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I aspire to disseminate Taiwan's screening model and experience throughout Asia

25.11.2025

Tags: Taiwan, National Taiwan University, Academica Sinica, Oncology, KOL

Professor Pan Chyr Yang is a clinician-scientist with an MD and PhD in pulmonary medicine, holding joint appointments at Academia Sinica and former university leadership roles in National Taiwan University. Recognised for pioneering non-smoker lung cancer screening methodologies in Asia, he has established national surveillance programmes now adopted across the region. His translational research achievements include spearheading biotech development initiatives and advancing precision medicine frameworks that challenge conventional Western-centric oncology paradigms.

Could you begin with an introduction to your background and clinical expertise?

I am a clinician with advanced training in pulmonary medicine, holding both MD and PhD credentials. Throughout my career, I have maintained a dual focus as a physician–scientist, conducting foundational and translational research whilst maintaining active clinical practice.

My research trajectory commenced with the investigation of respiratory medicine, including asthma, chronic obstructive pulmonary disease, and pulmonary critical care. Subsequently, I transitioned toward a concentrated focus on lung cancer, specifically examining molecular pathogenesis, genetic alterations, and precision medicine applications. I hold a joint appointment at Academia Sinica, where I direct a research laboratory conducting extensive basic and translational investigations. I have also fulfilled administrative responsibilities, including former

university presidency.

What prompted your concentrated focus on lung cancer research?

My specialisation in lung cancer emerged from clinical observations made over 30 years. Upon completing my pulmonary medicine training, I began clinical practice as an attending physician in Taiwan's hospital system. I observed a striking epidemiological pattern that contradicted established Western textbook doctrine: the predominance of lung cancer amongst female patients with no smoking history.

This observation fundamentally diverged from the conventional understanding that smoking represents the primary lung cancer aetiology. Yet in Taiwan, this paradigm proved inapplicable. I systematically examined Taiwan's lung cancer epidemiology and discovered a paradoxical phenomenon: despite implementing successful anti-smoking cessation campaigns beginning in 1997, which reduced male smoking prevalence from approximately 50% in the 1990s to approximately 20% currently, lung cancer incidence has continued increasing rather than declining.

Additionally, female smoking prevalence has remained persistently low at 3 – 5 percent without meaningful variation, yet females experience a substantial lung cancer burden. Evidently, this epidemiological pattern cannot be explained by smoking alone.

How did you approach investigating this epidemiological anomaly?

I collaborate with my colleagues, commence comprehensive molecular and genetic epidemiology investigations. What emerged proved remarkable: this disease pattern is not unique to Taiwan but rather characteristic across Eastern Asia – encompassing Korea, Japan, Hong Kong, Singapore, and mainland China. Throughout this region, female populations demonstrate very low smoking prevalence yet experience lung cancer as the leading cancer mortality cause.

This observation suggested a distinctly different disease entity requiring dedicated investigation. Approximately 10 – 15 years ago, we initiated systematic genetic epidemiology studies. Subsequently, I participated in the Cancer Moonshot project, commencing in 2017, which aimed to elucidate why non-smoking populations develop lung cancer, particularly in Taiwan and throughout Asia.

Our comprehensive genomic and proteogenomic investigations revealed critical findings: Eastern Asian populations harbour specific genetic susceptibilities predisposing them toward environmental carcinogen exposure. This genetic predisposition proves particularly pronounced in women.

We identified environmental factors – particularly air pollution – as critically important risk determinants. Specifically, we characterised polycyclic aromatic hydrocarbon components and nitrosamines as major environmental carcinogens. Notably, nitrosamines not only contaminate regional air pollution but also serve as food preservatives throughout East Asia, including Korea, mainland China, and Taiwan. This convergence of environmental carcinogenic exposure from multiple sources appears to play a substantial aetiological role.

Given lung cancer's disease burden, what strategic imperatives emerged from your findings?

Lung cancer represents the leading cancer mortality among both men and women in Taiwan. National health insurance systems allocate disproportionate resources toward lung cancer management, yet outcomes remain disappointingly poor. Historically, more than 50% of patients present with stage four disease. Even with contemporary therapeutics – including chemotherapy, targeted therapies, and immunotherapies – five-year survival rates remain modest at approximately 10 – 15% for advanced disease.

This clinical reality motivated me to consider alternative strategic approaches. I recognised that improving survival outcomes necessitated earlier disease detection. In stage 1 disease, five-year surgical cure rates exceed 90%. Conversely, stage 4 disease demonstrates a dramatically inferior prognosis.

