



Socio-Historical Aspects and Pharmacogenomics of the Chimilas Narakajmanta Based on CYP2C19, NAT2 and HLA Genes

Aspectos socio-históricos y farmacogenómica de los Chimilas Narakajmanta con base en los genes CYP2C19, NAT2 y HLA

ENIO ARMANDO HERNANDEZ AGUIRRE

MD, MSc. Human Genetics. Universidad Cooperativa de Colombia, Santa Marta.

Research group "Science and Pedagogy" Faculty of Medicine.

enarbulaver@gmail.com

<https://orcid.org/0000-0003-1196-3956> ID Scopus 57197726151

MARIA ROSA BALDVINO DIAZ

Microb. MSc Biomedical Sciences. Universidad Libre de Barranquilla. Bacteriology Program Director.

mbaldovino@gmail.com

<https://orcid.org/0000-0003-4189-5309>

ISIS ARIAS MADERA

Biol. MSc. Sciences with emphasis on Genetics. Fundación Universidad del Norte, Barranquilla.

isis.ariasm@gmail.com

<https://orcid.org/0000-0003-2188-9542>



Abstract

The Chimila (Ette Ennaka) are known for having resisted Spanish conquest without ever being fully subjugated. Their population declined dramatically in the early 20th century, leading some anthropologists to consider them nearly extinct. This study aimed to assess the health of the Ette community of Naara Kajmanta (Santa Marta), evaluate their capacity to metabolize medications via the CYP2C19 and NAT2 genes, and formulate a population hypothesis by identifying HLA alleles. Blood samples were collected with prior informed consent to conduct a complete blood count and to extract genetic material using molecular biology techniques. The results showed that all individuals possess the CYP2C19¹/CYP2C19² genotype, indicating that they are intermediate metabolizers. Regarding the NAT2 gene, 30% were classified as rapid acetylators, 41% as intermediate, and 29% as slow. The HLA alleles identified suggest an ancestral relationship with Indigenous peoples of the Pacific Islands and with groups from Peru, Bolivia, Panama, and Mexico.

Keywords: genes, indigenous health, genotype, Aboriginal, HLA antigens.

Resumen

Los chimilas se caracterizaron por ofrecer resistencia a los españoles durante la conquista sin llegar a ser sometidos. Su población disminuyó drásticamente a principios del siglo XX, siendo considerados en extinción por antropólogos. El objetivo de esta investigación fue indagar la salud de los chimilas de Naara Kajmanta (Santa Marta), conocer su capacidad de metabolizar medicamentos con los genes CYP2C19 y NAT2 y formular una hipótesis poblacional determinando los alelos HLA. Se tomaron muestras de sangre, con previo consentimiento, para elaborar un hemograma y obtener los genes mediante biología molecular. Los resultados mostraron que todos tienen el genotipo CYP2C19¹/CYP2C19² lo que indica que son metabolizadores intermedios, y con respecto al gen NAT2, el 30 % son acetiladores rápidos, el 41 % son intermedios y el 29 % son lentos. Los alelos HLA obtenidos sugieren una relación ancestral con aborígenes de las islas del Pacífico e indígenas del Perú, Bolivia, Panamá y México.

Palabras clave: genes, salud indígena, genotipo, aborigen, antígenos HLA.

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Introduction

The Ette people, the focus of this study, inhabit the village of Puerto Mosquito, southeast of the city of Santa Marta (Colombia), in the foothills of the Sierra Nevada de Santa Marta. Within this village lies the settlement of Naara Kajmanta, home to about 30 families and approximately 170 residents. The population size is not fixed and fluctuates due to patterns of mobility and kinship ties, which lead community members to move frequently between Naara Kajmanta and other settlements within the Issa Oristuna Indigenous *Resguardo*.

Mistakenly referred to as “Chimila” the Ette people are an Indigenous group of Amerindian origin whose language belongs to the Chibchan linguistic family. They identify themselves using the ethnonym *Ette*, which translates as “our people” or “the people themselves,” and speak *ette taara*, meaning “language of the people.” In November 1990, as a result of sustained Indigenous mobilization and research-based advocacy, the Colombian government formally established the Issa Oristunna Indigenous *Resguardo*, whose name can be rendered as the “Land of New Hope”. It spans parts of the municipalities of San Ángel, Ariguaní, and El Copey. Nearly two decades later, in 2009, the Constitutional Court of Colombia issued Auto 004, a legal directive aimed at protecting Indigenous peoples at risk of physical and cultural extinction due to the armed conflict and its related effects. This ordinance recognized 34 Indigenous groups as being in danger, including the Ette.

Brief History of the Ette People

We are the Ette Ennaka people, ancestral inhabitants of the central savannahs of the Colombian Caribbean. We are the children of Yaau, our creator and guide, who warns us of danger and prosperity through dreams. Thanks to him, we have survived five centuries of persecution, discrimination, and subjugation. Thanks to him, we continue to exist as a people with a vocation for the future (Plan de salvaguarda Pueblo Ette Ennaka).

