Elevated expression of placental growth factor is associated with airway-wall vascular remodelling and thickening in smokers with asthma

Dong Wu<sup>1,#</sup>, Tianwen Lai<sup>1,#</sup>, Yalian Yuan<sup>1,#</sup>, Min Chen<sup>1</sup>, Jun Xia<sup>2</sup>, Wen Li<sup>1</sup>, Guihai Pan<sup>2</sup>, Binfan Yuan<sup>1</sup>, Quanchao Lv<sup>1</sup>, Yanyu Li<sup>1</sup>, Dongmin Li<sup>1,\*</sup>, Bin Wu<sup>1,\*</sup>

<sup>1</sup> Institute of Respiratory Diseases, Department of Respiratory, The Affiliated Hospital of Guangdong Medical University, Zhanjiang 524001, China

<sup>2</sup> Department of Radiology, The Affiliated Hospital of Guangdong Medical University, Zhanjiang 524001, China

\*To whom correspondence should be addressed:

Prof Bin Wu

Institute of Respiratory, The Affiliated Hospital of Guangdong Medical University,

Zhanjiang 524001, China Tel: +86-07592386792 E-mail: wubin1190@126.com

Prof Dongmin Li

Department of Respiratory, The Affiliated Hospital of Guangdong Medical University,

Zhanjiang 524001, China Tel: +86-07592386792 E-mail: 3064264@qq.com

<sup>#</sup>These authors contributed equally to this work.

Supplemental Table 1. Association between serum, induced sputum PIGF levels and lung function in four groups.

	Groups	Pre-bronchodilator FEV <sub>1</sub> % pred	Post-bronchodilator FEV1% pred	Post-bronchodilator FEV1/FVC	DLCO% pred	FeNO <sub>50</sub>
serum PIGF levels	Smoking asthmatics	0.162 (-0.1840.494)	-0.735 (0.065–0.599)*	-0.139 (0.070-0.626)*	0.089 (-0.279–0.463)	0.168
	Non-smoking asthmatics	0.217	0.231 (-0.081–0.534)	0.181 (-0.134–0.465)	-0.098 (-0.398–0.229)	0.179 (-0.159-0.439)
	Smoking healthy control	0.284				-0.228 (-0.591–0.124)
	Non-smoking healthy control	0.201 (-0.103–0.567)				-0.255 (-0.567–0.421)

induced sputum	Smoking asthmatics	0.225	-0.568 (0.008-0.587)#		0.189	-0.172
PIGF		(-0.064–0.515)			(-0.159-0.503)	(-0.517–0.209)
levels	Non-smoking	0.151	0.173	0.113	-0.356	0.065
	asthmatics	(-0.179-0.451)	(-0.159-0.465)	(-0.184-0.413)	(-0.6350.138)	(-0.284-0.367)
	Smoking	0.131				-0.041
	healthy control	(-0.169-0.434)				(-0.357–0.279)
	Non-smoking healthy control	0.103				0.185
	ricalary control	(-0.249-0.425)				(-0.159-0.506)

\*Indicate significant associations for serum PIGF level. #Indicate significant associations for induced sputum PIGF level. FEV1: forced expiratory volume in 1s; FVC: forced vital capacity;  $D_{LCO}$ % pred COHb: diffusing capacity of the lung for carbonmonoxide corrected for haemoglobin and carboxyhaemoglobin, as a percentage of the predicted value;  $FeNO_{50}$ : exhaled nitric oxide fraction measured at a flow rate of 50 mL·s<sup>-1</sup>.

Supplemental Table 2. Association between serum, induced sputum PIGF levels and computed tomography RB10 airway dimensions in asthmatics

	Groups	RB10 %	RB10 wall	RB10 lumen
		wall area	thickness	area
serum PIGF	Smoking	0.069	0.545	-0.038
levels	asthmatics	(-0.254–0.383)	(0.102–0.668)*	(-0.364–0.312)
	Non-smoking	0.034	0.081	0.213
	asthmatics	(-0.276–0.415)	(-0.263–0.387)	(-0.067–0.551)
induced sputum	Smoking	0.076	0.571	0.169
PIGF levels	asthmatics	(-0.317–0.420)	(0.189–0.728)#	(-0.153–0.438)
	Non-smoking asthmatics	0.081	0.138	0.096
		(-0.243–0.444)	(-0.249–0.431)	(-0.253–0.432)

\*Indicate significant associations for serum PIGF level. \*Indicate significant associations for induced sputum PIGF level.; RB10: right bronchial division 10.