

Reversible smoking-dependent hPG₈₀ increase, a path to identifying NSCLC-negative individuals: an incentive to quit smoking?

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Background/Goal of the study

Minimally invasive method for **early detection of lung cancer** is an urgent need to improve patients' survival.

hPG₈₀ (circulating progastrin) has been previously described as a promising **multi-tumor blood biomarker** (You et al. Biomarker Research, 2025). hPG₈₀ is produced and released from cancer cells and can be detected in the blood at early steps of tumorigenesis.

In this study, we assess **hPG₈₀ levels in asymptomatic individuals** and in **non-small cell lung carcinoma (NSCLC)** patients, categorized by their smoking and chronic obstructive pulmonary disease (COPD) status.

Methods

Plasma hPG₈₀ levels were measured using the DxPG80.Lab kit (Biodena care, Grabels, France) across 5 cohorts:

(1) EDTA plasma samples were obtained from the Nice Hospital Biobank (BB-0033-00025; Nice, France) and included **396 treatment-naïve NSCLC patients** (collected at diagnosis) and **200 COPD patients**, with collection dates ranging from 2007 to 2022.

(2) EDTA plasma samples were prospectively collected from **369 never smokers**, **278 current smokers**, and **235 former smokers**, all asymptomatic, between April 2024 and March 2025.

ROC curves were used to evaluate the **diagnostic performance** of hPG₈₀ using the area under the curve (AUC).

