood.

While major breakthroughs in targeted therapy and immunotherapy have improved outcomes for advanced cancers, Zheng emphasized that early detection remains the most powerful determinant of survival—particularly in liver cancer, where Stage I patients can achieve long-term survival exceeding 10 years, compared with poor outcomes in late-stage disease.

His research focuses on leveraging biological principles of cancer evolution -specifically the accumulation of somatic mutations and genomic instability - to detect malignancy before clinical diagnosis. Rather than relying solely on mutation panels, Zheng's team developed innovative methods to analyze multiple circulating DNA features, including:

> **Telomere G-tail shortening**: A novel sequencing-preserving method captures the single-stranded 3' telomeric overhang typically lost in conventional library preparation. The team hypothesized that prematurely shortened telomere fragments released during accelerated tumor cell division could serve as early biomarkers.
>
> **Genome-wide fragmentation patterns**: Low-depth whole-genome sequencing revealed distinct fragmentation signatures that robustly distinguish clinical liver cancer cases from controls (AUC ~0.999).
>
> **Copy number variation–based tumor content estimation**: Using computational algorithms to infer circulating tumor DNA burden, the approach not only detected cancer but also monitored treatment response and predicted prognosis.

In a large longitudinal population cohort of nearly 20,000 individuals, the telomere-based assay achieved approximately 59% sensitivity at one year before clinical diagnosis while maintaining 98% specificity - an essential threshold for cost-effective population screening. In established clinical cases, detection sensitivity approached 100%.

Importantly, circulating DNA signatures also tracked surgical treatment response, showing marked reduction in tumor-derived signals after tumor removal, while persistent signals correlated with poorer prognosis.

Zheng concluded that while pre-diagnostic detection remains challenging, combining telomere features, genome-wide fragmentation, and copy number analysis offers a promising path toward non-invasive, highly specific early cancer screening. His work highlights the growing potential of liquid biopsy technologies to shift cancer management from late-stage treatment to proactive early intervention.

Bridging Research and Entrepreneurship: Building the Next Generation of Biotech Leaders

Dr. Sujuan Ba, founder and CEO of the Asian Fund for Cancer Research (AFCR), opened the session “Bridging Research from Academia to Cancer Entrepreneurship,” highlighting the critical factors for building successful biotech companies: innovative science, strong leadership, and robust funding. The program, held in partnership with CityU and AFCR, showcases how academic discoveries can be translated into patient benefits and billion-dollar biotech ventures. Participants learned from legendary scientist-entrepreneurs, including Dr. Kucherlapati and Dr. Liang Wang, whose pioneering work and company-building experiences demonstrate the journey from lab innovation to impactful therapies. The session emphasized mentorship, networking, and the importance of turning scientific breakthroughs into real-world solutions for cancer and other deadly diseases.

Raju Kucherlapati Shares Lessons from Building Billion-Dollar Biotech Companies

Raju Kucherlapati reflected on his journey from academic geneticist to co-founder and leader of multiple billion-dollar biotechnology companies, offering insights for young entrepreneurs in the audience.

Kucherlapati began by tracing the origins of his first company to a landmark 1985 *Nature* publication with Oliver Smithies, demonstrating targeted gene modification in mammalian cells. The breakthrough - later recognized with the 2007 Nobel Prize - enabled gene targeting in embryonic stem cells and laid the groundwork for genetically engineered mice. Building on this technology, Kucherlapati co-founded a company that developed fully human monoclonal antibody platforms. In partnership with Amgen, the company developed the EGFR-targeting antibody Vectibix (panitumumab), later acquired for $2.2 billion, generating more than 100-fold returns for early investors.

He next described the founding of Millennium Pharmaceuticals in 1993, alongside leaders including Eric Lander, during the early years of the Human Genome Project. Millennium pioneered genomics-driven drug discovery, secured major pharmaceutical partnerships, and ultimately developed the proteasome inhibitor bortezomib (Velcade), approved by the U.S. Food and Drug Administration in 2005. In 2008, Millennium was acquired by Takeda Pharmaceutical Company for $8.8 billion.

Kucherlapati also highlighted his role as chairman of PureTech Health, which incubates and spins out innovative therapeutic companies. One such venture, Karuna Therapeutics, developed KarXT for schizophrenia and was recently acquired by Bristol Myers Squibb for $14 billion following strong Phase III results. He further introduced Seaport Therapeutics, a newly launched company based on novel drug-delivery technology designed to reduce liver toxicity.

Across these case studies, Kucherlapati emphasized key principles for biotech entrepreneurship: patience over long development timelines, strong leadership and scientific talent, resilience during financial downturns, disciplined focus, and flexibility in seizing opportunities. While financial value creation is significant, he stressed that the ultimate reward lies in developing medicines that improve - and in many cases save - the lives of millions worldwide.

Advancing Drug Development: AI-Powered Screening and Comprehensive Gene & Cell Therapy Solutions

The session highlighted two pioneering companies transforming preclinical and translational drug development. **AniTech Limited**, presented by Vivian Chu, uses AI-assisted EEG analysis to optimize preclinical drug screening, predicting safety, toxicity, and efficacy with high accuracy. Their platform reduces screening time, costs, and animal use, while providing customizable studies and expert interpretation. Supported by City University of Hong Kong neuroscientists, their patented technology is already recognized with international awards.

