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Serum periostin levels in adults of Chinese descent: an observational study

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Abstract

Background: Periostin has been shown to be a marker of Type 2 airway inflammation, associated with airway eosinophilia. It has a potential role in identifying asthmatics who may be responsive to treatment with monoclonal antibody therapy directed against Type 2 cytokines, such as interleukin (IL)-13, IL-4 receptor subunit- α and immunoglobulin E. The clinical utility of periostin measurements depends on better understanding of factors that may affect serum periostin levels, such as race. We aimed to identify the ranges of serum periostin in Chinese adults both with and without asthma, and compare them with those previously identified in Caucasian adults.

Methods: A two-centred cross-sectional study, recruiting 188 Chinese adults, aged 18 to 75 years. 120 participants had no history of asthma or chronic obstructive pulmonary disease. 68 participants had a doctor's diagnosis of asthma and were on current treatment. Univariate comparisons of periostin by dichotomous variables were made using t-tests with logarithmic transformation as the distribution of periostin was skewed.

Results: In the Chinese non-asthma group, periostin levels were sex-, but not age-dependent, with females having higher periostin levels. The individual predicted (90% CI) reference range for periostin in females was 61.1 ng/ml (41.6 to 89.8) ng/ml and in males was 53.2 ng/ml (36.1 to 78.3) ng/ml. There was no difference in median serum periostin levels between Chinese non-asthmatics and Chinese asthmatics, 57.0 versus 56.8 ng/ml, difference (95% CI) 0.1 (−4.2 to 4.2) ng/ml, $P = 0.94$. The median serum periostin levels were higher in Chinese non-asthmatics than Caucasian non-asthmatics, 57.0 versus 49.7 ng/ml, difference (95% CI) 8.2 (5.8–10.6) ng/ml, $P < 0.001$.

Conclusions: Serum periostin does not discriminate between asthmatics and non-asthmatics and is therefore not a good biomarker to diagnose asthma. Serum periostin levels were higher in the Chinese compared to the Caucasian non-asthma group, and also sex dependent in the Chinese participants. There was no difference in serum periostin levels between Chinese non-asthma and asthma groups. This suggests that ethnicity should be considered in the interpretation of periostin levels in asthma patients and sex is an additional consideration in Chinese patients.

Trial registration This trial was prospectively registered with Australian New Zealand Clinical Trials Registry (ACTRN12614000122651)

Keywords: Adult, Asthma, Biomarkers, Chinese, Periostin

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31 Background

32 Periostin, a matricellular protein, has been shown
33 to be a marker of Type 2 inflammation associated
34 with airway eosinophilia [1, 2]. It has a potential role
35 in identifying asthmatics who may be responsive to
36 treatment with monoclonal antibody therapy directed
37 against Type 2 cytokines, such as interleukin (IL)-
38 13 [3, 4], IL-4 receptor subunit- α (IL-4R α) [5] and
39 immunoglobulin E (IgE) [6], and may have a role in
40 helping define asthma sub-phenotypes when used in
41 conjunction with other Type 2 biomarkers [7]. The
42 clinical utility of periostin measurements depends on
43 better understanding of factors that may affect serum
44 periostin levels, such as race.

45 We have recently reported reference ranges for
46 serum periostin both in an adult group without asthma
47 [8] and in an adult group with symptomatic airflow
48 obstruction [9]. In both these studies, participants
49 who identified as being 'Asian' had a trend towards
50 higher serum periostin levels than their Caucasian
51 counterparts. However, the interpretation of these
52 findings was difficult, as in both studies the proportion
53 of people from an Asian background was small,
54 comprising 34/480 (7%) and 9/386 (2%) of the clinical
55 cohorts, respectively, and the origin of the Asian
56 participants was not further defined.

57 In this study, we aimed to identify the range for
58 serum periostin in adult Chinese participants both
59 with and without asthma, and compare the ranges with
60 those previously described in Caucasian populations
61 [8, 9]. The methodology was based on the guidelines
62 of the Clinical and Laboratory Standards Institute for
63 determining reference values and reference intervals
64 for quantitative clinical laboratory tests [10]. We
65 also investigated whether periostin levels differed in
66 Chinese with and without asthma and whether or not
67 country of birth influenced serum periostin levels in
68 the Chinese groups.

