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Research Article

Prevalence of *GSTM1*0* and *CYP1A1*2A* (rs4646903) variants in the central Peruvian coastal population: Pilot Study of predictive genetic biomarkers for 4P medicine

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Abstract

The CYP1A1 isoenzyme is responsible for the biotransformation of procarcinogens, such as Benzo(a)pyrene, into reactive metabolites. Meanwhile, GSTM1 facilitates the detoxification of these metabolites by conjugating them with glutathione. The presence of the *CYP1A1*2A* genetic variant intensifies the production of these reactive metabolites, and the deletion of the *GSTM1* gene (*GSTM1*0*) impairs their detoxification. This enzymatic imbalance leads to the formation of DNA adducts, which are known to contribute to cancer and other diseases. Given the importance of studying these genes within the framework of 4P medicine (predictive, preventive, personalized, and participatory), the primary objective of this study was to investigate the prevalence of *GSTM1*0* and *CYP1A1*2A* in the central Peruvian coastal Population as genetic biomarkers. The study included 131 individual residents of the Peruvian towns of Ica and Lima. The results showed a frequency of 0.47 for *GSTM1*0* and an allele frequency of 0.68 for *CYP1A1*2A*. The genotype frequencies of *CYP1A1*2A* were 6% **1A/*1A*, 53% **1A/*2A*, and 41% **2A/*2A*. Notably, the population sample is not in the Hardy-Weinberg equilibrium ($\chi^2 = 5.324$) for *CYP1A1*. The reported frequencies of *GSTM1*0* and *CYP1A1*2A* in this study differ from those previously documented for other Latin American and tricontinental populations, potentially reflecting the unique

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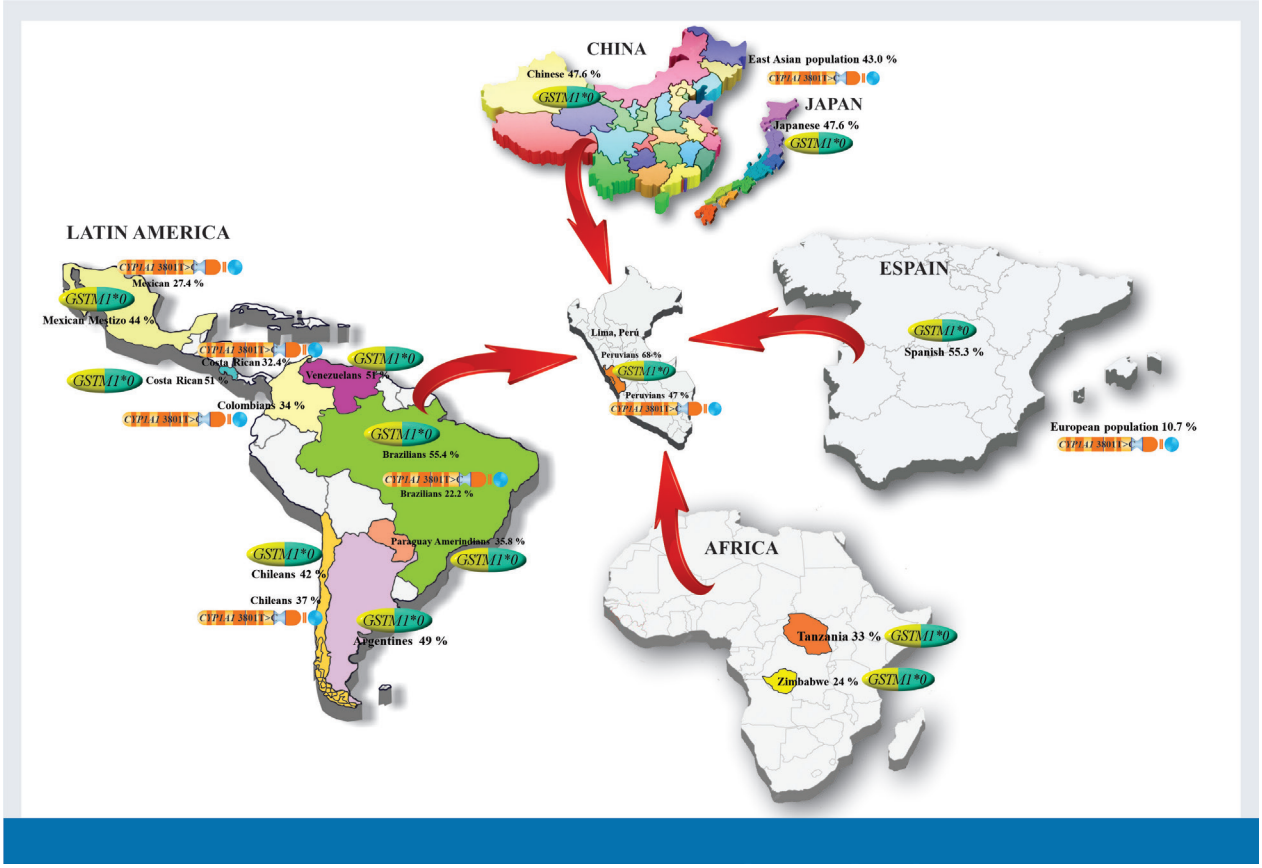
natural evolution and genetic admixture of the Peruvian population. The high prevalence of *GSTM1*0* and *CYP1A1*2A* identified in populations from Ica and Lima suggests a potentially elevated risk of exposure to procarcinogens such as polycyclic aromatic hydrocarbons (PAHs). This finding underscores the need for further research on a larger scale to validate and expand upon these results.