Cosmic Origin of the Ette people

According to the Ette people, Mother Earth, known as *Yunnari Kraari*, is unclean, and her creator, Yaau, seeks to purify her. They recount that earlier worlds once existed but were destroyed. In the first world lived the *Ette Chorinda*, the “ancient people,” who fought among themselves and brought about their own ruin. At that time, the *waacha*—understood as whites, and likely the Spaniards—did not yet exist. Yaau destroyed this world first with fire, which some interpret as volcanic

eruptions, and later with a great flood, until only the sky and water remained. A few of the *Ette Chorinda* survived and repopulated the earth. In the new world that followed, the *waacha* appeared, and wars again erupted—both among the Ette themselves and between the Ette and the *waacha*. Once more *Yunnari Kraari* was drenched in blood, and Yaau cleansed her first with fire and then with water.

After this, Yaau descended from the sky with Numirinta, and from two maize cobs they created the Ette Ennaka, also called the Ette Takke. Yaau then created the animals, trees, and plants, and taught the people how to cultivate the land, while Numirinta introduced the arts of cooking and weaving, including the making of mochila bags and *chinchorros*, the traditional hammocks. Yaau remained where the sun rises, and Numirinta where the sun sets. Yet once again the *waacha* defiled the land with blood, polluting both the air and the waters. For this reason, the Ette continue to perform ceremonies to safeguard health, to protect Mother Earth, and to keep this world clean so that Yaau does not destroy it once more.

The Ette say that four worlds have already existed, and that a fifth is waiting to descend, known as the land of the *Ette Kooronda* (Niño Vargas, 2020). *Yunnari Kraari* is not only Mother Earth but also the grandmother of Yaau and Numirinta, who remain in this fourth world, the present one. The fifth world of the *Ette Kooronda* lies in the sky, awaiting its descent. In the stars exist other cities and villages, inhabited by Ette, *waacha*, and other Yaau, who are creators and guides. This final world will come down when the present one ends, and it will be free of violence and death. Beneath the current world lies another realm, located under the sea, described as a dark domain filled with wild beasts (Rodríguez Villamil, 2020).

The Intervention of Spain

Before the arrival of the Spaniards in 1492, the Ette people occupied the central region of what is now the Department of Magdalena and part of the present-day Department of Cesar. These were areas rich in water resources, which supported diverse forms of agriculture, hunting, and fishing. The Ette settled both in riverside towns and in mountainous areas. Their social organization was based on villages composed of *rancherías*—small clusters of family farms similar to those of the Wayúu—whose members were linked by kinship and maintained ceremonial practices to sustain the myth of their origins. The *rancherías* were interconnected by a network of paths that allowed families to regroup with others in the event of conflict with neighboring communities. This system provided the foundation for their effective resistance to Spanish incursions.

In Ette society everyone worked and there were no slaves or servants. The land belonged to the community as a whole, and authority was exercised by *caciques* who combined the roles of priest and war chief. Two names survive from that period, Cacique Upar and Cacique Tamalameque. This form of social organization, grounded in principles of freedom, autonomy, rejection of slavery, and the ancestral mandate to keep the land clean, sustained the Ette people's capacity to resist both the Spanish and other groups well into the twentieth century (Rey Sinning, 2009).

By the seventeenth century the Spanish conquest was well underway. During the previous two centuries, the Ette people had resisted Spanish incursions through a form of guerrilla warfare. They burned the estates of Europeans who settled near their lands and disrupted trade and navigation along the Magdalena River, hampering the supply of goods to Santa Marta and Cartagena and moderately affecting the colonial economy. However, the relentless Spanish offensives forced the Ette to occupy new territories beyond their earlier domain. This prolonged conflict also drew in other groups, including the Orejones, some Arawak communities, and enslaved Africans who had escaped from the Spaniards. Coalitions with these groups appear to have been crucial for Ette survival. By the eighteenth century much of the region had become depopulated, and the Spanish established settlements in the forests. These settlements, protected by garrisons, further isolated the Indigenous peoples and intensified pressure on the Ette. The final decades of the eighteenth century and the early years of the nineteenth proved devastating for them, although their struggle persisted throughout the nineteenth century.

Independence from Spain

During the wars of independence from Spain, the Ette people were gradually subdued and confined to small enclaves. After independence, however, their lands came under capitalist exploitation. Many Ette sought refuge in the mountains of Magdalena, particularly in the regions of San Ángel, the Serranía del Perijá, along the Ariguaní River, and around Pivijay, while some established contact with Arawak groups. Scholars have suggested that the names of several towns, streams, and rivers in the region may derive from the word *Ette* (historically rendered as *Chimila*), including Chivolo, Chilloa, La China, La Chiespere, and Chimichagua (Rey Sinning, 2009).

Smallpox epidemics in 1782 and 1854, along with the displacement caused by capitalist exploitation, drastically reduced the Ette population. Historian José Alarcón of Santa Marta notes that by 1854, only around 200 Ette individuals remained

in the vicinity of Pivijay, describing them as “meek,” markedly different from their ancestors (Alarcón and Valdeblánquez, 1963). In contrast, a 1778 report by Antonio de Narváez y Latorre, then governor of the provinces of Santa Marta and Riohacha, estimated the Ette population at approximately 10,000 (Uribe, 1987).

