

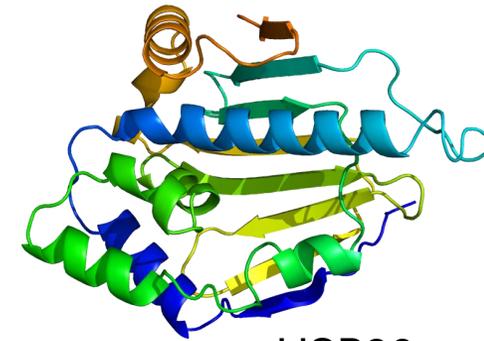
Systematic Validation of Using HSP90 α as a Lung Cancer Diagnostic Biomarker for Enhanced Clinical Screening

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Heat shock proteins (HSPs)

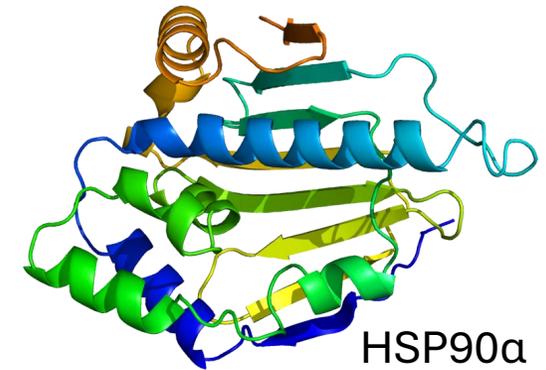
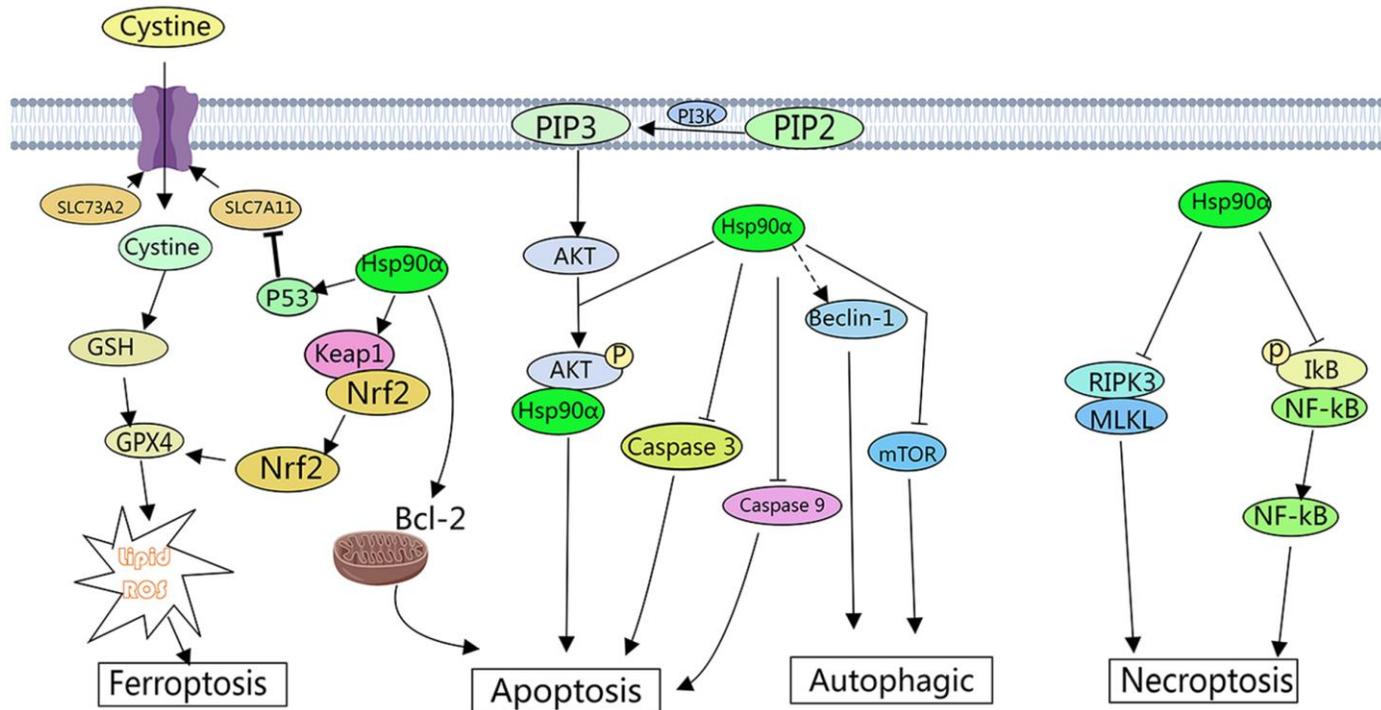
Type	Subtype
small HSPs	α B-crystallin, HSP27, HSP32
HSP40	HSP40, HSP47
HSP60	HSP60, TCP-1
HSP70	HSP70, HSP70hom, HSC70, Grp78/BiP, mtHSP70/Grp75
HSP90	HSP90 α , HSP90 β , Grp94/gp96/HSP100
HSP110	HSP110, Apg-1, HSP105