Graphical abstract:



Keywords

CYP1A1, *GSTM1*, 4P medicine, predictive genetic biomarker, procarcinogenic

Introduction

4P medicine is a new healthcare model that addresses predictive, preventive, personalized, and participatory medicine. Through genetic studies, we seek to identify predispositions to diseases before they manifest, allowing more precise predictions (predictive) and designing strategies that prevent their development (preventive) (Alonso et al. 2019). Genetic information allows individualized treatments to be adapted, considering their unique (personalized) biological characteristics, which optimizes the effectiveness of interventions. In addition, it actively involves various health professionals and patients in decision-making about their health (participatory), empowering them with detailed information about their genetic profile and encouraging greater responsibility in caring for their well-being; this allows for better adherence to the prevention and treatment of the disease (Alonso et al. 2019; Slim et al. 2021). To implement and apply 4P medicine effectively, it is essential to consider ethnic origin, as drug response and patient prognosis differ both interindividually and across populations. Notably, the frequencies of single nucleotide polymorphisms (SNPs), insertions/deletions, and microsatellites in pharmacogenes vary significantly with ethnic background (Cha et al. 2007; Gil et al. 2014; Sánchez-Siles et al. 2020).

The *CYP1A1* gene encodes the phase I cytochrome P450 isoenzyme that oxidizes various procarcinogenic compounds (e.g., polycyclic aromatic hydrocarbons) into their carcinogenic metabolites. Several genetic polymorphisms have been reported in this gene, the most relevant being *CYP1A1*2A*. The *CYP1A1* 3801T>C SNP (rs4646903) is one of the most common polymorphisms globally. This variant arises from a thymine (T) to cytosine (C) mutation at nucleotide 3801 in the 3′ untranslated region of the gene, increasing the expression of the CYP1A1 enzyme (Hashibe et al. 2003; Sánchez-Siles et al. 2020). On the other hand, the glutathione S-transferase mu-1 gene (*GSTM1*) encodes the

glutathione S-transferase M1 isoenzyme, which is a dimeric protein participating in phase II conjugation metabolism by incorporating glutathione into various drugs, oxidative stress products, environmental toxins, and procarcinogens to convert them into highly hydrophilic glutathione-conjugated molecules that are eliminated from the body (Strange et al. 2001; Acar et al. 2006; Alvarado et al. 2021a). A null allele called *GSTM1*0* can be generated by unequal recombination of the 5' and 3' end regions, and carriers of both null alleles due to homozygous deletion constitute the *GSTM1* genotype (-/- or del/del) in whom the enzyme is not expressed (Rosero et al. 2016; Heredia Ruiz et al. 2017; Satinder et al. 2017). This generates a metabolic imbalance, increasing reactive metabolite intermediates capable of interacting with DNA, inducing mutations, and thus increasing the individual risk of cancer (Sánchez-Siles et al. 2020). In various investigations, it has been reported that active allelic variants of *CYP1A1*, such as *CYP1A1*2A*, and homozygous deletions of *GSTM1* are associated with a higher risk of cancer (Hashibe et al. 2003; Lee et al. 2006; Sánchez-Siles et al. 2020; Alvarado et al. 2021a).