69 Methods

70 This was a two-centre, cross-sectional study which
71 recruited Chinese adults, aged 18 to 75 years, from
72 the Greater Wellington and Auckland regions. To
73 be eligible for inclusion, participants were required
74 to self-report both their own, as well as their
75 parents', race as Chinese. The study consisted of 188
76 Chinese participants, divided into non-asthma and
77 asthma groups. For each Chinese group there was a
78 comparator Caucasian group comprising participants
79 who self-reported their race as New Zealand European,
80 derived from previous studies [8, 9].

Participants

Non-asthmatic Chinese group

81 120 Chinese participants, without a doctor's diagnosis
82 of asthma or chronic obstructive pulmonary disease
83 (COPD), with at least 20 participants (10 male and 10
84 female) recruited to each of the following age bands:
85 18–30, 31–45, 46–60 and 61–75 years.
86
87

Non-asthmatic comparator Caucasian Group

88 420 Caucasian adults, without a doctor's diagnosis of
89 asthma or COPD, aged 18–75 years, were derived from
90 a previous study identifying reference ranges of periostin
91 in an adult non-asthmatic population [8].
92

93 For both non-asthmatic groups, participants were
94 excluded if they were current smokers, or former
95 smokers with a smoking history of greater than 10 pack
96 years; underwent surgery (including dental surgery),
97 were admitted to hospital, sustained a bone fracture or
98 received systemic corticosteroids within 3 months of
99 enrolment; were pregnant or breastfeeding; or had an
100 active (within 3 weeks prior to the study visit) respiratory
101 tract infection, as these scenarios could potentially
102 influence serum periostin levels.

Asthmatic Chinese group

103 68 Chinese participants with a doctor's diagnosis of
104 asthma whose current asthma treatment was either of:
105 (i) short-acting beta agonist (SABA) only, or (ii) SABA
106 and at least one controller. This group had the same other
107 exclusion criteria as the non-asthmatic groups.
108

Comparator asthmatic Caucasian Group

109 170 Caucasian adults, with a doctor's diagnosis of asthma
110 and aged between 18 and 75 years were derived from a
111 previous study of an adult population with symptomatic
112 airflow obstruction [9], and were stratified as above,
113 based on their asthma treatment.
114

115 The study conformed to the standards of the
116 Declaration of Helsinki. Ethical approval was given by
117 the Central Regional Ethics Committee of New Zealand
118 (13/NTB/190). Written informed consent was obtained
119 from all participants prior to testing. Participants
120 attended the nearest research facility for a single visit for
121 assessment of medical history, completion of a genogram
122 to document race and country of birth, measurement of
123 spirometry and fractional exhaled nitric oxide (FeNO),
124 and blood sampling for measurement of full blood count
125 (FBC), creatinine and electrolytes, serum IgE and serum
126 periostin. Asthmatic participants answered additional
127 validated respiratory health questionnaires, Asthma
128 Control Questionnaire (ACQ-5) [11] and Asthma Quality



of Life Questionnaire with Standardised Activities (AQLQ-S) [12], to establish their current asthma control. Medication history for all participants was recorded.

132 Spirometry and FeNO

133 Spirometry was performed for measurement of forced
134 expired volume in one second (FEV₁) and forced
135 vital capacity (FVC) using a Masterscreen Pneumo
136 (Masterscreen Version 2.0, Carefusion, Germany) in
137 accordance with the American Thoracic Society (ATS)
138 guidelines [13]. FEV₁ % predicted values were calculated
139 using the Global Lung Initiative equations [14]. FeNO
140 was assessed using a nitric oxide monitor (NiOX,
141 Aerocrine AB, Sweden) according to ATS guidelines [15].

142 Blood samples

143 All participants, including from the previous cohorts,
144 underwent venepuncture for measurement of serum
145 periostin, which was determined using the Elecsys®
146 Periostin immunoassay (Roche Diagnostics, Penzberg,
147 Germany). The Elecsys® Periostin assay was developed
148 according to the guidelines of the Clinical and Laboratory
149 Institute (CLSI) and is a fully automated immunoassay
150 operated on the e601 module of the cobas 6000 system
151 equipped with software version 05–01 or higher [16].
152 The assay has a high repeatability with coefficients of
153 variation across multiple sites and reagent lots of 1.7 to
154 3.1% [16]. Blood samples were coagulated, centrifuged
155 and serum aliquots stored at –80 °C prior to analysis.
156 FBC and white cell differential (Sysmex platform,
157 Mundelein, USA), urea and electrolytes (Roche, Cobas
158 501, NZ) and serum IgE (Roche modular, Indianapolis,
159 USA) were performed immediately in local laboratories.