In 1915, the Swedish anthropologist Gustav Bolinder, accompanied by an Indigenous guide, departed from a village in the Upar Valley (present-day Valledupar) and ventured into the forests near the Ariguaní River. There, he encountered only two huts inhabited by two women, two men, a young boy, and an infant. The treatment of these Ette individuals was marked by distrust, and the following day, Bolinder and his companion were asked to leave. When he returned in January 1920, this time better prepared, residents of Fundación informed him that only 14 Ette people remained in the area. These individuals, reportedly having intermarried with Creoles, were said to be living in a village between Fundación and the Magdalena River. Revisiting the banks of the Ariguaní River, where he had been five years earlier, Bolinder found the two original huts burned. Nearby, he encountered two more settlements—one with eight huts and another with two—most of which were uninhabited. The ten Ette individuals he met there were visibly distressed by the discovery of their refuge.

Bolinder noted that these individuals showed clear signs of malnutrition and had bodies covered with wounds. All of them exhibited bluish patches on their skin, consistent with a disease locally known as *carate* or *jovero*. He observed that this illness was also common among Arawak groups, the Goajiro and Motilón peoples, as well as among mulatto populations living in the lowlands and forests of the Magdalena region. According to the Ette, the disease originated through sexual contact and appeared in children from a young age, which could suggest a hereditary or congenital etiology. At the time, their diet was based primarily on maize and sweet cassava.

Drawing on evidence such as hut construction (Figure 2), body painting, ceramic techniques, subsistence practices, and language, Bolinder argued that the Ette shared cultural ties with Indigenous groups of southern Costa Rica and northwestern Panama. He also noted affinities with Indigenous peoples of the Caribbean and southern Central America, particularly in social traits such as warfare and aggressiveness. Bolinder published his research in both German and Swedish, and in it he described the Ette as a dying people condemned to extinction (Bolinder, 1987). Prior to his 1915 expedition, the Magdalena region had experienced

outbreaks of measles and a flu-like illness (possibly influenza?), which may have contributed to the drastic population decline of the Ette.

Most classifications place the Ette language within Colombia's Chibchan linguistic family. However, the ethnographic research conducted by Gerardo Reichel-Dolmatoff among the Ette people (Reichel, 1946; 1947), along with the absence of more recent ethnolinguistic studies, casts doubt on this classification (Uribe, 1987).



Source: Gustaf Bolinder (1921, p. 203).

Figure 1. One of the last Ette survivals, historically referred to as Chimila



Source: Ette Ennaka Village Safeguard Plan (p.11). Ministry of the Interior.

Figure 2. “Case et indiens Chimilas” by E. Gotorbe. *Le tour du monde*, 1898, p. 4G3

In addition to Bolinder, other anthropologists predicted the extinction of the Chimila. In his book, Bolinder wrote: “The last independent remnants of a once large and powerful tribe” lived in misery, surviving on meager crops and scarce hunting, with limited opportunities to find partners to ensure future descendants. Surrounded by mestizos and land-hungry enterprises that had begun destroying the forests, they were forced to hide in caves and in the dense thickets of the *manigua*, perhaps explaining why they were difficult to locate. For most ethnic groups on Earth, the universe must exist in a state of balance; for the Ette people, the universe has a beginning and an end, and in the course of this process, natural catastrophes are normal events that bring about the annihilation of humanity, followed by its rebirth from the earth. This extinct Ette group may correspond to the Ette Chorinda of the second or third earth (“the ancient people”), and from these survivors, the Ette Ennaka or Takke (“new people”) would emerge. For this reason,

some historians argue that the Ette Ennaka are mistakenly referred to as Chimila (Niño Vargas, 2010).

From State Abandonment to Recognition: The Role of the Colombian Government

Starting in 1920, the forests of the Magdalena region began to be exploited for timber extraction and for clearing land for cattle ranching. The few Ette individuals who had remained hidden and isolated were eventually subjected to the authority of the *waacha* (non-Indigenous outsiders) and mestizos, working as laborers on the newly established farms. However, the constant buying and selling of land prevented them from achieving any form of stability, dignified labor, or social organization. They were forced to move from place to place. For the Ette, the destruction of the forest signifies the destruction of *Naara Kajmanta* (the skin of Mother Earth).

In 1940, the Colombian government granted the multinational company Shell 405,287 hectares for oil exploration and exploitation, a concession that included the Sabana de San Ángel and El Difícil. This triggered an increase in the white and mestizo population and a corresponding reduction of the ancestral territory of Indigenous peoples, deepening social, cultural, and spiritual disruption. The oil well dried up by 1980 (Rodríguez Villamil, 2020). Between 1946 and 1960, Ette refuges were attacked by ranchers, who burned settlements and forced their inhabitants to serve as laborers on their estates under the feudal *terraje* system. By 1989, the Ette were fragmented, working on farms across the Ariguaní plain between Monte Rubio and El Difícil.