Therefore, I advocated for implementing lung cancer screening programmes to increase early-stage disease detection and reduce advanced-stage diagnoses. This represented a fundamental paradigm shift in our approach to lung cancer management.

You initiated the TALENT study, a milestone lung cancer screening investigation. Can you describe this initiative?

The TALENT study, commencing in 2015, proved instrumental in establishing evidence supporting our screening approach. Our clinical trial consortium recognised that achieving improved lung

cancer control required shifting diagnosis toward earlier, potentially curative disease stages whilst simultaneously reducing stage four presentations.

Our investigation differed fundamentally from existing screening studies. Global lung cancer screening initiatives – including the NLST study in the US and the NELSON study in Europe – concentrated exclusively on heavy smokers, typically with 30 pack-year smoking histories. However, our patient population analysis demonstrated that approximately two-thirds of Taiwanese lung cancer patients had no smoking history, whilst only one-third were smokers.

We recognised that applying Western-derived screening guidelines would capture only one-third of our patient population, rendering this approach clinically insufficient for addressing Taiwan's disease burden. Consequently, we advocated to government authorities for a low-dose computed tomography screening programme to encompass non-smoking populations with identifiable risk factors.

We recruited 12,011 participants demonstrating risk factor profiles including family history of lung cancer, prior chronic lung diseases such as tuberculosis or pulmonary fibrosis, second-hand smoke exposure, and notably, occupational cooking-related fume exposure, which proved particularly significant for women.

What were the TALENT study's key findings?

The baseline lung cancer detection rate proved remarkably elevated – 2.6 percent – substantially exceeding NLST and NELSON detection rates of 0.9 – 1.1 percent. This elevated detection rate did not reflect exceptionally high lung cancer population incidence but rather our strategic risk stratification methodology successfully identifying high-risk populations.

The study's most consequential finding involved disease stage distribution: 96.5% of detected cancers presented at stage 0 or stage 1 disease – essentially curable through surgical intervention. This contrasted sharply with our historical baseline, where only 20 – 25% of cases presented as early-stage disease, with 50% presenting as stage 4.

These findings provided compelling evidence supporting government investment in systematic screening infrastructure. Consequently, the government allocated resources to establish a nationwide low-dose computed tomography screening programme commencing in July 2022.

How has the national programme evolved since its implementation?

The programme currently targets two populations. First, smokers with modified inclusion criteria – originally 30 pack-years but reduced to 20 pack-years in 2024, appropriately capturing heavier smokers without excessive restriction. Second, family history of lung cancer in non-smoking or light-smoking populations or identifiable occupational and environmental exposures.

To date, we have screened over 200,000 individuals across more than 200 participating hospitals nationwide. The overall lung cancer detection rate has achieved 1.3 percent – an excellent result. This programme has become internationally recognised as an exemplary model, particularly given our success in establishing systematic screening for non-smoking populations with risk factors.

How does your experience inform global lung cancer screening strategy?

This initiative holds profound international significance. Global trends demonstrate that smoking cessation programmes prove remarkably successful, yet non-smoker lung cancer incidence continues escalating worldwide. Currently, approximately 30% of global lung cancer patients have no smoking history – an increasing proportion.

Taiwan demonstrates that conventional Western-derived screening paradigms prove insufficient for addressing this emerging epidemiology. We have established international examples through consensus meetings and clinical trial consortium activities throughout Eastern Asia. Singapore has implemented identical screening criteria based on our model since earlier this year. The United States has established the FANS programme – Focus on Asian, Non-smoker Study – specifically targeting Asian female populations, reflecting the importance of our findings.

We regularly present outcomes at the World Congress of Lung Cancer, demonstrating how screening programmes can be tailored to non-smoking populations, identifying appropriate screening candidates, and documenting clinical impact.

Shifting toward treatment modalities, how do you evaluate current therapeutic options?

Lung cancer exemplifies precision medicine application. If we identify druggable driver mutations, we can prescribe targeted therapies specifically inhibiting those genetic alterations, achieving substantially high response rates.

We participated in the pioneering IPASS trial, which evaluated EGFR-targeted therapy for lung cancer. Gene testing emerged as the critical foundation enabling precision medicine implementation. I advocated strongly to government authorities to include comprehensive cancer gene testing panels within reimbursement coverage for all lung cancer patients.

Taiwan's national health insurance system – providing coverage for 99% of the population – subsequently began reimbursing genetic testing panels for all lung cancer patients, enabling identification of druggable mutations and targeted therapy prescription. This represented a crucial advancement in democratising access to precision medicine.

You have advocated for government funding of cancer drug access. Can you describe these efforts?