160 Study power

161 The sample size of 120 non-asthmatic Chinese adults (60
162 male; 60 female) was based on the recommendations of
163 the Clinical and Laboratory Standards Institute [10], to
164 allow 90% confidence intervals to be computed by non-
165 parametric methods if normal distribution assumptions
166 were not met. Based on the standard deviation (SD) of
167 logarithm periostin of 0.22, a sample size of 120 Chinese
168 participants and 420 Caucasian participants had 90%
169 power with alpha 5% to detect a difference in mean
170 logarithm periostin of 0.074 which is equivalent to a ratio
171 of mean periostin of 1.08.

172 Statistical methods

173 Data descriptions for continuous variables were by
174 mean, median, and minimum to maximum ranges.
175 Serum IgE, FeNO and serum periostin had skewed
176 distributions, so were analysed on the logarithm
177 transformed scale. For univariate comparison of

continuous variables by dichotomous variables, t-tests
were used, using a logarithm transformation when
needed. For completeness, for those variables analysed
on the logarithm transformed scale, the univariate
association by a Mann–Whitney test and Hodges-
Lehmann estimator of location shift were also shown.
Where a logarithm transformation of a response variable
was carried out, the exponent of this was shown and was
interpreted as the ratio of geometric means.

Estimates of the mean and median periostin levels
and 90% confidence intervals for prediction were
determined for the Chinese non-asthma group with
an analysis of variance (ANOVA). The sex and age
adjusted reference range for periostin was estimated by
analysis of co-variance (ANCOVA). We performed the
analysis on the logarithm transformed scale with a back
transformation to establish the 90% confidence interval
for prediction.

An estimate of the difference between the Chinese
and Caucasian groups was calculated by a general linear
model (ANOVA). An exploratory analysis, comprising
a *t* test, was done to examine the effects of country
of birth on serum periostin levels. Finally, ANOVA
and ANCOVA were used to examine the association
between periostin (using logarithm periostin as the
response variable) and the interaction between race and
asthma status without (ANOVA) and with (ANCOVA)
adjustment of the continuous co-variables body mass
index (BMI) and FEV₁% predicted.

SAS version 9.4 was used.

178 Results

179 The flow of Chinese participants through the study is
180 shown in Fig. 1. Participants were recruited between
181 May and November 2015 from both sites. A total of
182 182 people were screened, of which nine were excluded.
183 12 participants, who self-identified as Chinese from a
184 previous study [8] were included in the Chinese non-
185 asthma group, and were part of the final analysis. A total
186 of 185 Chinese participants had complete data, which
187 was analysed and is presented here.

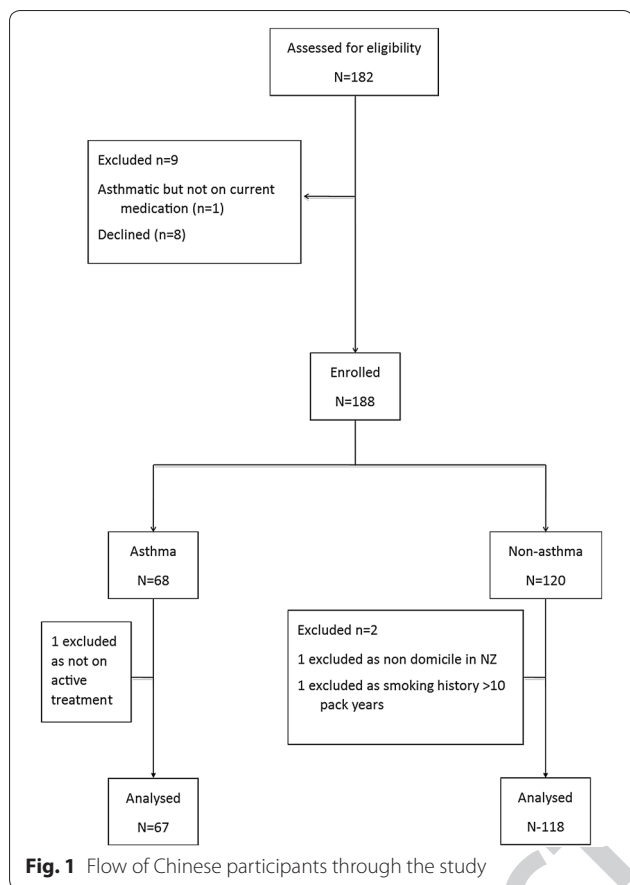
188 Participant characteristics

189 Participant characteristics are described in Table 1
190 (non-asthmatic Chinese and Caucasians) and Table 2
191 (asthmatic Chinese and Caucasians).