In their struggle to reclaim their rights, the Ette Ennaka received support from various governmental and non-governmental organizations addressing the longstanding challenges faced by the community. Their advocacy led the Colombian Institute for Agrarian Reform (Incora) to grant them, through Resolution 075 of November 19, 1990, a total of 1,764 hectares as an protected Indigenous land, known in Latin America as a *resguardo*. This included 280 hectares of the La Sirena farm, donated to the Ette by its former owner, Alejandro Manco, upon his death. The territory was named *Issa Oristunna* (“New Hope”) and is located between the municipalities of Sabanas de San Ángel and Las Mulas. The community soon began to reorganize around a cabildo, which enabled dispersed Ette individuals to return and settle. As the population grew, they formally requested an expansion of the *resguardo*, and on April 2, 1992, they were granted an additional property, La

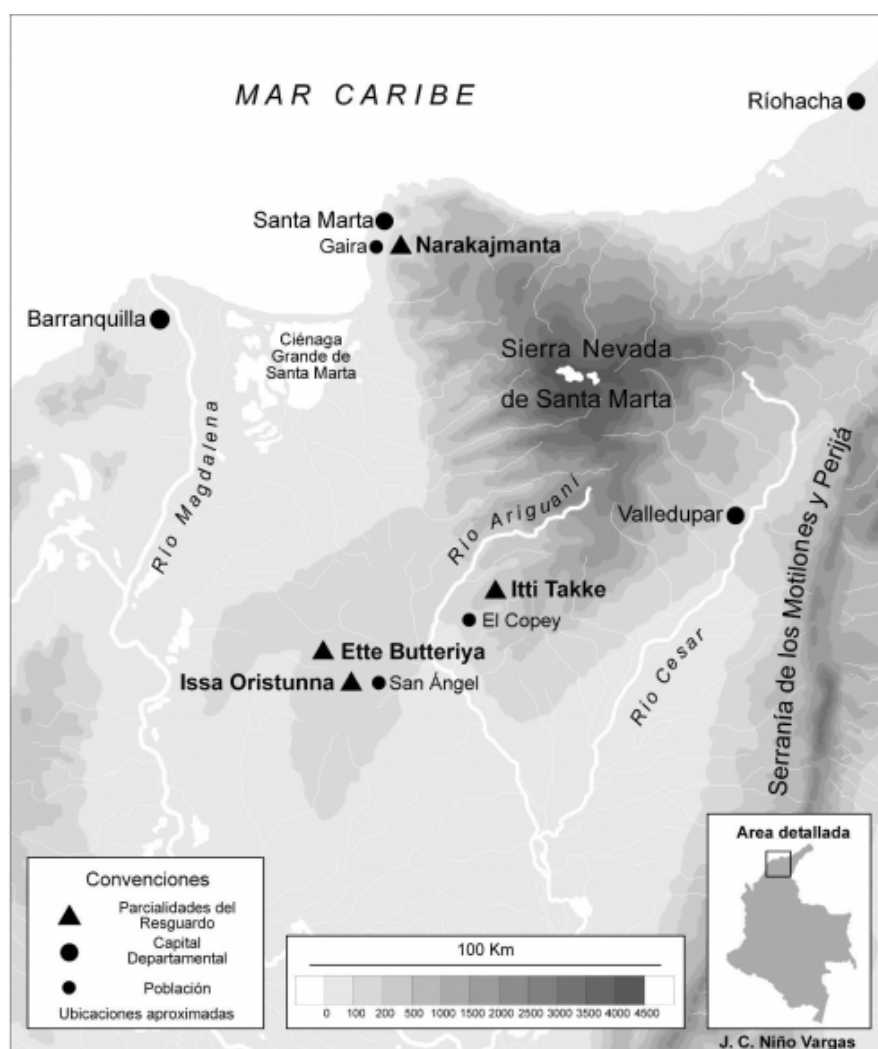
Alemania, located in the Las Mulas district of the municipality of Plato. This territory was renamed *Ette Butteriya* (“own thought”).

Today, the Ette live primarily from agriculture, and dreams and myths continue to play a central role in their culture (Rodríguez Villamil, 2020). With Resolution 1410 of September 30, 2005, the Ministry of Environment, Housing, and Territorial Development authorized a further expansion of their land. According to the Colombian Institute of Rural Development (Incoder), the Ette *resguardo* now covers a total of 1,828 hectares and 515 square meters. The Ette currently represent just 0.065% of Colombia’s Indigenous population, estimated at 1,392,693 people, according to DANE (*Diagnóstico de la situación del pueblo indígena Chimila–Ette Ennaka*).

In 1997, due to public order disturbances, several Ette families were displaced from the *resguardos* in the municipality of Sabanas de San Ángel. A significant number sought refuge in the city of Santa Marta, where they remained dispersed and in urgent need of support. By the year 2000, efforts to reorganize and relocate these families within the district of Santa Marta had begun.

To achieve this, we began to organize and knock on doors to secure resources and acquire a piece of land where we could live, and where our children could speak our own language, because our traditions were being lost and no one was hearing the *ette taara* anymore. (*Diagnóstico de la situación del pueblo indígena Chimila–Ette Ennaka*).

In 2002, with the approval of the *cabildo* governor of the *resguardo*, the U.S.-based company Merck Sharp & Dohme purchased a piece of land and transferred it to the displaced Indigenous population. Today, the property is known as *Naara Kajmanta* (“skin of Mother Earth”) and is located near the *corregimiento* of Gaira. This community is considered a resettlement site, covering an area of 92 hectares and home to 164 people. It now forms an integral part of the Issa Oristunna *resguardo* (see Map 1).



