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IMPLEMENTING COMPREHENSIVE GENOMIC PROFILING IN SOUTHEAST ASIA: REAL-WORLD FEASIBILITY AND PERFORMANCE ACROSS MULTIPLE CANCER TYPES

Nam HB Tran[1], Thien-Phuc Hoang Nguyen[1], Dao Nhat Anh[1], Khanh PB Le[1], Lan N Tu[1,2]

[1]Medical Genetics Institute, Ho Chi Minh City, Vietnam [2]Gene Solutions, Ho Chi Minh City, Vietnam

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BACKGROUND

Suboptimal DNA quantity and quality of FFPE specimens could reduce the success rate of comprehensive genomic profiling (CGP).

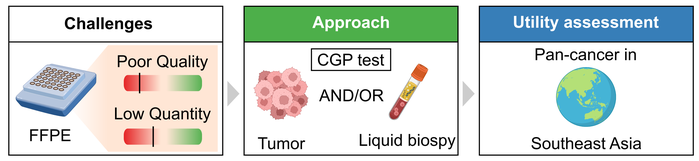
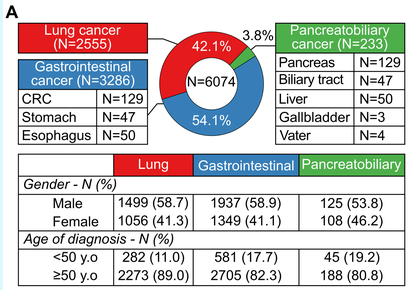


Figure 1. Background. FFPE tissue is readily available in routine clinical practice, but DNA quality and quantity could be insufficient for CGP. **This study evaluated feasibility and performance of tumor CGP combined with liquid biopsy ctDNA profiling in a real-world Southeast Asian cohort.**

TUMOR GENOMIC PROFILING AND LONGITUDINAL ctDNA MONITORING



	Lung	Gastrointestinal	Pancreatobiliary
Gender - N (%)			
Male	1499 (58.7)	1937 (58.9)	125 (53.8)
Female	1056 (41.3)	1349 (41.1)	108 (46.2)
Age of diagnosis - N (%)			
<50 y.o	282 (11.0)	581 (17.7)	45 (19.2)
≥50 y.o	2273 (89.0)	2705 (82.3)	188 (80.8)

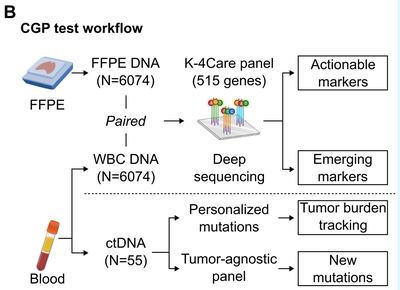


Figure 2. Methods. (A) Archived FFPE tumor samples were collected from 6074 patients with lung, gastrointestinal, or pancreatobiliary cancers. **(B)** Paired tumor and blood gDNA underwent sequencing using a custom 515-gene panel (K-4Care, Gene Solutions) to identify actionable and emerging biomarkers. Longitudinal plasma samples from 55 metastatic lung cancer patients were analyzed using a hybrid tumor-informed & tumor-agnostic approach to profile additional actionable mutations and monitor ctDNA-MRD.

Ethical approval: FFPE-derived biomarker analysis (03/2024/CT-VDTYH) and the real-world ctDNA monitoring study (03/2023/CT-VDTYH)

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Conflict of Interest: L. Tu is a current employees of Gene Solutions, Vietnam. The remaining authors declare no conflict of interest

Contact information: lantu@genesolutions.vn

FFPE CGP achieved high success rate of >80%

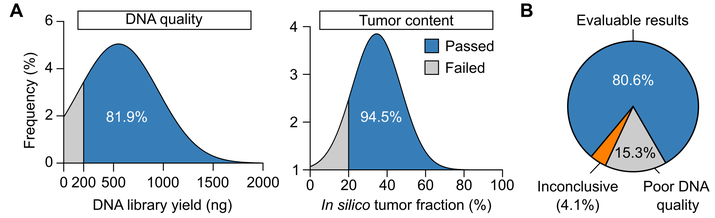


Figure 3. FFPE DNA quality. (A) Distribution of DNA library yield (left) and in silico tumor fraction (right) in archived FFPE tumor samples; blue areas indicate samples passing QC thresholds. **(B)** Pie chart showing proportions of samples having satisfactory CGP results, inconclusive results or failure due to poor DNA quality.

