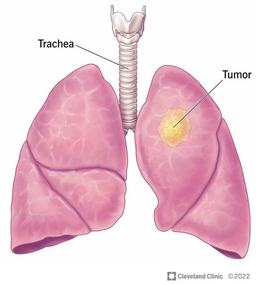
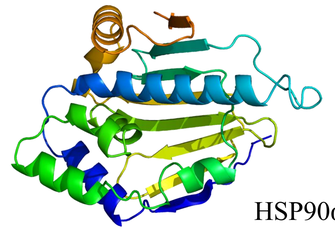
Systematic Validation of Using HSP90α as a Lung Cancer Diagnostic Biomarker for Enhanced Clinical Screening

Chase Zhou



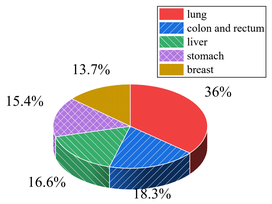
Lung cancer



HSP90α

Background

Lung cancer is responsible for over 2 million deaths every year, largely because 84% of patients receive medical treatment late. Current methods of diagnosis such as biopsies are inaccurate and very costly. Biomarkers offer a more cost-efficient and accurate solution. Heat Shock Proteins (HSPs) are chaperones that ensure correct folding. HSPs are frequently overexpressed in tumor cells to help them survive environmental stress. Because HSPs correlate with drug resistance, metastasis, and poor patient survival, they can serve as valuable biomarkers for diagnosis. However, limited studies have been done to synthesize its accuracy in lung cancer diagnosis.



Top 5 Deadliest types of Cancer

Graph created using Excel with data from World Health Organization

Objective

The goal of this study was to perform a systematic analysis to evaluate the diagnostic performance and clinical utility of HSP90α as a biomarker for detecting lung cancer.

Materials and Methods

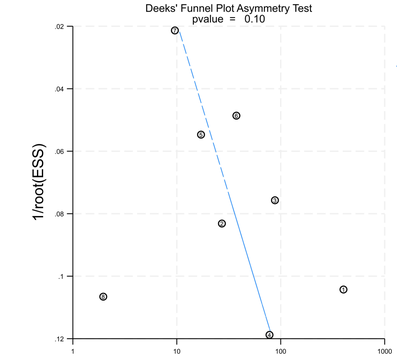
Literature on HSP90α and lung cancer was found using PubMed and PROSPERO, and 8 studies out of 632 papers and 2 registers were selected for this study. Information on 3,624 patients (2,080 lung cancer patients and 1,544 healthy controls) was analyzed.

	Healthy control	Cancer patient
High HSP90α	False Positive (FP)	True Positive (TP)
Low HSP90α	True Negative (TN)	False Negative (FN)

Specificity = $\frac{TN}{FP+TN}$ Sensitivity = $\frac{TP}{TP+FN}$

Results

Flow chart of included and excluded studies



Information on Patients in Included Studies

HSP90α Cut-off value (ng/mL)	Number of cancer patients	Number of Healthy Controls	Total number of patients	Sensitivity	Specificity	Reference
49.8	45	45	90	82.2%	100.0%	(Jain et al., 2025)
101.8	76	69	145	55.3%	95.2%	(Wang et al., 2022)
114.8	92	83	175	68.5%	97.3%	(Wang et al., 2022)
103.0	37	34	71	70.3%	96.0%	(Wang et al., 2022)
50.0	175	160	335	88.1%	69.7%	(Yuan et al., 2022)
71.5	312	160	472	66.3%	95.0%	(Wang et al., 2021)
56.3	1,294	953	2,247	72.2%	78.7%	(Shi et al., 2014)
NA	49	40	89	59.0%	58.0%	(Zhong et al., 2003)

Summary data and performance estimates

- Number of studies = 8
- ROC Area, AUROC = 0.84 [0.80 - 0.87]
- Heterogeneity (Chi-square): LRT_Q = 97.894, df =2.00, LRT_p =0.000
- Inconsistency (I-square): LRT_I2 = 98, 95% CI = [97- 99]

Parameter	Estimate	95% CI
Sensitivity	0.71	[0.63, 0.78]
Specificity	0.92	[0.80, 0.97]
Positive Likelihood Ratio	9.3	[3.4, 25.3]
Negative Likelihood Ratio	0.31	[0.24, 0.41]
Diagnostic Odds Ratio	30	[10, 91]

Fagan's Nomogram

Assuming pretest probability = 20%;
Positive = 70% likelihood, Neg = 7% likelihood

Graph created by finalist using STATA software

Deeks' Funnel Plot

The diagnostic accuracy of HSP90α is consistent across studies of varying power.

Graph created by finalist using STATA software

AUROC Curve

Negative correlation between sensitivity and specificity of using HSP90α as an effective biomarker for lung cancer diagnosis; AUROC curve = 0.84

Graph created by finalist using STATA software

Conclusions

- Analysis of 3,624 patients with high accuracy **establish HSP90α as a robust, scalable biomarker for cancer screening and clinical monitoring**.
- Despite varying clinical cut-off values (49.8 to 114.8 ng/mL), diagnostic performance remained statistically stable ($p>0.05$), showing HSP90α is a widely applicable biomarker.
- Fagan's Nomogram reveals that a positive test result dramatically increases the probability of disease by 50%, and can be used to strengthen clinical decision-making.
- Extremely efficient AUROC Curve of 0.84, showing HSP90α can properly distinguish between cancerous and non-cancerous patients 84% of the time.
- Substantially more cost-efficient and non-invasive diagnostic tool compared to current treatment options such as biopsies.

References

Ahn et al. (2025) *Front Pharmacol* **16**: 1522285; Board of Governors of the Federal Reserve System (2025); Capan et al. (2025) *Drug Dev Res* **86**(3): e70092; Chiu et al. (2021) *Clinicoecon Outcomes Res* **13**: 191–200; Ciocca et al. (2005) *Cell Stress Chaperones* **10**(2): 86–103; Cyran et al. (2022) Front Oncol **12**: 860320; Dwamena, B. (2007) *Statistical Software Components*; Guo et al. (2021) Oncol Lett **22**(2): 630; Hu et al. (2022) MedComm **3**(3): e161; Jain et al. (2025) Asian Pac J Cancer Prev **26**(10): 3797–3803; Kabut et al. (2025). Cells **14**(20); Liu et al. (2024). Discov Oncol **15**(1): 151; Mazurakova et al. (2023). Adv Med Sci **68**(2): 464–473; Nakamura et al. (2024). World J Gastrointest Oncol **16**(4): 1578–1595; Page et al. (2021) BMJ **372**: n71; Pockley (2003) The Lancet **362**(9382): 469–476; Shi et al. (2014) Clin Cancer Res **20**(23): 6016–6022; Tustumi et al. (2022) Cells **11**(17); Wang et al. (2022). Turk J Med Sci **52**(3): 747–753; Wang et al. (2021) Oncol Res Treat **44**(11): 583–589; World Health Organization (2025); Yuan et al. (2022) J Clin Lab Anal **36**(6): e24462; Zhang et al. (2020) Lung Cancer Manag **9**(4): Lmt40; Zhong et al. (2003) Cancer Detect Prev **27**(4): 285–290; Zuo et al. (2024). *J Hematol Oncol* **17**(1): 81.