In this sense, Fig. 1A proposes a scheme of the metabolism of benzopyrene; in route 1, it is observed that the CYP1A1 isoenzyme (encoded by *CYP1A1*1A*) biotransforms benzopyrene into 4,5-epoxide benzopyrene, which, by action of GST mu (encoded by *GSTM1* (+) wild type), is converted into 4,5-dihydroxy-benzopyrene and conjugated to glutathione benzopyrene that is eliminated through the bile. In route 2, it is observed that the CYP1A1 protein biotransforms benzopyrene into 7,8-epoxide benzopyrene, which is converted into 7,8-dihydroxy benzopyrene with the participation of the epoxide hydrolase protein; immediately the aforementioned metabolite is biotransformed by CYP1A1/CYP3A4 into benzopyrene-7,8-dihydroxy-9,10-epoxide, and by the action of GST mu is reduced into benzopyrene-7,8,9,10-tetrahydroxy-7,8,9,10-tetrahydro and conjugated to form a hydrophilic metabolite called benzopyrene glutathione that is also eliminated via the bile. Fig. 1B proposes the biotransformation of benzopyrene into benzopyrene-7,8-epoxide by the action of CYP1A1 (encoded by *CYP1A1*2A* (T3801C)); then by epoxide hydrolase, it is converted into benzopyrene-7,8-dihydroxy, and by the action of CYP1A1/CYP3A4, it is biotransformed into the reactive metabolite called benzopyrene-7,8-dihydroxy-9,10-epoxide (Lee et al. 2006); and due to *GSTM1*0*, the GST mu protein is not expressed, so it is not possible to conjugate the reactive metabolite (Satinder et al. 2017). Therefore, the metabolite benzopyrene-7,8-dihydroxy-9,10-epoxide binds to guanine (G), forming a benzopyrene-DNA adduct. For this reason, the conjugation process is important to eliminate free radicals and reactive molecules (García-Martínez et al. 2017).

The literature regarding these enzymes, their genes, and their variants in Peruvian populations is still very scarce, particularly considering local ethnic variations, so it is justified to carry out these studies in populations with a high percentage of Amerindian admixture, such as those from the Ica regions (mestizo 70.9%, Quechua 14.3%, Caucasian 5.8%, Afro-Peruvian 5%, Tusan and Nikkei 1%, others 3%) and Lima (mestizo 67.7%, Quechua 16.4%, Caucasian 7.1%, Afro-Peruvian 2.8%, Tusan and Nikkei 1.8%, others 4.2%) (National Institute of Statistics and Informatics 2018) to generate scientific evidence and contribute to 4P medicine and its implementation in Peru. Therefore, the objective of this work was to describe the prevalence of *GSTM1*0* and *CYP1A1*2A* (rs4646903) variants in the central Peruvian coastal Population and to be used as predictive genetic biomarkers for 4P medicine.

Materials and methods

Design, sampling, and study population

Descriptive observational study with prospective recruitment, non-probabilistic, and convenience sampling. The study population was composed of 131 volunteer residents (sex: 45 females and 86 males; age 19–30, mean 23.21 SD ± 2.33) from the regions of Ica and Lima that are in the coastal area of Peru.

Ethical considerations

The study was developed in accordance with the criteria of the Belmont Report, Declaration of Helsinki of 1964 with the current revision. The Research Ethics Committee of the National University San Luis Gonzaga of Ica approved the protocol and informed consent of the study through CEI-UNICA certificate Nº023/09-2023. The subjects signed the informed consent before their participation and were called volunteers; then they completed a questionnaire with their personal data on age, sex, and lifestyle and authorized them to donate a blood sample. Each volunteer was assigned a code to ensure anonymity and confidentiality.