Source: Retrieved from <https://doi.org/10.4000/jsa.13726>.

Map 1. Ette Indigenous Resguardos

Health of the Ette People

The Ette notion of health is dual and holistic, encompassing both material and immaterial dimensions, as well as ethical and moral principles that guide individual and collective conduct. These dimensions must remain in balance. Health is understood as the result of an interwoven set of environmental, social, and cultural factors, all of which are embodied in the territory. The equilibrium among these elements is essential to achieving a state of well-being. When this balance is disrupted—which, according to the Ette, is often caused not only by internal factors but also by the influence of broader national society—illness emerges. Disease,

then, is not simply the result of internal imbalance within Indigenous communities, but also a consequence of external pressures on their territories, beliefs, and practices. Historically, various models have been proposed to conceptualize disease. One such framework is offered by Canguilhem, who identifies three conceptions: the ontological, the dynamic, and the social (Moreno-Altamirano, 2007).

The Ette's traditional health systems have been preserved through the knowledge and practices of elders, *sobanderos*, and healers, who continue to apply ancestral medicine to address illness within the cultural and communal context. These practitioners draw on Indigenous knowledge systems to diagnose and treat disease in ways that are grounded in Ette worldviews. In the city of Santa Marta, the Ette Ennaka Gonawindua Indigenous Health Provider Institution (IPS) reports on health conditions within the *resguardo*, despite lacking a centralized database. Among the most prevalent health issues are malnutrition—especially in children under five—skin diseases affecting both children and adults, acute diarrheal disease (more frequent in children), zoonotic infections (particularly among children), dengue, and parasitic infections. The health conditions experienced by the Ette are closely linked to their environmental surroundings and to traditional understandings of illness, including cultural syndromes and local treatment methods. State and municipal health programs, however, often take a welfare-based approach that fails to recognize the Ette's current living conditions or cultural perspectives. In contrast, local universities have undertaken research efforts aimed at understanding these health challenges from their roots.

The continued practice of Ette health traditions reflects their cultural struggle for recognition and the defense of their own system in the face of biomedical models that seek to homogenize health programs. These biomedical approaches are promoted by various actors attempting to exert influence over Ette society, knowledge systems, and territories. Health and illness are not merely conditions or states of the individual, understood in terms of organic function or personality; they are also culturally and institutionally recognized phenomena embedded within the social structures of each society (Moreno-Altamirano, 2007).

Genetic Markers Analyzed in Naara Kajmanta

Our research group at the Universidad Cooperativa de Colombia, based in Santa Marta, in collaboration with the Genetics and Molecular Medicine research group at Universidad del Norte (Barranquilla), conducted a study among various Indigenous groups of the Colombian Caribbean. The aim was to analyze the genes

CYP2C19 and NAT2, which code for enzymes involved in drug metabolism, and the HLA genes, which are related to population genetics. One objective of this study was to determine the polymorphisms of these genes in order to identify the different metabolizer types within these ethnic groups and to infer their physiometabolic responses to medications processed by these enzymes. Depending on an individual's ability to metabolize xenobiotics, certain drugs may produce adverse effects or prove ineffective.

A second objective was to identify HLA molecules, which play a key role in generating immune responses against pathogens and in monitoring the production of peptides within cells—functioning as a kind of quality control system. HLA analysis is also widely used in population genetics and anthropology to help determine, among other things, the ancestral origins of human groups. This article presents the analysis of the genetic results obtained from the Ette population living in the Naara Kajmanta *resguardo* (NK).

The research team contacted the *cabildo* of the Ette Ennaka in the Naara Kajmanta *resguardo* and agreed to carry out a health brigade-style visit to examine individuals with symptoms of illness and to assess overall health status through complete blood counts (CBCs). Using the same blood samples, and with informed consent approved by the Bioethics Committee for Research at the Universidad Cooperativa de Colombia, Santa Marta campus (Resolution 024 of 2010), participants authorized the collection of blood and the extraction of DNA for the analysis of the CYP2C19, NAT2, and HLA genes.

The team conducted three visits in total. During the first, they coordinated the work plan with community leaders. For the second, they returned with a health team—including two registered nurses, medical students, and supplies requested by the community to meet specific needs. During this visit, they carried out medical examinations for several children and adults and collected venous blood samples after obtaining signed consent. The third visit focused on delivering the CBC results, distributing the appropriate medications based on those results, and providing protective skin lotions. Figures 3 and 4 document the visit.



Source: Photo taken by project researchers.

Figure 3. A Chimila child, examined



Source: Photo taken by project researchers.