FFPE actionable biomarkers identified in >40% of patients

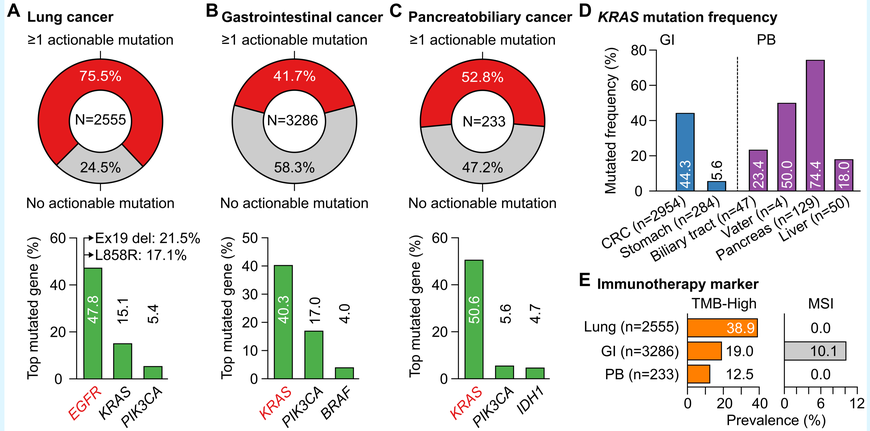


Figure 4. Actionable alterations and immunotherapy biomarkers across multiple cancer types. Proportion of patients with at least one actionable mutation (red) and the most frequently mutated actionable genes in **(A)** lung, **(B)** gastrointestinal (GI), and **(C)** pancreatobiliary (PB) cancers. In **(A)**, the two most common *EGFR* mutation subtypes, exon 19 deletion and L858R, are indicated. **(D)** *KRAS* mutation frequency by GI and PB cancers; subtypes with no detected *KRAS* mutations are not shown. **(E)** Prevalence of immunotherapy-relevant biomarkers, tumor mutational burden - high (TMB-high) and microsatellite instability (MSI), by cancer type.

FFPE emerging biomarker *MTAP–CDKN2A* co-deletion detected in >20% of lung and pancreatobiliary cancers

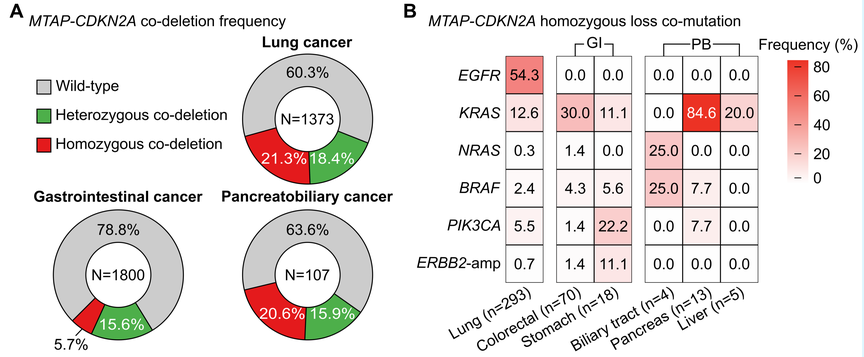


Figure 5. Frequency of *MTAP-CDKN2A* co-deletion across cancer types. (A) Frequency of *MTAP-CDKN2A* co-deletion status in lung, gastrointestinal (GI), and pancreatobiliary (PB) samples. **(B)** Co-mutation frequencies of actionable alterations among homozygous M*TAP-CDKN2A* co-deletion cases, by cancer type.

Liquid biopsy profiling detected additional tumor-agnostic mutations & predicted disease progression early

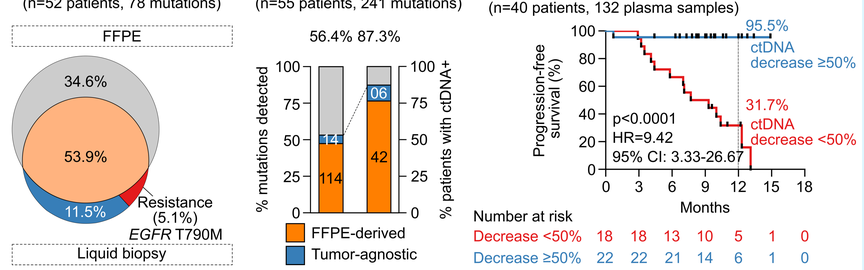


Figure 6. Plasma ctDNA monitoring to detect tumor-agnostic mutations and predict disease progression. (A) Overlap between FFPE- and liquid biopsy-derived actionable mutations, including resistance mutations. **(B)** Plasma detection of 241 monitored mutations and pretreatment ctDNA positivity in 55 patients. **(C)** Progression-free survival by ≥50% versus <50% ctDNA reduction from baseline in 40 patients.

CONCLUSION: Combining tissue-based CGP with plasma ctDNA profiling was both feasible and clinically valuable to maximize biomarker identification and enable treatment response monitoring