DNA isolation and genotyping

Genomic DNA was obtained from the buffy coat of blood samples using a standard manufacturer's protocol. The polymerase chain reaction (PCR) was carried out using the following program: initial denaturation at 94 °C for 3 min, samples were subjected to 30 cycles for 30 s at 94 °C, 30 s at 55 °C, and 1 min at 72 °C, ending with a final extension at 72 °C for 5 min. A fraction of the PCR product was subjected to electrophoresis in a 2% agarose gel, and the presence of amplicons was identified by staining with GelRed (Biotium®) and ultraviolet transilluminator. The *CYP1A1*2A* rs4646903 polymorphism was determined by restriction fragment length polymorphism (RFLP) analysis, using the direct primer 5' CAGTGAAGAGTGTGTAGCCGCT-3' and the reverse primer 5' TAGGAGTCTTGT TCATGCCT-3'. As an internal amplification control, the amplicon obtained with the primers for rs4646903 was used. Deletion of the *GSTM1* gene was detected using the forward primer 5'GAACTCCCTGAAAGCTAAAGC-3' and the reverse primer 5'GTTGGGCTCAAAATACGTGG-3'. The *GSTM1*0* genotype was visualized by the absence of a 215 bp amplification fragment, while wild-type (+) *GSTM1* was determined by the presence of the 215 bp fragment (Pérez-Morales et al. 2008; Alvarado et al. 2019, 2021a).