Figure 4. Signed consent and sample collection

Methodology

A total of 4 ml of venous blood was collected from each participant and placed in EDTA test tubes. Genomic DNA was isolated from lymphocytes using the UltraClean™ Blood kit (Mo-BIO). The CYP2C gene cluster is located at 10q23.33 and includes CYP2C18, CYP2C19, CYP2C9, and CYP2C8, all of which encode enzymes involved in the hepatic metabolism of approximately 25% of commonly prescribed medications. CYP2C19 alone metabolizes around 15% of the drugs approved by the

U.S. Food and Drug Administration (FDA). This gene has three principal alleles—CYP2C19¹*, CYP2C19²*, and CYP2C19³*—which are distinguished by polymorphisms in exons 4 (G636A) and 5 (G681A). To identify the different alleles, a PCR method using confronting two-pair primers (PCR-CTPP) was employed, with four forward and four reverse primers. This technique produced the following bands: 131 bp for 681G (*allele 1), 105 bp for 681A (*allele 2), a shared band of 191 bp for *alleles 1 and 2, 377 bp for 636G (*allele 1), 255 bp for 636A (*allele 3), and a shared band of 597 bp for *alleles 1 and 3.

The NAT2 gene is located at 8p22, and more than 100 allelic variants have been identified across human populations. These variants include one to four nucleotide substitutions at positions 191, 282, 341, 434, 481, 590, 803, 845, and 857. Four main NAT2 alleles are recognized. NAT2⁴* is the wild-type allele, while NAT2⁵*, NAT2⁶*, and NAT2⁷* are mutant alleles associated with single nucleotide polymorphisms (SNPs) at 481C>T, 590G>A, and 857G>A, respectively. These three SNPs—C481T (rs1799929), G590A (rs1799930), and G857A (rs1799931)—were analyzed by real-time polymerase chain reaction (qRT-PCR) using TaqMan allelic discrimination assays C_1204092_20, C_1204091_10, and C_572770_20, respectively, on an ABI PRISM 7500 system (Applied Biosystems). These assays identify the four main NAT2 alleles: NAT2⁴*, NAT2⁵*, NAT2⁶*, and NAT2⁷*.

The HLA genes form part of the major histocompatibility complex (MHC) and are located at locus 6p21.3, spanning approximately 3×10^6 base pairs. These genes were typed using the method developed by Yoshiki Itoh and collaborators, which combines PCR and sequencing. A protocol based on sequence-specific oligonucleotide probes (SSOP) was implemented using the Luminex 100 x MAP dual-laser flow cytometry system to quantify fluorescently labeled oligonucleotides bound to color-coded microspheres. In total, 48 probes were used for the HLA-A locus, 61 for HLA-B, 34 for HLA-C, and 51 for HLA-DRB1 and DQB1.

Results

The studied population consisted of 47 individuals from the Ette Ennaka people (Table 5), 51% of whom were men and 49% women. The samples were selected based on the characteristic phenotypic traits of this population, its geographic location, the preservation of traditional activities and rites in accordance with their sociocultural condition, and their original cultural behavior during the pre-Hispanic period. Based on the Ette people's accounts of their cosmic origin, it is deduced that they have experienced three historical events of near-extinction, possibly due

to natural forces, followed by demographic resurgence guided by their beliefs and the internal strength of their spirituality. A fourth event of near-extinction was caused by human intervention, leading to the emergence of the present-day Ette community. According to their worldview, the current Earth will one day come to an end, giving rise to a fifth Earth in which harmony and peace will prevail.

1) The CYP2C19 Gene

The CYP2C19 gene has three recognized alleles: CYP2C19^{*}1, 2, and 3. Among the Indigenous population of the Ette ethnic group, alleles CYP2C19^{*}1 and CYP2C19^{*}2 were found in 47 healthy individuals. The frequency of the functional native allele CYP2C19^{*}1 was 50%, and that of the non-functional allele CYP2C19^{*}2 was also 50%. This indicates that all individuals analyzed in **Naara Kajmanta** have the CYP2C19^{*}1/CYP2C19^{*}2 genotype and are therefore classified as intermediate metabolizers. The results are presented in Tables 1 and 2 (Hernández et al., 2013).

Table 1. Allele frequencies of the CYP2C19 gene in the Naara Kajmanta population

Alleles	No. of persons	Frequency %
CYP2C19 [*] 1	47	100
CYP2C19 [*] 2	47	100
CYP2C19 [*] 3	0	0

Source: Hernández et al. (2013).

Table 2. Genotypic frequencies of the CYP2C19 gene and metabolizer type

Genotype	N. individuals	Frequency %	Metabolizer Type
CYP2C19 [*] 1*1	0	0	Quick
CYP2C19 [*] 1*2	47	100	Intermediate
CYP2C19 [*] 1*3	0	0	Intermediate
CYP2C19 [*] 2*2	0	0	Poor
CYP2C19 [*] 3*3	0	0	Poor

Source: Hernández et al. (2013).

2) The NAT2 Gene

Although multiple alleles have been reported for this gene, the most frequent ones were analyzed. The NAT2^{*}4 allele is the most common across all human popula-

tions and is therefore considered the wild-type or original allele; it has normal enzymatic function. In contrast, the other alleles listed in the table exhibit reduced function. The enzymes encoded by these genes metabolize drugs through acetylation, including antibiotics such as Isoniazid and Rifampicin, which are first-line treatments for tuberculosis. The results for the NAT2 gene are presented in Tables 3 and 4 (Arias et al., 2014).