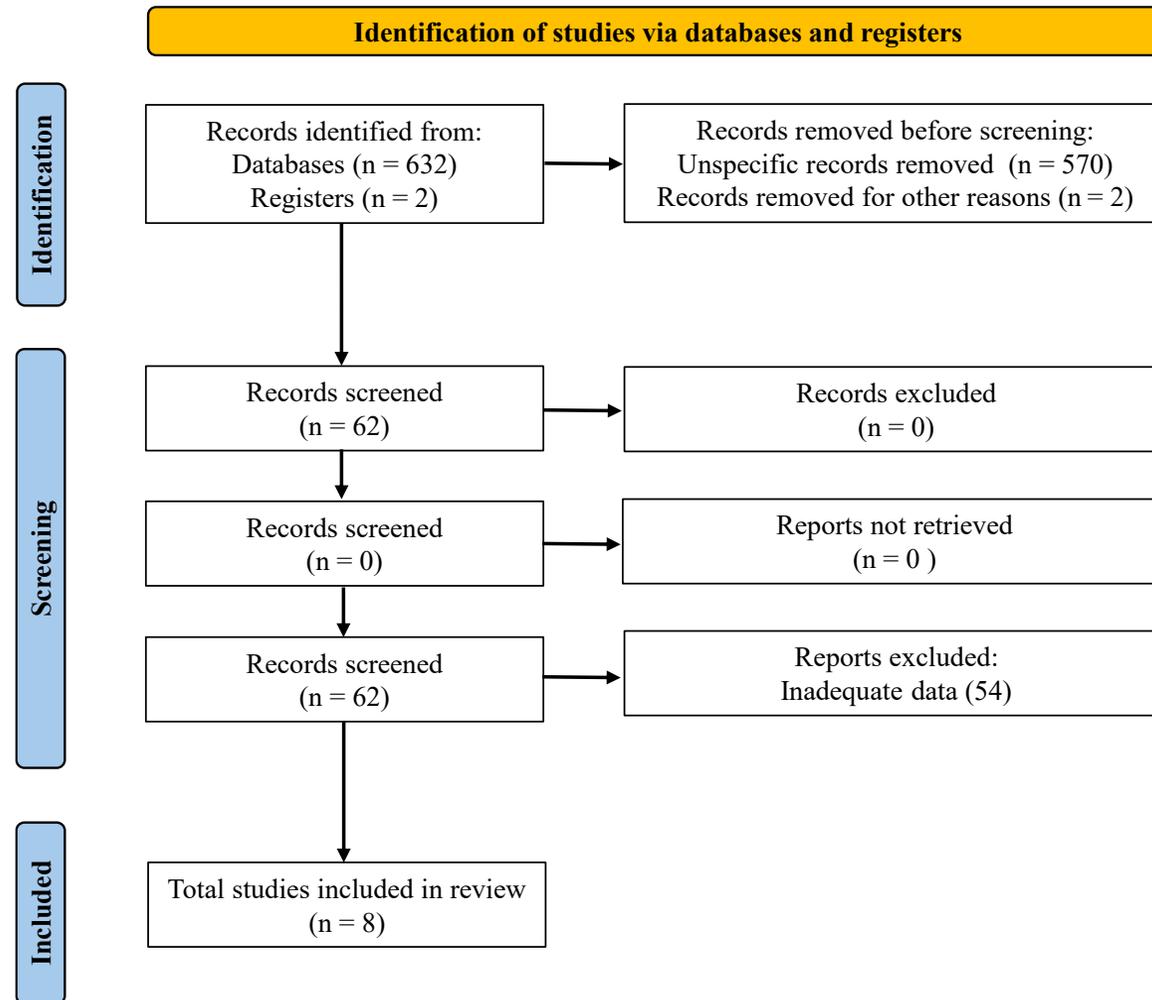
HSP90 α

- help proteins fold correctly and protect cells from stressful conditions
- Hsp90 α is involved in many different cell death pathways and may be used as a biomarker

Hsp90 α is involved in many different cell death pathways and may be used as a biomarker