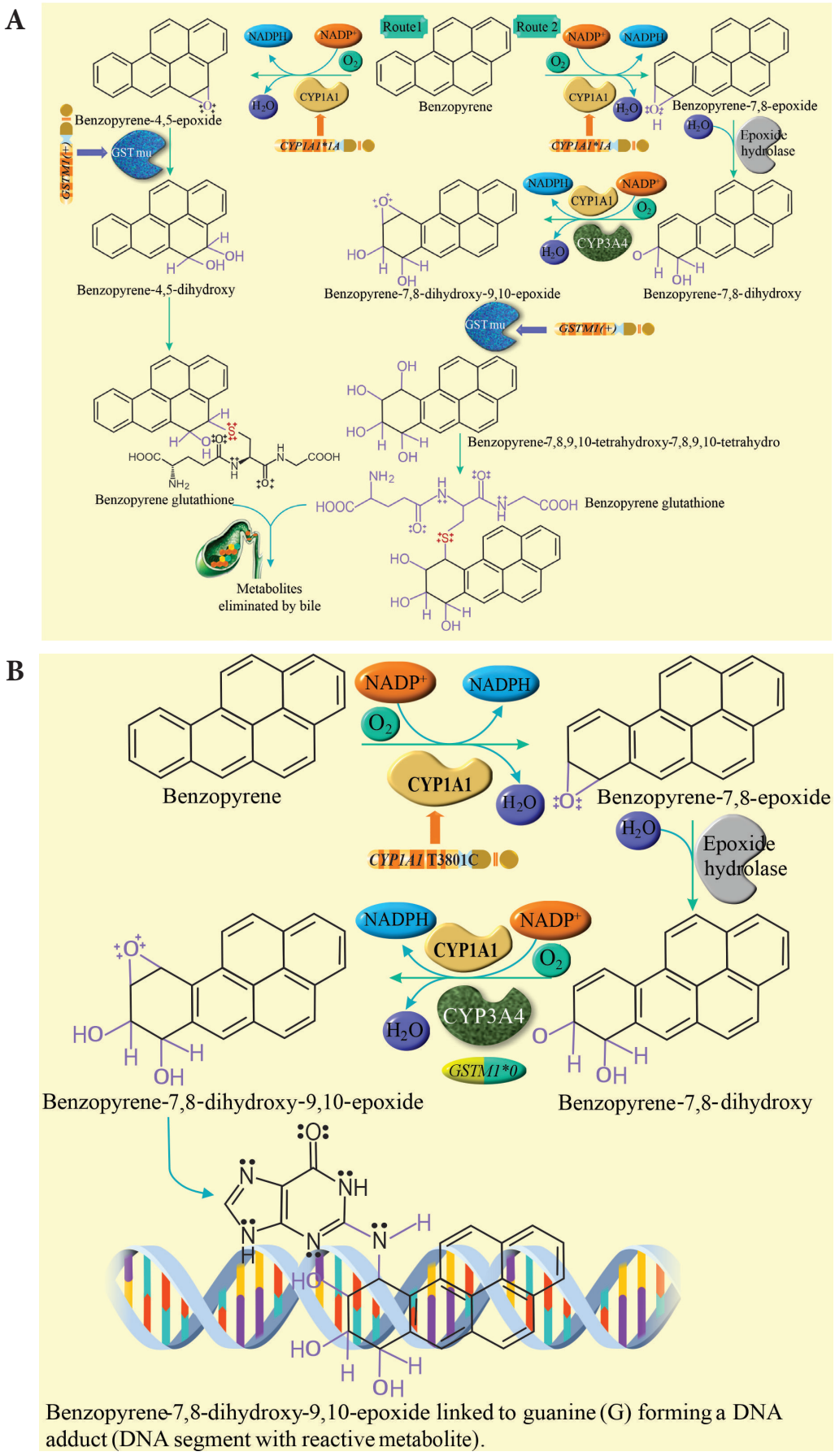


Figure 1. Biotransformation of benzopyrene and formation of DNA adducts. **A.** Shows the biotransformation of benzopyrene through phases 1 and 2 of conjugation for its elimination; **B.** Shows the formation of the DNA adduct by the allelic variant of *CYP1A1*2A* and by the deletion of *GSTM1*0* that does not conjugate the reactive metabolite.

Statistical analysis

To determine whether the distribution of *CYP1A1* genotypes is in Hardy-Weinberg equilibrium (HWE), the Chi-square goodness-of-fit test (χ^2) was used, considering one degree of freedom and a p-value < 0.05. The χ^2 values greater than 3.88 in the comparison indicated the rejection of the null hypothesis, therefore, the observed frequencies differed significantly from those expected. The analysis included the allele frequencies described in Latin American and tricontinental populations (Europeans, Africans, and East Asians) and the analysis of published studies with the possible association of *GSTM1*0* and *CYP1A1*2A* rs4646903 with susceptibility to different types of cancer. GraphPad Prism 9 statistical software was used. Version 9.1.2.

Results and discussion

Table 1 shows the ethnic-linguistic and demographic characteristics of the populations of the Ica and Lima regions. It is observed that 65.65% are male (n = 86) and mostly from Ica (n = 48), and additionally, a high percentage of Amerindian mixture has been reported in both regions, with the mestizo population predominating (National Institute of Statistics and Informatics 2018).

The frequencies obtained for the homozygous genotype *GSTM1*0* (*GSTM1* null) are 47% and 53% for the wild type *GSTM1* (+) genotype (Table 2). A previous study conducted by Alvarado et al. (2021a) in Peruvian mestizo populations (n = 81) from the jungle regions of Iquitos and the coastal regions of Lima (Alvarado et al. 2021a) found a similar frequency (Table 3). In populations from India, Pakistan, and New Delhi, who are carriers of *GSTM1*0* genotypes, an association with a higher risk of developing cervical cancer was found (Hasan et al. 2015; Sharma et al. 2015; Satinder et al. 2017). Similarly, in populations from northeastern Thailand, chronic smokers and carriers of *GSTM1*0* have been associated with an increased risk of developing cervical cancer (Settheetham-Ishida et al. 2020). In other studies and populations, no association was evident between ovarian cancer in Serbian women (Pljesa et al. 2017) and in Brazilian patients (Tacca et al. 2019).

While the frequencies of the *CYP1A1*2A* allele in the sample of coastal Peruvians is 0.68 (68%), which expresses the genotypes *CYP1A1*1A/*2A* (T/C) and **2A/*2A* (C/C), and applying the Chi-square χ^2 test, it was found that the comparison value is greater than 3.84, indicating that it is not in Hardy-Weinberg equilibrium. However, when determining the HWE independently in the ICA or Lima sample, they turn out to be in HWE. These antecedents indicate that they are different population samples and that a global analysis is not appropriate (Table 2).

In another study carried out in Peruvian mestizo populations, 69% (n = 81) of this allele was found (Alvarado et al. 2021a); while the study by Harrison et al. (2024) showed a higher frequency in populations of Lima and with a difference of 7.3% (Table 4). *CYP1A1* variants have been associated with the development of various types of cancer, including laryngeal (Sánchez-Siles et al. 2020), prostate (Hoidy et al. 2019), breast (Martínez-Ramírez et al. 2021), cervical (Das et al. 2022; Barek et al. 2023; Helaoui et al. 2023), and chronic lymphocytic leukemia (Al-Adl et al. 2023). However, such associations must be studied and confirmed through case-control studies with a larger number of samples, considering the two genes *GSTM1* and *CYP1A1*.