Table 3. The 4 main alleles of NAT2* and the percentage of each allele found in the Naara Kajmanta population

ALLELE	NAT2*4	NAT2*5	NAT2*6	NAT2*7
SNP polymorphism identifying each allele				
C481	C	T	C	C
G590	G	G	A	G
G857	G	G	G	A
Percentage (%) of each allele in Naara Kajmanta				
Chimila	51.6	17.6	6.6	24.2

Source: Arias et al. (2014).

Table 4. Genotypes found in Naara Kajmanta and their percentage in the population

NAT2* gene genotypes and types of acetylators based on genotype								
Genotype	NAT2* 4/4	NAT2* 4/5	NAT2* 4/6	NAT2* 4/7	NAT2* 5/5	NAT2* 5/6	NAT2* 5/7	NAT2* 7/7
Acetylator	Quick	Intermediates			Slow			
Chimila	29.5%	9.1%	9.1%	22.7%	6.8%	4.5%	9.1%	9.1%

Source: Arias et al. (2014).

3) HLA Genes

These genes determine the HLA molecules of the same name. Class II molecules activate the immune response to fight external pathogens, while Class I molecules present proteins produced by cells as part of an internal surveillance mechanism. Research has also highlighted the relevance of these molecules in understanding ancestral origins, population evolution, and migration patterns. Table 5 presents the HLA gene results for the Naara Kajmanta population (47 Ette individuals). The table was compiled using data from the following open-access source: www.allelefrequencies.net No3426 (Arnaiz-Villena et al., 2018).

Table 5. HLA Haplotypes. Chimila Amerindians (Naara Kajmanta), Colombia

1	A * 02: 01	A * 24: 02	B * 35: 43	B * 51: 24	C * 01: 02	C * 15: 02	DRB1 * 03: 02	DRB1 * 04: 07	DQB1 * 03: 01	DQB1 * 03: 04
2	A * 24: 02	A * 24: 02	B * 40: 09	B * 51: 10	C * 03: 04	C * 15: 02	DRB1 * 03: 02	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
3	A * 24: 02	A * 30: 01	B * 15: 47	B * 35: 43	C * 01: 02	C * 02: 10	DRB1 * 04: 07	DRB1 * 15: 03	DQB1 * 03: 02	DQB1 * 06: 02
4	A * 23: 01	A * 23: 01	B * 08: 01	B * 51: 10	C * 07: 01	C * 15: 02	DRB1 * 04: 07	DRB1 * 11: 01	DQB1 * 03: 02	DQB1 * 06: 02
5	A * 02: 01	A * 24: 02	B * 51: 10	B * 51: 10	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
6	A * 24: 03	A * 29: 02	B * 39: 09	B * 45: 01	C * 06: 02	C * 07: 05	DRB1 * 08: 04	DRB1 * 15: 01	DQB1 * 04: 02	DQB1 * 06: 02
7	A * 02: 01	A * 02: 01	B * 51: 10	B * 51: 46	C * 15: 02	C * 15: 02	DRB1 * 03: 02	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
8	A * 24: 02	A * 24: 02	B * 51: 10	B * 51: 10	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
9	A * 24: 02	A * 68: 01	B * 39: 05	B * 51: 10	C * 03: 04	C * 15: 02	DRB1 * 04: 04	DRB1 * 04: 17	DQB1 * 03: 02	DQB1 * 04: 02
10	A * 68: 01	A * 68: 01	B * 35: 43	B * 39: 01	C * 01: 02	C * 03: 04	DRB1 * 04: 04	DRB1 * 04: 17	DQB1 * 03: 02	DQB1 * 04: 02
11	A * 24: 02	A * 68: 23	B * 35: 43	B * 51: 10	C * 15: 02	C * 01: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 03
12	A * 24: 02	A * 24: 02	B * 35: 43	B * 51: 10	C * 01: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 03
13	A * 29: 02	A * 31: 08	B * 44: 03	B * 51: 10	C * 15: 02	C * 16: 01	DRB1 * 04: 07	DRB1 * 07: 01	DQB1 * 02: 02	DQB1 * 03: 02
14	A * 24: 02	A * 24: 02	B * 08: 50	B * 51: 10	C * 07: 01	C * 15: 02	DRB1 * 03: 01	DRB1 * 04: 07	DQB1 * 02: 01	DQB1 * 03: 02
15	A * 01: 01	A * 02: 58	B * 08: 01	B * 35: 44	C * 01: 02	C * 07: 01	DRB1 * 03: 02	DRB1 * 15: 01	DQB1 * 03: 01	DQB1 * 06: 02
16	A * 24: 02	A * 68: 01	B * 35: 43	B * 51: 10	C * 01: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
17	A * 02: 46	A * 02: 87	B * 51: 10	B * 51: 10	C * 15: 02	C * 15: 02	DRB1 * 03: 02	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
18	A * 24: 02	A * 68: 01	B * 35: 43	B * 51: 10	C * 01: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
19	A * 24: 02	A * 24: 02	B * 51: 10	B * 51: 10	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
20	A * 02: 04	A * 24: 02	B * 51: 10	B * 78: 02	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 17	DQB1 * 03: 02	DQB1 * 04: 02
21	A * 24: 02	A * 30: 01	B * 15: 47	B * 51: 10	C * 02: 10	C * 15: 02	DRB1 * 04: 07	DRB1 * 15: 03	DQB1 * 03: 02	DQB1 * 06: 02
22	A * 24: 03	A * 68: 23	B * 35: 43	B * 38: 01	C * 01: 02	C * 12: 03	DRB1 * 04: 07	DRB1 * 13: 01	DQB1 * 03: 02	DQB1 * 06: 03

Continue...