632 papers were screen and 8 studies were identified for further analysis



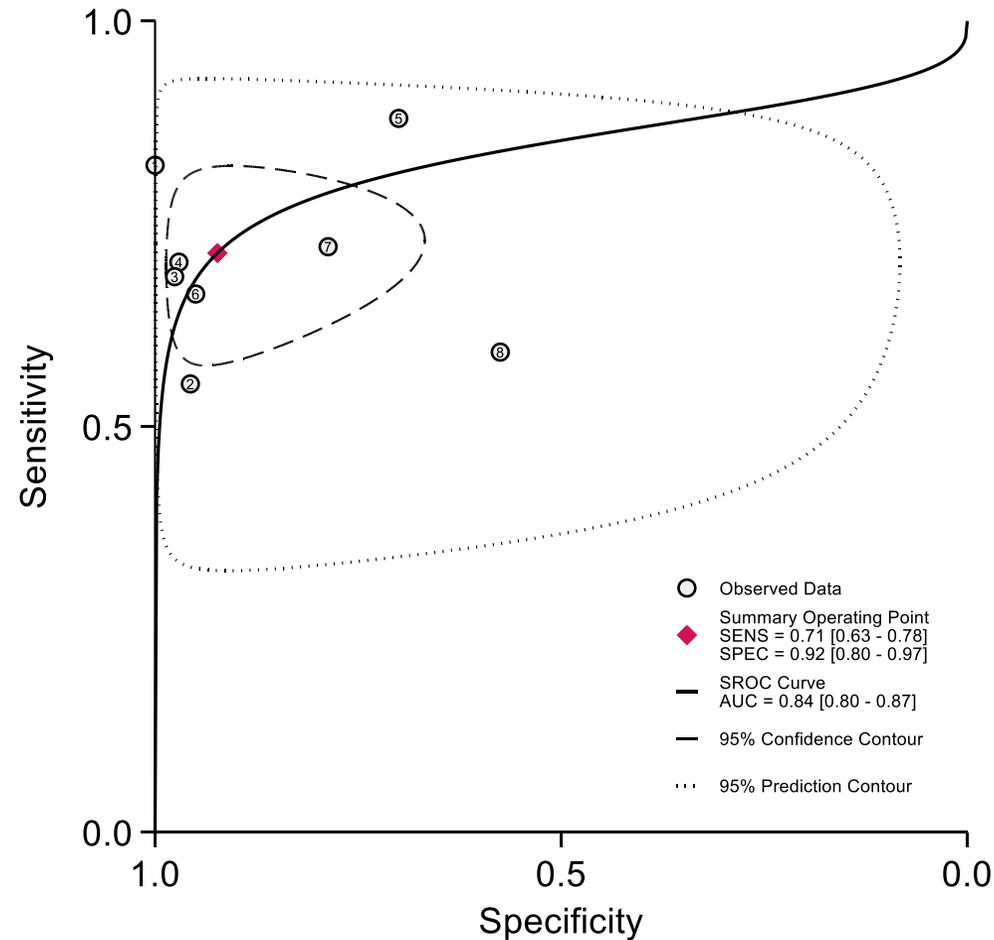
3,624 patients (2,080 lung cancer patients and 1,544 healthy controls) were selected for this study

HSP90 α 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)