The frequency of *GSTM1*0* genotypes in Latin American populations related to Peruvians are variable (Table 3). Montero et al. (2007) and Palma-Cano et al. (2017) observed frequencies of 42.6% (n = 150) and 44.0% (n = 211) in mestiza Mexican populations, respectively, which are related to those found in the present study (Montero et al. 2007; Palma-Cano et al. 2017). In another research carried out by Pérez-Morales et al. (2008), it was reported that the frequency of *GSTM1*0* is lower (33.5%) with a greater number of mestizo Mexican populations (n = 529) (Pérez-Morales et al. 2008). In the Argentine (Fundia et al. 2014), Costa Rican (Cornelis et al. 2007), Venezuelan (Chiurillo et al. 2013), and Brazilian populations, this genotype is higher than that observed in Peruvians (Gattás et al. 2004); however, in Amerindian Brazilians the frequency is lower (26.5%) (Magno et al. 2009). In Amerindian Paraguayans, the frequency is lower (35.8%) (Gaspar et al. 2002); and in Chileans, it goes from 63.6% (Roco et al. 2012) to 21.4% (Quiñones et al. 1999). This is due to their greater American (44.34 ± 3.96%) and European (51.85% ± 5.44%) ancestry (Fuentes et al. 2014).

In research carried out in Asian, African and European populations that are considered the ancestral ancestors of Peruvians (Alvarado et al. 2023; Rojas-Macetas et al. 2023), the study by Garte et al. (2001) who found a similar frequency to Peruvians in Japanese populations (n = 639, 47.6%) (Garte et al. 2001); However, Fujihara et al. (2009) indicates a small difference between the Japanese and Peruvian population (3.8%) (Fujihara et al. 2009); while Hishida et al. (2005) proposes that the difference is 5% (Hishida et al. 2005). Liu et al. (2009) reported that the frequency of *GSTM1*0* is 52.0% in the Chinese population with a difference greater than 5% compared to Peruvians (Liu et al. 2009). It has been found that the frequency of this genotype is major in Spanish (8%) (Piacentini et al. 2011), and in the African population the frequency is lower (23–33%); therefore, the difference is 20% from what was found in the present study (Dandara et al. 2002).

Table 1. Ethnic-linguistic and demographic characteristics of the studied subjects.

Population	Gender		Age (years)	Ethnic-linguistic characteristics*					
	Male n (%)	Female n (%)	Mean ± SD	Mestizo (%)	Quechua (%)	Caucasian (%)	Afro-Peruvian (%)	Tusanes/ Nikkei (%)	Others (%)
Ica	48 (36.65)	22 (16.80)	23.33 ± 2.05	70.9	14.3	5.8	5	1	3
Lima	38 (29.00)	23 (17.55)	21.95 ± 2.06	67.7	16.4	7.1	2.8	1.8	4.2

*Data from the National Institute of Statistics and Informatics (INEI); SD: standard deviation.

Table 2. Frequency of *CYP1A1* genotypes and *GSTM1* phenotype in a sample of the central Peruvian coastal population.

Gene	Allele			Genotype			
				Observed			
	Type	n	f	Type	Nucleotide change	n	f
CYP1A1	**1A*	85	0.32	**1A/*1A*	T/T	8	0.06
	**2A*	177	0.68	**1A/*2A*	T/C	69	0.53
				**2A/*2A*	C/C	54	0.41
GSTM1	Total	262	1.00		Total	131	1.00
					Phenotype		
				Positive		70	53%
				Null		61	47%
					Total	131	100%

n: sample number; f: allele frequency.

The frequency of *CYP1A1* rs4646903 observed in Latin American populations is highly variable (Table 4); according to published studies, a higher frequency was found in the Mexican population of Baja California (39.8%, n = 51) (Harrison et al. 2024); however, Porchia et al. (2017) mention that the frequency in the Guadalajara-Mexican population is 27.4% (n = 125) (Porchia et al. 2017). Meanwhile, in Chilean populations (Santiago), a frequency of 37% (n = 94) has been reported (Roco et al. 2012); in Medellin-Colombia populations, 34% (n = 64) (Harrison et al. 2024); in Costa Ricans (San José), 32.4% (n = 33) (Porchia et al. 2017); in Brazilians (Campinas, Sao Paulo), 22.2% (n = 329) (Oliveira et al. 2015); the frequency being less in Puerto Ricans (20.2%, n = 42) (Harrison et al. 2024).