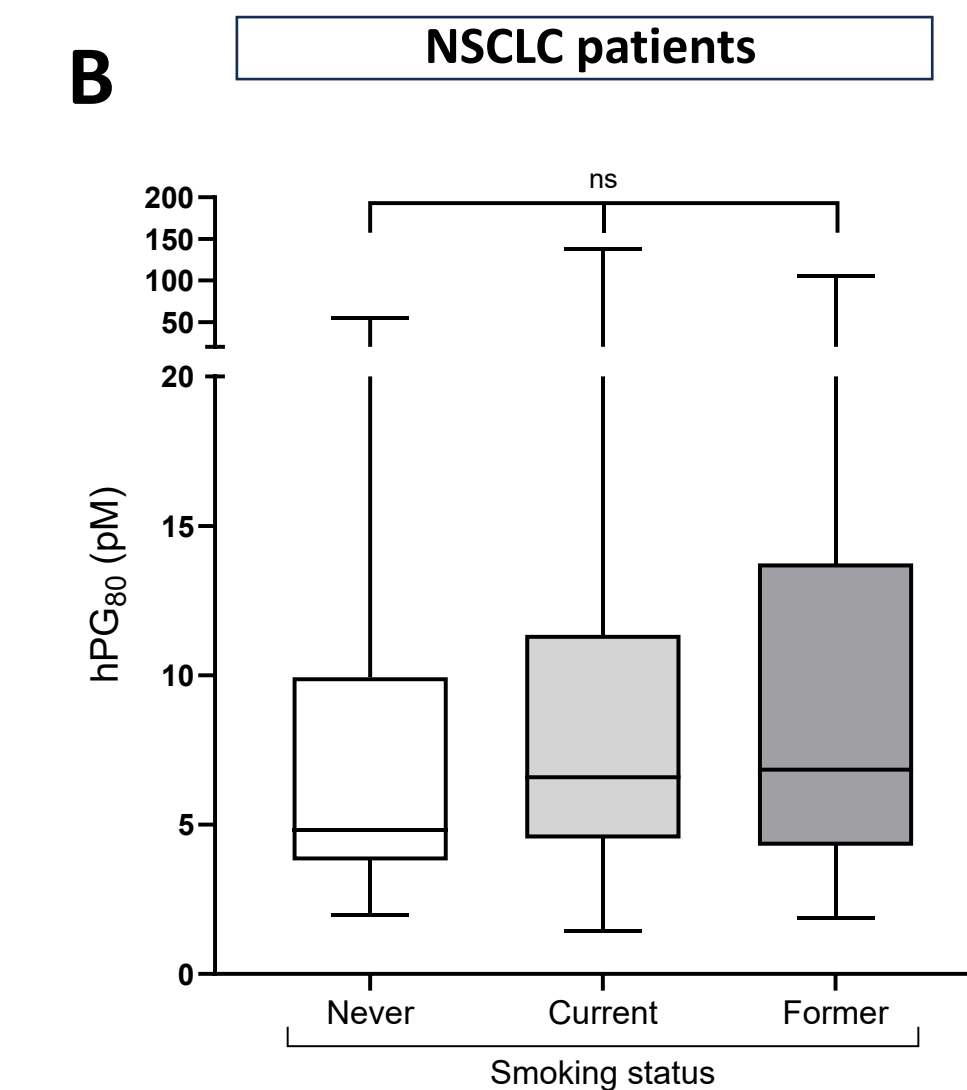
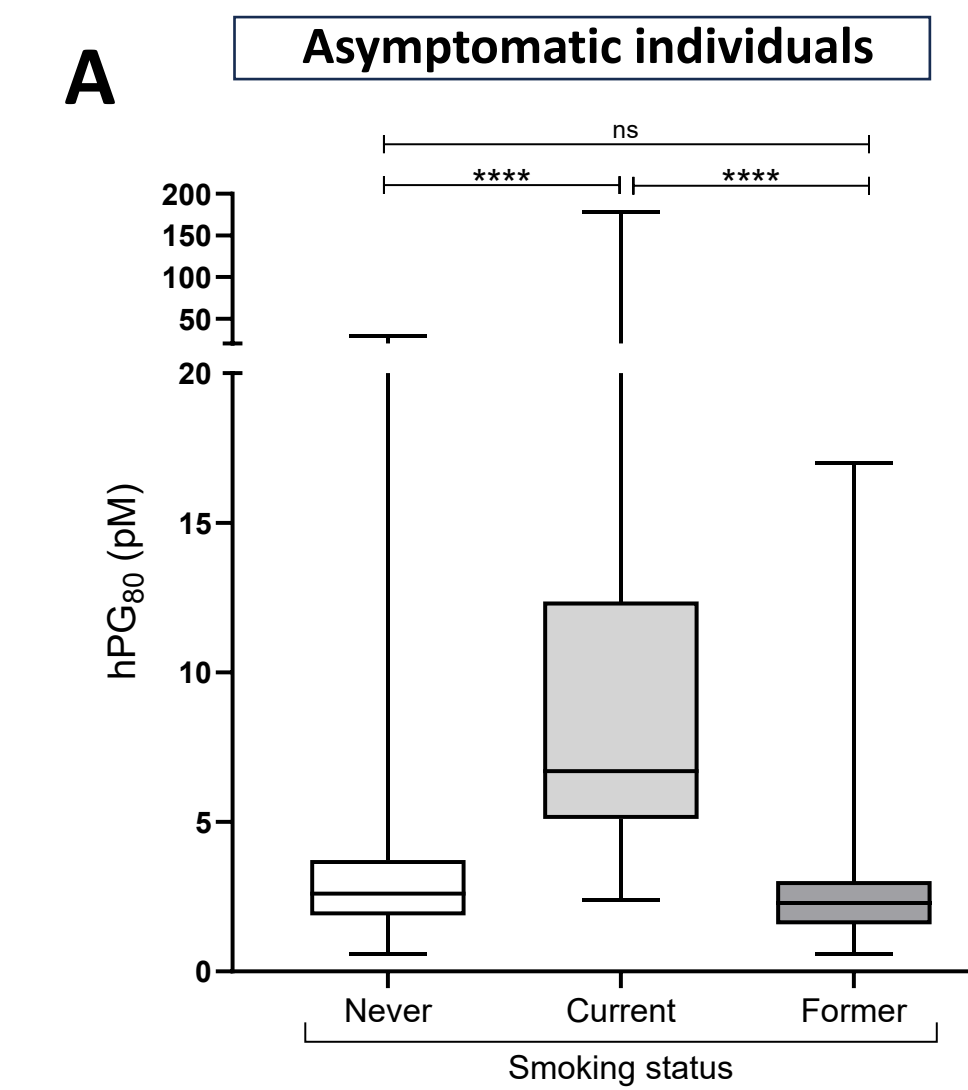
Clinical characteristics