192 Serum periostin reference range in non-asthmatic Chinese

193 In the Chinese non-asthma group, periostin levels were
194 sex-, but not age-dependent, with females having higher
195 periostin levels, with a ratio of geometric mean periostin
196 (95% CI) 1.15 (1.05 to 1.26), *P*=0.001. Using the mean
197 age in this group (42.2 years), the back-transformed





individual predicted (90% CI) reference range for periostin in females was 61.1 ng/ml (41.6 to 89.8) ng/ml and in males was 53.2 ng/ml (36.1 to 78.3) ng/ml. There was an inverse relationship between logarithm serum periostin and BMI ($r = -0.28, P = 0.002$).

Group comparisons

Non-asthmatic Chinese and non-asthmatic Caucasians

The Chinese non-asthmatic group had more females (77/118, 68% of total) and a lower mean BMI than the Caucasian group. Atopic conditions, such as seasonal rhinoconjunctivitis or eczema, were less prevalent in the Chinese group, 32.2%, compared to 48.3% in the Caucasian group. The median (interquartile range; IQR) serum periostin level was higher in Chinese non-asthmatics, 57.0 (50.3 to 67.9) ng/ml, than in Caucasian non-asthmatics, 49.7 (42.8 to 56.5) ng/ml. The Hodges-Lehmann estimate (95% CI) of the difference was 8.2 (5.8 to 10.6), $P < 0.001$. Figure 2 shows comparative frequency histograms of logarithm transformed serum periostin in Chinese and Caucasian non-asthmatics. With respect to other biomarkers of Type 2 asthma, serum IgE was higher in the Chinese non-asthmatic group compared to

the Caucasian group. There was no difference between the groups with respect to peripheral blood eosinophils or FeNO.

Asthmatic Chinese and non-asthmatic Chinese

The Chinese asthma group had a higher proportion of males, 37/67 (55%), and were younger than the Chinese non-asthmatics (Tables 1 and 2). A history of atopic conditions, including nasal disorders, was more prevalent in Chinese asthmatics, 48/67 (71.6%). There was no significant difference in serum periostin between the Chinese asthma and non-asthma groups, median 56.8 ng/ml and 57.0 ng/ml respectively, with a Hodges-Lehmann estimate of (95% CI) $-0.1 (-4.2 \text{ to } 4.2)$, $P = 0.94$. Peripheral blood eosinophils, FeNO and serum IgE, were higher in Chinese asthmatics.

Asthmatic Chinese and asthmatic Caucasians

The Chinese asthma group had a lower BMI than the Caucasian group and a higher mean FEV₁/FVC ratio and higher FEV₁% predicted values. Spirometric differences were consistent with a lower proportion of Chinese participants being on Global Initiative for Asthma (GINA) treatment Step 2 or higher; 33/67 (49%) in the Chinese group and 106/170 (62%) in the Caucasian group. Median serum periostin levels between the two groups were similar (56.8 ng/ml in Chinese and 54.9 ng/ml in Caucasians). There was evidence of modest interaction between race and asthma status on serum periostin levels with an unadjusted value $P = 0.01$, and a value of $P = 0.024$ after adjustment for BMI and FEV₁% predicted. With respect to other biomarkers of Type 2 asthma, blood eosinophils were similar with means (SD) of $0.29 (0.19) \times 10^9/L$ and $0.27 (0.22) \times 10^9/L$ in Chinese and Caucasian asthmatics. However, FeNO and IgE were higher in Chinese asthmatics with a mean (SD) FeNO of 64.4 (54.8) ppb and IgE 537.6 (632.9) IU/ml compared to 39.3 (33.2) ppb and 372.8 (1429) IU/ml in Caucasian asthmatics.