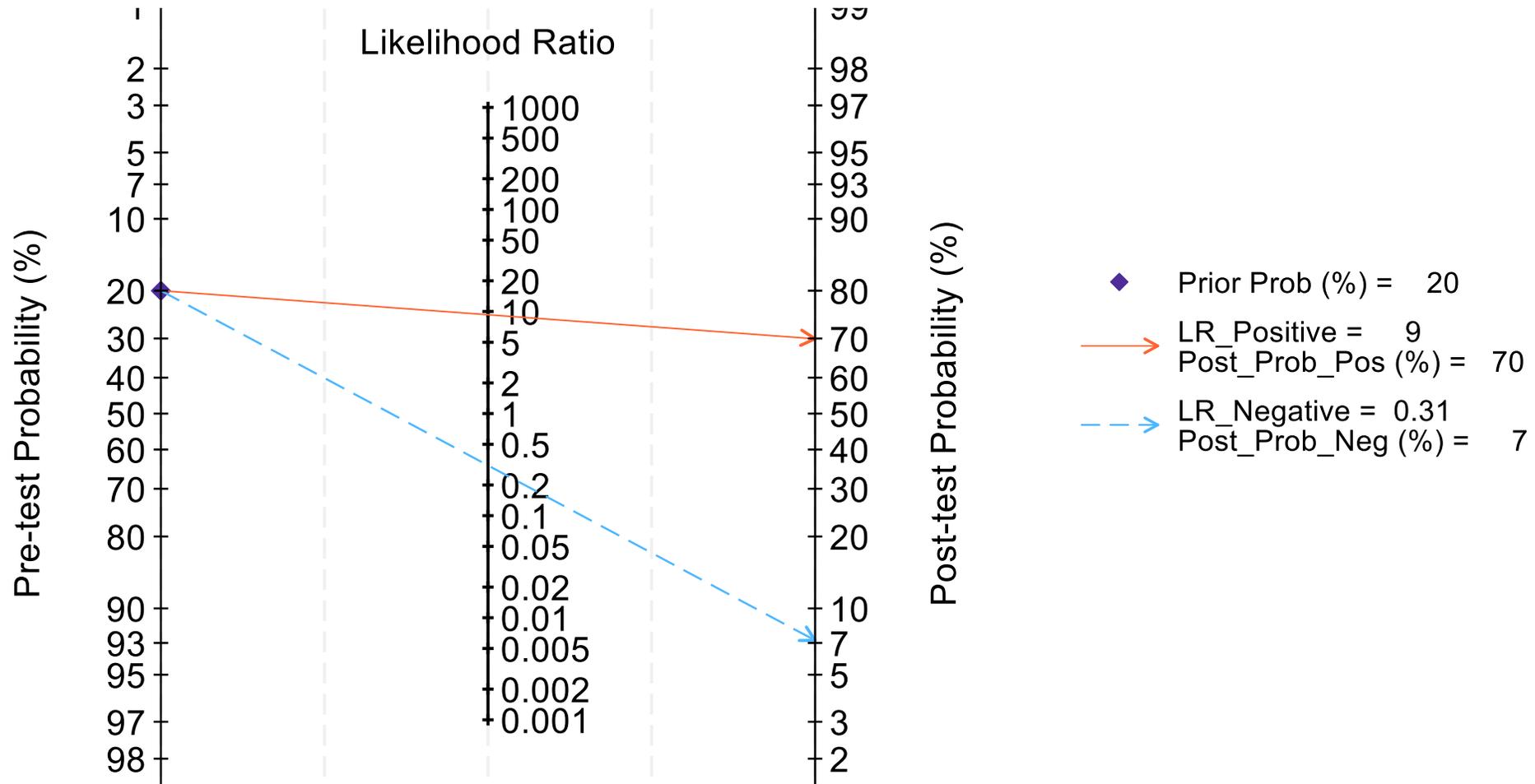
Summary data and performance estimates

- 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]