	NSCLC		COPD		Never smokers	Current smokers	Former smokers	p-value
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)		
No. of patients/individuals	396	200	369	278	235			
Age								
Median (range), years	68 (41-94)	65 (60-69)	63 (22-92)	45 (18-80)	68 (21-93)			<0.0001
Gender								
Male	254 (64.1%)	147 (73.5%)	128 (34.7%)	133 (47.8%)	149 (63.4%)			
Female	142 (35.9%)	53 (26.5%)	241 (65.3%)	145 (52.2%)	86 (36.6%)			<0.0001
Smoking history								
Never	40 (10.1%)	-	369 (100%)	-	-			
Current	224 (56.6%)	27 (13.5%)	-	278 (100%)	-			
Former	127 (32.1%)	18 (9.0%)	-	-	235 (100%)			
Unknown	5 (1.3%)	155 (77.5%)	-	-	-			
Pack-years (mean, SD)	44.7 (18.9)	-	NA	12.6 (17.2)	-			<0.0001
Cancer stage								
I	100 (25.25%)	-						
II	100 (25.25%)	-						
III	97 (24.5%)	-						
IV	99 (25.0%)	-						
NSCLC subtype								
Adnocarcinoma (LADC)	234 (59.1%)	-						
Squamous (LSCC)	135 (34.1%)	-						
Large cell (LLCC)	17 (4.3%)	-						
Other	11 (2.8%)	-						
GOLD stage								
GOLD1	-	50 (25.0%)						
GOLD2	-	76 (38.0%)						
GOLD3	-	63 (31.5%)						
GOLD4	-	11 (5.5%)						

hPG₈₀ levels in asymptomatic individuals and NSCLC patients

	n	Age, median (IQR), years	hPG ₈₀ , median (IQR), pM	p-value
Asymptomatic individuals				
All				\$0.0004
Never	369	63.00 (45.00-73.00)	2.90 (2.00-4.25)	s
Current	278	45.00 (30.75-57.00)	5.51 (3.97-8.00)	
Former	235	68.00 (57.00-75.00)	2.40 (1.60-3.40)	
Age-matched never, current and former				<0.0001
Never	110	58.50 (48.00-66.25)	2.29 (1.61-2.97)	s
Current	110	58.00 (48.75-66.00)	6.70 (5.13-11.29)	
Former	110	58.50 (48.00-67.00)	2.50 (1.70-3.70)	
NSCLC				
All	396	68.00 (60.00-73.00)	6.52 (4.31-12.04)	0.2011
Never	40	74.00 (67.25-79.00)	4.83 (3.80-9.94)	s
Current	127	70.00 (64.00-74.00)	6.84 (4.30-13.74)	
Former	224	65.00 (57.25-71.00)	6.59 (4.54-11.36)	
Age-matched never asymptomatic smokers and all NSCLC				<0.0001
Never asymptomatic	289	67.00 (57.00-74.50)	3.20 (2.20-4.80)	s
NSCLC	289	66.00 (58.00-73.00)	6.11 (4.11-11.22)	
Age-matched never smoker				0.0019
Asymptomatic	39	73.00 (67.00-79.00)	3.73 (2.36-5.06)	s
NSCLC	39	74.00 (67.00-79.00)	4.82 (3.79-9.95)	
Age-matched current smoker				0.4442
Asymptomatic	113	59.00 (54.00-66.00)	7.00 (5.10-12.20)	s
NSCLC	113	59.00 (54.00-66.00)	6.60 (4.36-11.22)	
Age-matched former smoker				<0.0001
Asymptomatic	127	70.00 (65.00-74.00)	2.40 (1.81-3.65)	s
NSCLC	127	70.00 (64.00-74.00)	6.84 (4.30-13.74)	
COPD				0.1088
Yes	32	70.00 (62.50-74.75)	7.46 (5.71-14.48)	s
No	364	68.00 (60.00-73.00)	6.41 (4.19-11.91)	
COPD				
All	200	64.50 (60.00-69.00)	6.07 (3.99-11.69)	0.3283
Current	27	65.00 (60.00-67.00)	9.03 (6.34-1.60)	s
Former	18	64.50 (59.50-72.25)	6.18 (4.44-21.35)	
Age-matched never asymptomatic smokers and all COPD				<0.0001
Never asymptomatic	145	67.00 (62.00-70.50)	3.30 (2.40-5.05)	s
COPD	145	67.00 (62.00-70.50)	6.35 (4.10-13.31)	