Country of birth and serum periostin levels in Chinese participants

Of the 185 Chinese participants with periostin data, 93 participants were born in New Zealand and 92 participants were immigrants to New Zealand. All participants had lived in New Zealand for at least 1 year prior to enrolment into the study. As there was no difference in serum periostin between the Chinese asthma and non-asthma groups, this analysis was performed on all Chinese participants, irrespective of their asthma status. There was no difference in periostin levels between those who were born in New Zealand and

Table 1 Participant characteristics of non-asthma groups

Variable	Chinese				Caucasian				P-value	
	N	Median (IQR)	Mean (SD)	Min to max	N	Median (IQR)	Mean (SD)	Min to max		
Age (years)	118	42.5 (24 to 58)	42.2 (17.6)	18 to 73	420	47.5 (32 to 61)	46.4 (16.9)	18 to 74	-4.3 (-7.8 to -0.8)	0.017
BMI (kg/m ²)	118	23.1 (20.4 to 25.5)	23.4 (3.5)	17.6 to 33.6	420	25.3 (22.8 to 28.5)	26.1 (4.7)	18.2 to 57.5	-2.7 (-3.6 to -1.8)	<0.001
FEV ₁ /FVC ratio ^c	118	0.82 (0.78 to 0.88)	0.83 (0.08)	0.61 to 1.26	419	0.78 (0.73 to 0.82)	0.77 (0.07)	0.48 to 0.99	0.05 (0.04 to 0.07)	<0.001
FEV ₁ %	117	106.0 (97.6 to 113.6)	104.9 (13.7)	64.0 to 135.9	419	104.0 (95.0 to 112.0)	103.7 (12.4)	71.3 to 148.5	1.25 (-1.36 to 3.85)	0.35
Serum periostin ^b (ng/mL)	118	57.0 (50.3 to 67.9)	59.6 (15.4)	22.1 to 132.1	420	49.7 (42.8 to 56.5)	50.9 (12.1)	28.1 to 136.4	8.8 (6.1 to 11.4)	<0.001
FeNO ^b (ppb)	118	19 (13 to 29)	28.8 (34.2)	5.0 to 300.0	420	19 (14.5 to 27)	23.3 (14.1)	2.5 to 99.0	5.5 (1.36 to 9.64)	0.009
Serum IgE ^b (U/L)	118	68 (25 to 216)	270.9 (717.8)	2.0 to 5888	420	31 (11 to 78)	94.3 (247.3)	0.5 to 2608	176.6 (94.7 to 258.6)	<0.001
Blood eosinophils x10 ⁹ /L (units)	117	0.1 (0.07 to 0.18)	0.15 (0.12)	0 to 0.72	419	0.1 (0.1 to 0.2)	0.16 (0.12)	0 to 0.8	0.1 (0.1 to 0.2)	

SD standard deviation, IQR interquartile range, 95% CI 95% confidence intervals, BMI body mass index, FEV₁ forced expiratory volume in one second, FVC forced vital capacity, FE_{NO} fractional exhaled nitric oxide, IgE immunoglobulin E

^a Comparison of variables using t-test: Chinese minus Caucasian means

^b For illustration: better analysed on the logarithm transformed scale

^c Based on pre-bronchodilator spirometry



Table 2 Participant characteristics of asthma groups

Variable	Chinese				Caucasian			
	N	Median (IQR)	Mean (SD)	Min to max	N	Median (IQR)	Mean (SD)	Min to max
Age (years)	67	32 (22 to 52)	37.3 (16.3)	18.4 to 72.4	170	46 (35 to 57)	46.0 (14.5)	19 to 75
BMI (kg/m ²)	67	24.9 (22.2 to 26.6)	24.9 (3.9)	17.6 to 37.4	170	26.5 (22.7 to 30.9)	27.7 (6.7)	15.7 to 57.1
FEV ₁ /FVC ratio ^a	67	0.76 (0.70 to 0.81)	0.74 (0.11)	0.43 to 0.96	170	0.74 (0.66 to 0.79)	0.72 (0.11)	0.38 to 0.95
FEV ₁ % predicted	67	99.5 (83.3 to 107.5)	95.3 (16.6)	50.1 to 130.5	170	84.8 (74.4 to 94.1)	83.1 (16.3)	32.6 to 121.8
Serum periostin ^b (ng/mL)	67	56.8 (47.8 to 70.4)	59.9 (15.3)	36.4 to 128.2	170	54.9 (47.3 to 68.0)	58.9 (19.9)	15.0 to 148
FeNO ^b (ppb)	67	41 (23 to 96)	64.4 (54.8)	7.0 to 242	170	30.5 (16.5 to 49.4)	39.3 (33.2)	2.7 to 194.1
Serum IgE ^b (U/L)	66	308 (128 to 738)	537.6 (632.9)	7.0 to 3454	170	125.4 (34 to 283.1)	372.8 (1429.0)	1 to 18,083
Blood eosinophils x 10 ⁹ /L (units)	67	0.24 (0.14 to 0.40)	0.29 (0.19)	0.02 to 0.78	170	0.2 (0.1 to 0.3)	0.27 (0.22)	0 to 1.5