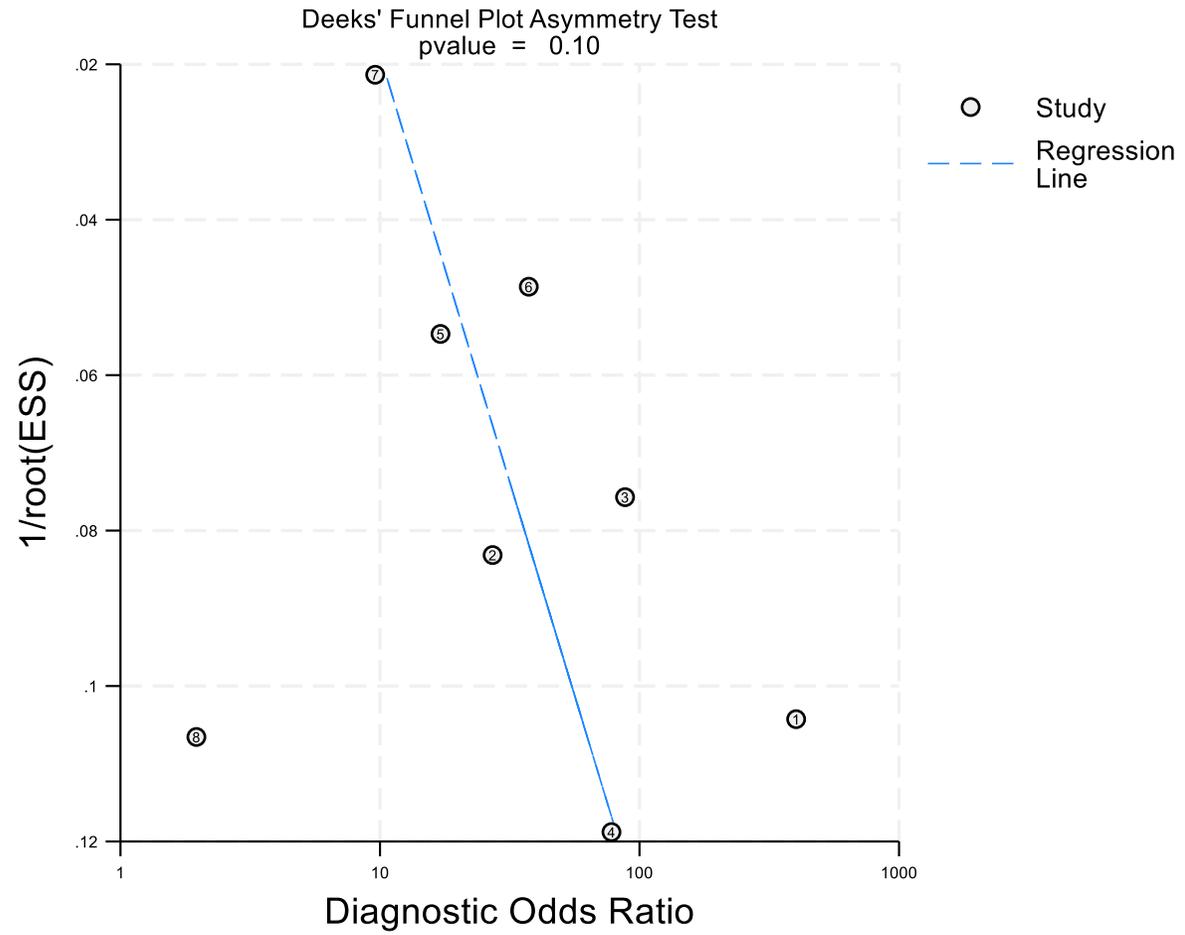
SROC curve shows HSP90 α is highly reliable and precise to detect lung cancer patients



Clinical utility test shows HSP90α has a good clinical power



There is no statistically significant evidence of publication bias in the current dataset



Conclusion

- Analysis of 3,624 patients with high accuracy **establish HSP90 α as a robust, scalable biomarker for cancer screening and clinical monitoring.**
- Despite varying clinical cut-off values (49.8 to 114.8 ng/mL) in different projects, diagnostic performance remained statistically stable ($p > 0.05$), showing HSP90 α is a stable biomarker.
- Fagan's Nomogram reveals that a positive test result of HSP90 α dramatically increases the probability of disease from an assumed 20% to 70% and can be used as an important parameter to support clinical decision-making.
- Extremely efficient AUROC Curve of 0.84, showing HSP90 α can properly distinguish between cancerous and non-cancerous patients 84% of the time
- Substantially more cost-efficient compared to current treatment options such as biopsies