Studies of these allelic variants were also found in the East Asian population, whose frequency is lower (43%) than what was observed in our study; and in Europeans, it is much lower (10.7%) (Harrison et al. 2024). The *CYP1A1*2A*, *CYP1A1*2C* and *CYP1A1*3* alleles have been described in African populations; and *CYP1A1*4*, in German, Polish and Turkish populations (Rahal et al. 2013). The differences in the frequencies of Peruvians with their Latin American, Spanish, African, and East Asian ancestry (Chinese and Japanese) are explained by the χ^2 analysis,

Table 3. Frequency of *GSTM1* null phenotype in the coastal Peruvian population in relation to Latin American and tricontinental ancestry.

Populations	*GSTM1 Null*		Reference
	n	%	
Latin Americans			
Peruvians (Coastal)	61	47.0	Current study
Ica	34	48.6	
Lima	27	44.0	
Peruvian Mestizo	38	47.0	(Alvarado et al. 2021a)
Mexican Mestizo	150	42.6	(Montero et al. 2007)
Mexican Mestizo	211	44.0	(Palma-Cano et al. 2017)
Mexican Mestizo	529	33.5	(Pérez-Morales et al. 2008)
Mexico Amerindians	258	16.8	(Montero et al. 2007)
Argentines	69	49.0	(Fundia et al. 2014)
Costa Rican	2042	51.0	(Cornelis et al. 2007)
Venezuelans	120	51.0	(Chiurillo et al. 2013)
Brazilians	137	55.4	(Gattás et al. 2004)
Amerindian Brazilians	35	26.5	(Magno et al. 2009)
Amerindian Paraguayans	67	35.8	(Gaspar et al. 2002)
Chileans Mestizo	161	36.4	(Roco et al. 2012)
Asian			
Japanese	639	47.6	(Garte et al. 2001)
Japanese	128	50.8	(Fujihara et al. 2009)
Japanese	476	52.0	(Hishida et al. 2005)
Chinese	763	52.0	(Liu et al. 2009)
European			
Spanish	94	55.3	(Piacentini et al. 2011)
African			
Tanzania	220	33.0	(Dandara et al. 2002)
Zimbabwe	150	24.0	(Dandara et al. 2002)

n: sample number.

Table 4. Frequency of *CYP1A1*2A* genotypes in the coastal Peruvian population in relation to Latin American and tricontinental ancestry.

Populations (n)	*CYP1A1* gene										HWE $\chi^2 < 3.84$	Ref.
	Allele				Genotype							
	T		C		**1A/*1A*		**1A/*2A*		**2A/*2A*			
	n	(f)	n	(f)	n	(%)	n	(%)	n	(%)		
Latin Americans												
Peruvians (131)	85	0.324	177	0.680	8	6.1	69	52.6	54	41.2	5.324	Current study
Ica (70)	43	0.307	97	0.693	4	5.7	35	50.0	31	44.3	2.138	
Lima (61)	42	0.344	80	0.656	4	6.6	34	55.7	23	37.7	3.355	
Peruvian mestizo (81)	8	0.31	154	0.690	4	4.9	43	53.1	34	42.0	4.304	(Alvarado et al. 2021a)
Peruvian mestizo, Lima (85)	42	0.247	128	0.753	3	3.5	36	42.4	46	54.1	1.628	(Harrison et al. 2024)
Colombians (94)	124	0.660	64	0.340	39	41.5	46	48.9	9	9.6	0.757	(Harrison et al. 2024)
Mexicans from Baja California (64)	77	0.602	51	0.398	26	40.6	25	39.1	13	20.3	2.193	(Harrison et al. 2024)
Mexican from Guadalajara (228)	331	0.726	125	0.274	121	53.0	89	39.0	18	7.8	0.083	(Porchia et al. 2017)
Costa Ricans (51)	69	0.676	33	0.324	22	43.1	25	49.0	4	7.8	0.733	(Porchia et al. 2017)
Chilean Mestizo (253)	319	0.630	187	0.370	112	44.3	95	37.5	46	18.2	9.539	(Roco et al. 2012)
Brazilians (742)	1155	0.778	329	0.222	456	61.4	243	32.7	43	57.9	1.931	(Oliveira et al. 2015)
Puerto Ricans (104)	166	0.798	42	0.202	68	65.4	30	28.8	6	5.8	1.146	(Harrison et al. 2024)
East Asian population (504)	575	0.570	433	0.430	166	32.9	243	48.2	95	18.8	0.132	(Harrison et al. 2024)
South Asian population (489)	646	0.661	332	0.339	218	44.6	210	42.9	61	12.5	0.879	(Harrison et al. 2024)
European population (503)	898	0.893	108	0.107	399	79.3	100	19.9	4	0.8	0.699	(Harrison et al. 2024)