SD standard deviation, IQR interquartile range, 95% CI 95% confidence intervals, BMI body mass index, FEV₁ forced expiratory volume in one second, FVC forced vital capacity, FeNO fractional exhaled nitric oxide, IgE immunoglobulin E

^a Based on pre-bronchodilator measurements

^b For illustration: better analysed on the logarithm transformed scale

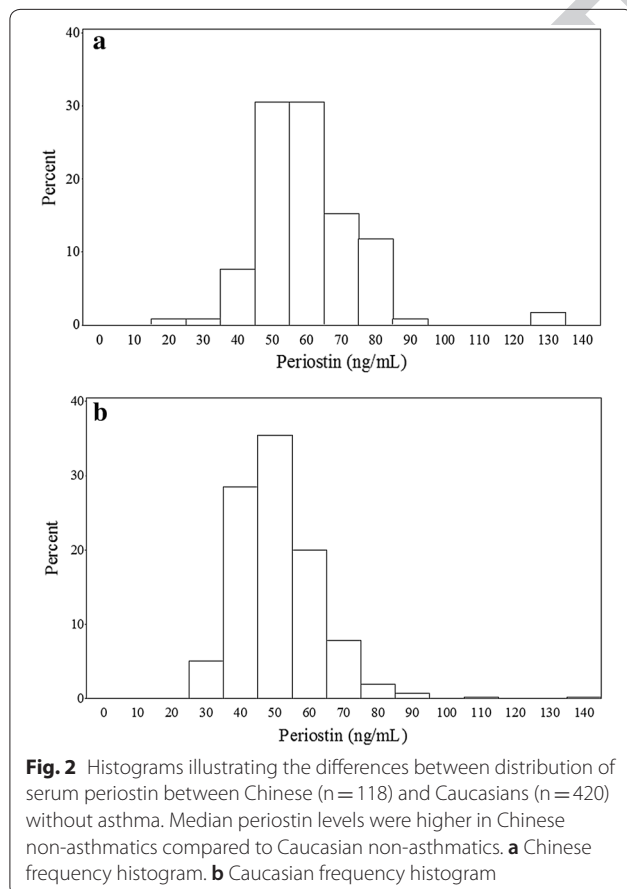


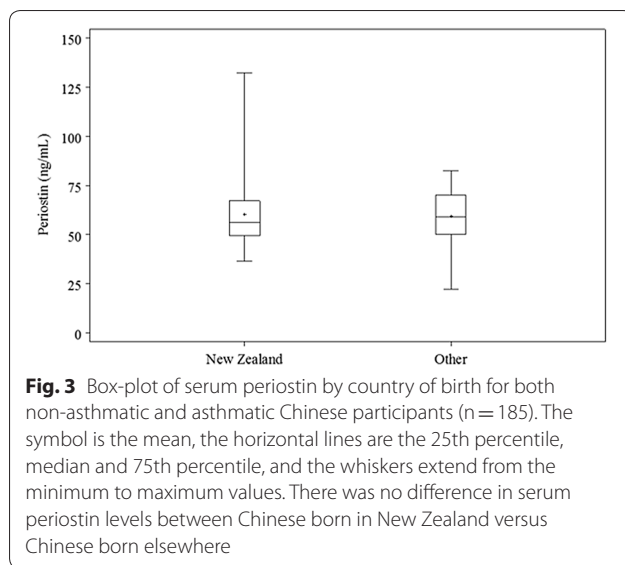
Fig. 2 Histograms illustrating the differences between distribution of serum periostin between Chinese (n = 118) and Caucasians (n = 420) without asthma. Median periostin levels were higher in Chinese non-asthmatics compared to Caucasian non-asthmatics. **a** Chinese frequency histogram. **b** Caucasian frequency histogram

those born elsewhere, with a Hodges-Lehmann estimate (95% CI) of -1.3 (-5.1 to 2.6), P = 0.51, (Fig. 3).