I advocated for establishing a dedicated cancer drug fund to support access to innovative therapeutics. Working through the government's Biotechnology Committee, we pursued initiatives to establish resources supporting novel cancer drug availability. This fund has expanded significantly, with current projections reaching approximately 500 million Taiwan dollars – representing 15 million USD – enabling patient access to emerging therapeutics.

Your research emphasises translational science. Can you describe successful translational research examples emerging from Academia Sinica?

My laboratory has developed multiple therapeutic interventions through translational research. One of the most significant achievements involves developing siRNA therapeutics targeting COVID-19 pathogenesis.

Initially, global efforts concentrated exclusively on vaccination approaches. However, I recognised a fundamental problem: COVID-19 exhibits extremely high mutation frequency, with the spike protein mutating multiple times monthly – sometimes undergoing major alterations. Vaccines targeting the spike protein cannot prevent infection or provide durable immune protection because viral mutations escape antibody binding.

I concluded this approach represented a fundamentally flawed strategy. My team subsequently identified an alternative target – the RNA-dependent RNA polymerase – representing the most conserved viral sequence component, unchanged since SARS-CoV-1 in 2003. We developed siRNA

specifically targeting this sequence, theoretically effective against all coronavirus variants given the genetic sequence's absolute conservation.

We published findings and patents, subsequently completing Phase I and Phase II clinical trials. We established a spinoff company – Diamond Biopharm – to advance this therapeutic development.

How did Diamond Biopharm emerge from your research programme?

Our Academia Sinica research group made significant scientific discoveries, yet we lacked structured pathways supporting start-up company development. Diamond Biopharm was established to provide exemplary support for spinoff startup companies, supplying necessary resources to conduct preclinical studies, research, and extend through Phase I clinical investigations.

I continue advocating through the government Biotechnology Committee to promote investment in biotech company development. Taiwan has experienced remarkable success in information and communications technology collaboration. I advocate for similar integration between technology companies and biotech enterprises – utilising artificial intelligence to augment biotech development, particularly supporting precision medicine applications.

Beyond drug development, I emphasise integrating medical device development and leveraging Taiwan's national health insurance database – with appropriate de-identification – to support artificial intelligence applications in precision medicine.

What is Taiwan's global role in lung cancer research?

Taiwan occupies a critically important position. Over 60% of global lung cancer – approximately 63% in 2022 – occurs in Asia, and 63% of lung cancer mortality occurs in Asia. Therefore, achieving improved global lung cancer control necessitates focused attention on Asian disease patterns.

Our experience demonstrates that lung cancer management must expand beyond advanced-disease precision therapy. We advocate for precision screening methodologies, emphasising regional and local differences. Different countries and regions possess differing resources, requiring customised screening and prevention strategies reflecting local epidemiology.

We have established an exemplary model demonstrating that management involves not merely advanced-disease precision therapy for mature pharmaceutical companies, but also requires precision screening and precision prevention – fundamentally important concepts advancing beyond traditional advanced-disease focus.

Looking forward, what outcomes would you envision for Taiwan's lung cancer fight?

I aspire to disseminate Taiwan's screening model and experience throughout the Asian region, promoting lung cancer screening programme implementation across Asia based on our evidence and strategic approach. Our methodology can improve early detection throughout the region and potentially prevent lung cancer development.

Asia experiences exceptionally high environmental pollution, particularly PM2.5 air pollution. We must address these air quality challenges. Air pollution contributes not only to lung cancer carcinogenesis but also to cardiovascular disease and stroke. Comprehensive environmental health improvement represents an important broader public health imperative.

I am investigating specific air pollution components involved in lung cancer carcinogenesis – an initiative with parallels in British Columbia. Environmental exposure reduction and prevention strategies represent critical complementary approaches alongside screening and early detection.

On a personal level, what motivates your career trajectory?

As a clinician, patients represent my paramount consideration. In daily clinical practice, one encounters patients with advanced disease in late stages. Despite access to excellent contemporary therapies, outcomes frequently remain disappointing and deeply frustrating – even with optimal treatment, many patients do not achieve satisfactory outcomes.

This clinical frustration motivated me to conceptualise comprehensive strategies capable of effectively helping patients. Rather than merely treating advanced disease, I recognised that early diagnosis and ultimately disease prevention represent essential objectives. I progressively advanced from advanced-disease precision medicine toward precision early detection and ultimately precision prevention.

This philosophical trajectory – from treatment optimisation toward prevention – represents the most meaningful clinical contribution I can make toward improving patient outcomes. This

perspective drives my continued commitment to advancing lung cancer management in Taiwan, Asia and globally.

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