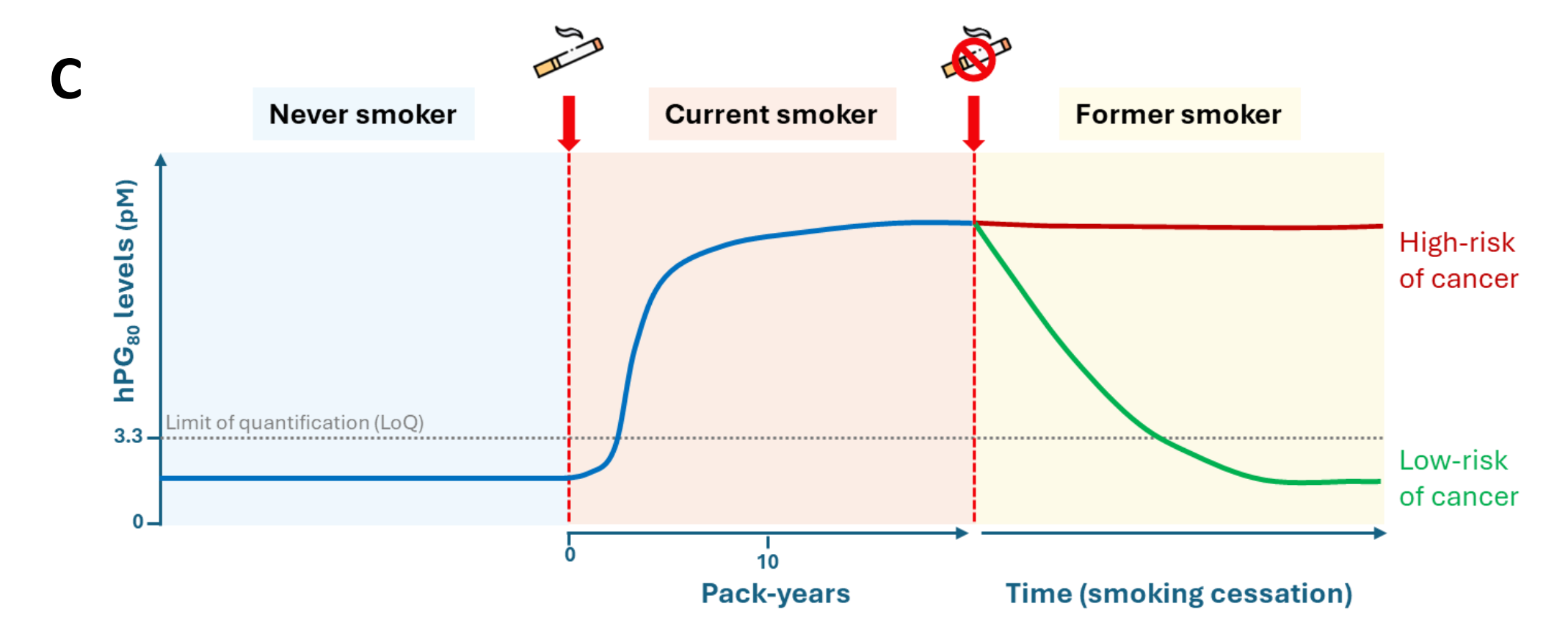
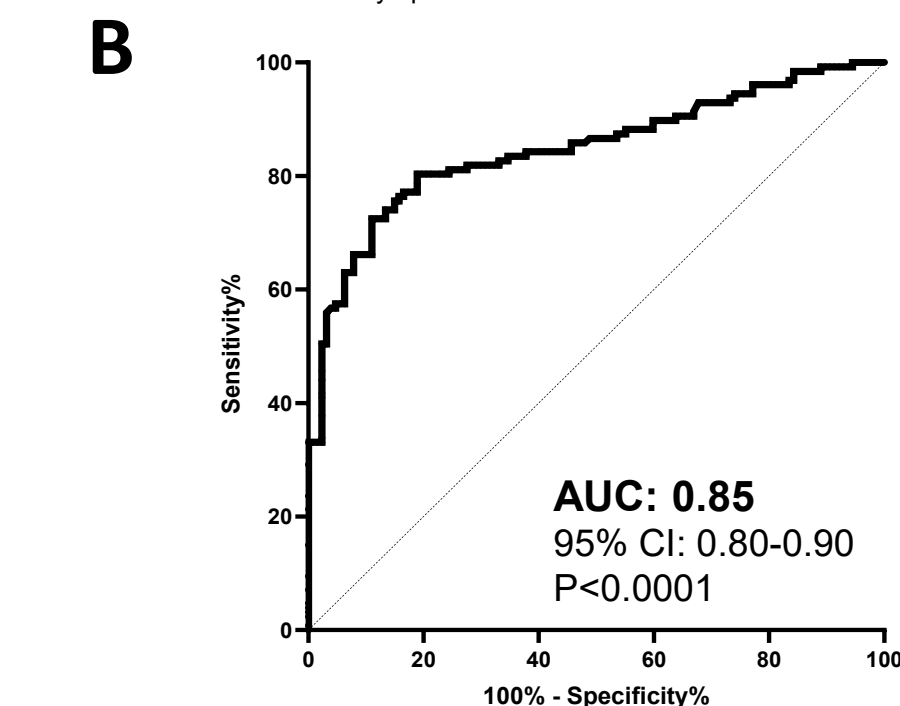
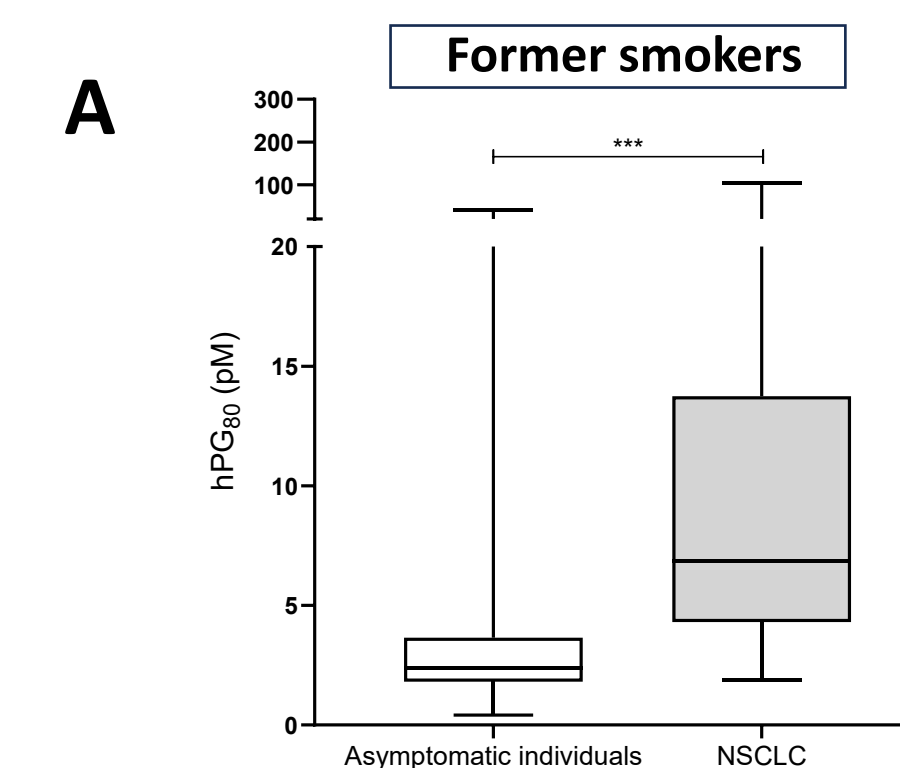
hPG₈₀ levels in asymptomatic individuals and NSCLC patients stratified by smoking status