Discussion

The main findings of this study were that serum periostin levels were higher in non-asthmatic Chinese compared to non-asthmatic Caucasians and there was no difference in periostin levels between Chinese adults with and without asthma.

Some of the associations we have found should be interpreted cautiously. As this was an exploratory study investigating a potential difference in serum periostin levels between Chinese and Caucasian populations, performing multiple statistical tests may have resulted in Type I error inflation. Secondly, we recruited people who self-reported their race as Chinese. To mitigate against issues around race identity, participants completed a genogram in which both of their parents were also required to identify as Chinese. Thirdly all participants were resident in New Zealand for at least a year prior to enrolment, in order to minimise potential confounding of environmental factors, such as indoor or outdoor air pollution, on serum periostin levels. Consequently, these results may not be generalisable to Chinese people domiciled outside of New Zealand. Despite data from different participant cohorts being used in this study, serum for periostin levels were processed and stored using the same methodology [8] and using the same assay in a single clinical laboratory for all participants [16].



327 The Elecsys[®] Periostin immunoassay is a fully automated
 328 assay based on the sandwich principle and was developed
 329 for diagnostic purposes and use in clinical practice.
 330 Therefore, the CSLI guidelines were followed to develop
 331 an accurate, precise and reliable assay that is sufficiently
 332 sensitivity, accuracy with regard to an established
 333 target value, precision of the assay across instruments,
 334 lots and sites, and low susceptibility towards potential
 335 interferences, resulting in comparable results between
 336 separate measured cohorts over periods of time. Thus
 337 the comparisons between these groups in this study are
 338 unaffected by the intervening times between testing.
 339 Finally, the Chinese asthmatics had less severe asthma
 340 as measured by FEV₁% predicted and asthma medication
 341 use, although this is unlikely to be of significance, as
 342 serum periostin levels are not related to asthma severity
 343 [7, 9].

344 In the Chinese non-asthma population periostin
 345 levels were sex-dependent, with females having higher
 346 periostin levels. This was an unexpected finding as it was
 347 not observed in the previous study of a predominantly
 348 Caucasian population without asthma [8], which was a
 349 larger study defining a reference range for non-asthmatic
 350 adults. It is possible that differences in key environmental
 351 or personal characteristics that influence serum periostin
 352 levels may differ between Chinese and Caucasian
 353 people, based on sex. To clarify the uncertainty, further
 354 robust data describing sex-dependent reference ranges
 355 in Chinese and other populations defined by racial
 356 background are needed.

357 Serum periostin levels were similar in the Chinese
 358 asthma and non-asthma groups with median values
 359 56.8 ng/ml and 57.0 ng/ml respectively. This finding

360 is in agreement with previous studies undertaken in
 361 predominantly Caucasian participants [8, 9] where
 362 serum periostin levels did not discriminate between
 363 asthmatic and non-asthmatic groups, suggesting that
 364 measurement of periostin is not a useful biomarker in
 365 establishing a diagnosis of asthma. Of note, the Chinese
 366 asthma group consisted of a range of asthmatics, some
 367 of who were not taking regular ICS. From previous
 368 studies [9], it is clear that ICS use can lower serum
 369 periostin levels by approximately 10% and whilst this
 370 is statistically significant, it is unlikely to be clinically
 371 meaningful.

372 However, differences between asthmatic and non-
 373 asthmatic groups have been observed in a Japanese
 374 population [17]. This could be due to differences
 375 in populations included in the studies, including
 376 polymorphisms that have been associated with periostin
 377 levels.

378 The observation that serum periostin was similar
 379 between the Chinese and Caucasian asthma groups
 380 is difficult to interpret given that the two groups were
 381 recruited using different methodology. The Caucasian
 382 asthmatics were recruited from the electoral roll
 383 and were not excluded if they underwent surgery or
 384 dental procedures, or sustained bone fractures prior to
 385 enrolment and had less severe asthma, as periostin was
 386 not the main focus of this study [9]. Consequently, formal
 387 statistical analysis was not performed between these
 388 asthma groups, as any meaningful conclusion would be
 389 difficult to interpret given the different approaches to
 390 recruitment between the two groups of participants.
 391 However, the serum for periostin measurement was
 392 processed in the same way, utilising the same assay [16].