f: frequency; χ^2: Pearson Chi-square test, significance when $p < 0.05$, for Peruvians current study vs. other populations, and American population vs. other regional places; HWE: Hardy-Weinberg equilibrium; Ref. Reference.

which indicates that the studied samples of Peruvians are not in HWE, and this is due to their genetic derivation and the mechanism of evolution that changes over several generations due to chance, mutations, internal migrations of Peruvians, and the mixture that has been generated through the years since the first arrival of the ancestors (Alvarado et al. 2021b, 2023); therefore, the frequencies of allelic variants in the world are different (Zanger et al. 2004).

Current medicine is 4P based on predictive, preventive, personalized, and participatory medicine (Alonso et al. 2019; Slim et al. 2021); through predictive medicine, the genetic variants of *CYP1A1* and the null genotype *GSTM1* that are associated with the risk of different types of cancer should be studied, and through preventive medicine, the minimum consumption of roasted meats (Bulanda and Janoszka 2023), roasted turkey, beef salami, smoked ham and other processed foods containing polycyclic aromatic hydrocarbons (PAHs) such as benzopyrene, phenanthrene, anthracene and fluorene (Cheng et al. 2021); also avoid exposure to chemical compounds generated by ignition of wood (Satinder et al. 2017) and continue promoting non-consumption of tobacco, as they are considered mutagenic and carcinogenic compounds (Settheetham-Ishida et al. 2020). In various studies, it has been proposed that PAHs, persistent organic pollutants (POPs), environmental chemicals, and endogenous compounds bind to the aryl hydrocarbon receptor (AHR) to generate toxic effects and induce the expression of very active *CYP1A1* genes that encode enzymes that activate procarcinogenic compounds into carcinogens (Vogel et al. 2020).

However, the results of our research must be considered in the context of several limitations. The main reason is that it has only been studied in a small sample (n = 131) from the central coast of Peru and therefore is not representative for all Peruvians. To validate our study, it is necessary to increase the population sample and to be from the three regions of the country (coast, Andes, and jungle). In addition, other allelic variants of *CYP1A1* should be studied in populations and in cancer patients. All these limitations are being considered for future research. Despite these limitations, these findings could be relevant as scientific evidence to promote predictive and preventive medicine as part of the application of 4P medicine in Peru.

Conclusion

High prevalence of *GSTM1*0* and *CYP1A1*2A* (rs4646903) variants was observed in the central Peruvian coastal population, which can be considered as predictive genetic biomarkers for 4P medicine. Carriers of these genetic variants appear to have an active phase I metabolism, along with no activity of phase II conjugation, which could increase the risk of procarcinogen activation. Additionally, published studies showing a significant association with cervical cancer and other types of cancer were reviewed.

Likewise, differences were identified in the frequency of the *GSTM1*0* and *CYP1A1*2A* rs4646903 alleles among Peruvians with diverse ancestry: Latin American, Spanish, African, and East Asian (Chinese and Japanese). These variations can be attributed to natural evolution and genetic mixing that occurred over the years since the arrival of these populations to Peru. However, additional observational and case-control studies are required to validate these findings.

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Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that experiments on humans or human tissues were performed for the present study.

Informed consent from the humans, donors or donors' representatives: The Research Ethics Committee of the National University San Luis Gonzaga of Ica approved the protocol and informed consent of the study through CEI-UNICA certificate N°023/09-2023.

The authors declared that no experiments on animals were performed for the present study.

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Data availability

All of the data that support the findings of this study are available in the main text.

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