(A) Comparison of hPG₈₀ levels in age-matched asymptomatic never-, current- and former smokers (n=110 each cohort). In current smokers, hPG₈₀ levels were significantly higher than those in age-matched never smokers (6.70 pM vs 2.29 pM, P<0.0001).

(B) Comparison of hPG₈₀ levels in NSCLC patients stratified by smoking status: never (n=40), former (n=127) and current (n=224). No significant differences were observed according to the smoking status: 4.83 pM, 6.84 pM and 6.59 pM (in never, former and current smokers, respectively).

hPG₈₀ diagnostic performance in former smoker NSCLC and potential use for cancer risk stratification



Comparison of hPG₈₀ levels between former smoker NSCLC patients and their respective age-matched asymptomatic controls (n=127). (A) Median hPG₈₀ concentration was significantly higher in former smoker NSCLC patients than in former smoker asymptomatic individuals (6.84 pM vs 2.40 pM, P<0.0001). (B) ROC curve analysis in the former smoker NSCLC cohort (vs former smoker asymptomatic donors) yielded an AUC of 0.85. (C) This figure illustrates a potential association between hPG₈₀ levels and the risk of developing cancer in individuals who have quit smoking.

Conclusions: hPG₈₀ is a promising, accurate and non-invasive blood biomarker to help stratify non-COPD former smokers based on lung cancer risk.