393 Serum periostin levels were higher in Chinese,
 394 irrespective of the participant's country of birth. This
 395 finding is consistent with previous studies [8, 9] which
 396 have found higher serum periostin levels in those of
 397 Asian origin. Together with studies that described
 398 polymorphisms of the POSTN gene influencing
 399 serum periostin levels [17], this suggests that genetic
 400 background may play a role in determining levels of
 401 serum periostin. The clinical relevance is that race and
 402 ethnicity may be important factors to consider when
 403 interpreting serum periostin values.

404 The finding that different patterns for other Type 2
 405 biomarkers between the groups were observed supports
 406 previous observations that these biomarkers may identify
 407 different aspects of Type 2 mediated inflammation [8,
 408 18–20]. Between non-asthmatics, the periostin and
 409 serum IgE levels were higher in Chinese compared with
 410 Caucasians, whereas there was no significant difference
 411 in FeNO or blood eosinophils. In the Chinese population
 412 those with asthma had higher levels of FeNO, IgE and



413 blood eosinophils, but not periostin, when compared
414 with those without asthma.

415 The observation of a higher serum IgE in Chinese
416 compared with Caucasian populations is consistent
417 with previous findings identifying differing serum IgE
418 levels between races and socio-economic groups [21–
419 23] and specifically a trend towards higher serum IgE in
420 Chinese compared with ‘White’ people in England [23].
421 Smoking, which is associated with elevated levels of
422 serum IgE [24] was unlikely to be a confounding factor
423 in our study as current smokers, or former smokers
424 with a pack year history of over 10 years, were excluded.
425 However, participants were not assessed with regards to
426 passive smoking, which can be a contributing factor to
427 higher levels of serum IgE [24]. The finding that blood
428 eosinophil levels were similar in Chinese and Caucasians
429 without asthma is consistent with the previous
430 observation that blood eosinophil levels are comparable
431 between ethnicities, including ‘Orientals’ (defined as
432 those who were from South East Asia, or who identified
433 as Chinese) [25]. Our finding of similar FeNO levels
434 between Chinese and Caucasians without asthma adds
435 to the literature of inconsistent findings between FeNO
436 and race [26–30]. Significantly elevated FeNO levels have
437 been reported in Asians versus their Caucasian peers in
438 both asthmatic [27] and non-asthmatic [29] children.
439 The National Health and Nutrition Examination Survey
440 (NHANES) cohort [26] found only a difference between
441 races in children, but not in adults in a population free of
442 respiratory diagnoses. However, Ko and colleagues report
443 higher FeNOs in Chinese adults compared to Caucasians
444 without chronic respiratory disease [30].

445 **Conclusions**

446 In conclusion, we have determined that serum periostin
447 levels are higher in a Chinese non-asthmatic population
448 compared with a Caucasian non-asthmatic population,
449 suggesting that genetic background may influence
450 serum periostin levels. If serum periostin is to be used
451 to identify patient phenotypes in asthma or to make
452 treatment decisions in the clinical context of asthma,
453 these factors would need to be taken into account.
454

455 **Abbreviations**

456 ACQ: Asthma Control Questionnaire; AQLQ-S: Asthma Quality of Life
457 Questionnaire—Standardised activities; ATS: American Thoracic Society;
458 COPD: chronic obstructive pulmonary disease; FeNO: fractional exhaled
459 nitric oxide; FEV1: forced expiratory volume in one second; FVC: forced vital
460 capacity; ICS: inhaled corticosteroid; Ig: immunoglobulin; IL: interleukin; LABA:
461 long-acting beta agonist; LAMA: long-acting muscarinic antagonist; NZRHS:
462 New Zealand Respiratory Health Survey; SABA: short-acting beta agonist.

463 **Authors’ contributions**

464 Study conception and design: ET, RV, RCS, MW, RB, IB; Acquisition of data: ET,
465 RV, BM, RS, RCS; Analysis: MW; Interpretation of data: All authors; Drafting of

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467 the work in ensuring that questions related to the accuracy or integrity of any
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Competing interests

Dr. Olsson and Dr. Holweg are employees of Genentech Inc., a member of the
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Availability of data and materials

The datasets used and/or analysed during the current study are available from
the corresponding author on reasonable request.
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Consent for publication

Not applicable
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Ethics approval and consent to participate

This trial conformed to the standards of the Declaration of Helsinki, and was
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