Following, **Betagen Scientist Limited**, presented by Vivian Yan, specializes in cell and gene therapy development and biologics manufacturing. With a team of internationally experienced scientists, Betagen offers one-stop services including viral vector development, circular RNA stabilization, and process optimization. Their solutions reduce time and costs for clients while overcoming bottlenecks in RNA delivery and CMC readiness. Since 2019, the company has leveraged government grants and aims to expand to North America, supporting startups and established biotech firms in bringing therapies from concept to clinical impact.

Hong Kong Biotech Startups Showcase Innovations in Diagnostics, Drug Delivery, AI Surgery, and Environmental Health

At the Hong Kong Bio entrepreneurship showcase, a diverse group of early-stage biotech and health-tech companies presented innovations spanning diagnostics, therapeutics, digital health, and environmental monitoring.

Cimple Biotechnology introduced a quantitative rapid test platform designed to bring laboratory-level measurement into the home setting. Its first application targets chronic kidney disease (CKD) through urine albumin detection, aiming to replace qualitative dipstick tests with affordable, visually readable quantitative results supported by a mobile health app.

Greater Bay Biotechnology Limited presented microneedle-based transdermal drug and cell delivery technology, including insulin delivery for diabetes and stem-cell applications. The company highlighted preclinical and early human studies and its ambition to address China's large diabetic population with minimally invasive, pain-free alternatives to injections.

Focusing on preventive health, **GUTolution Limited** showcased a personalized gut microbiome platform using metagenomic sequencing and AI-driven disease risk assessment. The company offers customized probiotic formulations and reports high detection accuracy for microbiome-associated conditions such as colorectal cancer.

In the extracellular vesicle field, **JotBody Hong Kong Limited** unveiled EV engineering kits designed for drug loading and surface functionalization, building on published research in advanced drug delivery systems. The company is seeking funding to scale production and move toward GMP-grade manufacturing.

Environmental health innovation came from **NerOcean Limited**, which developed low-cost "artificial mussels" capable of monitoring heavy metals and radionuclides in water. The technology, endorsed in international collaborations, aims to become a global standard for environmental monitoring.

In smart rehabilitation, **Sharpsight Limited** introduced computerized embodiment therapy systems integrating multimodal feedback to support neurological and motor recovery, addressing shortages in rehabilitation resources amid global aging.

Cardiovascular diagnostics company **Sramek Insight Limited** presented portable, non-invasive impedance cardiography devices for home and clinical use, targeting improved hypertension management through hemodynamic monitoring.

Surgical innovation was highlighted by **Syngular Technology Limited**, which combines AI, AR, and 3D modeling to provide real-time surgical visualization and guidance, aiming to improve precision and reduce dependence on complex robotic systems.

Food safety startup **ZenxTag Technology** introduced a spoilage marker dosimetric tag that detects biogenic amine gases to visually indicate food freshness, addressing food waste and safety challenges in retail and hospitality sectors.

Collectively, the 11 presenting teams demonstrated Hong Kong's growing biotech ecosystem, emphasizing translational science, commercialization strategies, and global market ambitions across healthcare and sustainability sectors.

VIII. Conclusion

The AFCR - CityU Symposium on Precision and Digital Medicine at BIOHK2024 reflected the accelerating convergence of molecular science, artificial intelligence, translational medicine, and biotechnology entrepreneurship. Across two days of keynote addresses, scientific presentations, and innovation showcases, speakers demonstrated how genomics, targeted therapeutics, digital diagnostics, and AI-driven modeling are reshaping modern healthcare.

From public health strategies addressing hepatitis-related liver cancer to breakthrough targeted therapies in glioma, breast cancer, pancreatic cancer, cardiovascular disease, and mental health, the symposium highlighted both scientific depth and translational momentum. Equally significant was the emphasis on commercialization pathways, regulatory reform, and cross-border collaboration within the Greater Bay Area and the broader Asia-Pacific region.

By convening global leaders in academia, industry, and government, the symposium reinforced Hong Kong's emerging role as a nexus for precision medicine innovation. It underscored AFCR's ongoing commitment to advancing impactful cancer research while fostering sustainable ecosystems that translate discovery into clinical benefit.

About AFCR

The **Asian Fund for Cancer Research Limited (AFCR)** is a Hong Kong–based non-profit organization dedicated to accelerating breakthroughs in cancer research through strategic funding and international collaboration. Founded in 2003 by Dr. Sujuan Ba, AFCR supports high-impact, translational research projects that advance precision medicine, early detection technologies, and innovative therapeutic strategies.

AFCR works closely with leading academic institutions, research hospitals, and biotechnology partners worldwide to bridge the gap between laboratory discovery and clinical application. By prioritizing interdisciplinary science and fostering cross-border collaboration - particularly between Asia and the global research community - AFCR seeks to ensure that promising scientific advances translate into tangible benefits for patients.

Over the past two decades, AFCR has funded pioneering work in genomics, immunotherapy, molecular diagnostics, and targeted drug development. In addition to research funding, the organization actively convenes global scientific leaders, policymakers, and industry innovators through forums such as the AFCR–CityU Symposium on Precision and Digital Medicine, strengthening Hong Kong's role as an emerging hub for biomedical innovation.

Through its commitment to scientific excellence, collaboration, and patient impact, AFCR continues to advance its mission of improving cancer outcomes and expanding access to next-generation precision therapies.