23	A * 24: 03	A * 24: 03	B * 38: 01	B * 51: 10	C * 12: 03	C * 15: 02	DRB1 * 04: 07	DRB1 * 13: 01	DQB1 * 06: 03	DQB1 * 06: 03
24	A * 02: 93	A * 24: 03	B * 35: 68	B * 51: 10	C * 04: 01	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
25	A * 24: 02	A * 24: 02	B * 51: 10	B * 51: 10	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
26	A * 02: 04	A * 68: 01	B * 35: 43	B * 78: 02	C * 01: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 17	DQB1 * 03: 02	DQB1 * 04: 02
27	A * 01: 01	A * 24: 02	B * 08: 50	B * 57: 01	C * 07: 01	C * 07: 01	DRB1 * 01: 01	DRB1 * 03: 01	DQB1 * 02: 01	DQB1 * 05: 01
28	A * 02: 04	A * 24: 02	B * 51: 10	B * 78: 02	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 17	DQB1 * 03: 02	DQB1 * 04: 02
29	A * 02: 04	A * 24: 02	B * 51: 10	B * 78: 02	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 17	DQB1 * 03: 02	DQB1 * 04: 02
30	A * 24: 02	A * 24: 02	B * 40: 09	B * 51: 10	C * 03: 04	C * 15: 02	DRB1 * 03: 02	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
31	A * 24: 03	A * 68: 01	B * 35: 43	B * 39: 04	C * 01: 02	C * 07: 27	DRB1 * 04: 07	DRB1 * 08: 04	DQB1 * 03: 02	DQB1 * 04: 02
32	A * 24: 02	A * 30: 02	B * 35: 31	B * 51: 10	C * 03: 04	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 03
33	A * 29: 02	A * 68: 01	B * 35: 43	B * 45: 01	C * 01: 02	C * 06: 02	DRB1 * 04: 07	DRB1 * 15: 01	DQB1 * 03: 02	DQB1 * 06: 02
34	A * 24: 02	A * 26: 01	B * 07: 08	B * 51: 10	C * 07: 01	C * 15: 02	DRB1 * 04: 07	DRB1 * 15: 01	DQB1 * 06: 02	DQB1 * 06: 02
35	A * 29: 02	A * 68: 01	B * 39: 01	B * 45: 01	C * 03: 04	C * 06: 02	DRB1 * 04: 04	DRB1 * 15: 01	DQB1 * 04: 03	DQB1 * 06: 02
36	A * 02: 01	A * 24: 02	B * 15: 01	B * 40: 09	C * 01: 02	C * 03: 04	DRB1 * 03: 02	DRB1 * 16: 02	DQB1 * 03: 01	DQB1 * 03: 01
37	A * 24: 02	A * 31: 01	B * 39: 13	B * 51: 10	C * 17: 01	C * 15: 02	DRB1 * 04: 07	DRB1 * 08: 07	DQB1 * 03: 02	DQB1 * 04: 02
38	A * 24: 02	A * 30: 02	B * 14: 02	B * 51: 10	C * 08: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 15: 03	DQB1 * 03: 02	DQB1 * 06: 02
39	A * 24: 02	A * 74: 01	B * 15: 03	B * 35: 43	C * 01: 02	C * 02: 10	DRB1 * 04: 07	DRB1 * 11: 02	DQB1 * 03: 02	DQB1 * 03: 02
40	A * 24: 02	A * 24: 02	B * 35: 43	B * 51: 10	C * 01: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
41	A * 24: 02	A * 24: 02	B * 48: 01	B * 51: 10	C * 08: 01	C * 15: 02	DRB1 * 04: 07	DRB1 * 14: 06	DQB1 * 03: 02	DQB1 * 03: 02
42	A * 24: 02	A * 68: 16	B * 39: 01	B * 40: 09	C * 03: 04	C * 03: 04	DRB1 * 03: 02	DRB1 * 04: 04	DQB1 * 03: 01	DQB1 * 04: 02
43	A * 24: 02	A * 24: 02	B * 51: 10	B * 51: 10	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 02
44	A * 02: 01	A * 24: 03	B * 15: 01	B * 40: 89	C * 01: 02	C * 03: 04	DRB1 * 03: 02	DRB1 * 16: 02	DQB1 * 03: 01	DQB1 * 03: 01
45	A * 24: 02	A * 24: 02	B * 08: 01	B * 51: 10	C * 07: 01	C * 15: 02	DRB1 * 03: 07	DRB1 * 04: 07	DQB1 * 02: 01	DQB1 * 03: 02

Continue...

46	A * 32: 01	A * 68: 01	B * 15: 17	B * 39: 05	C * 03: 04	C * 17: 01	DRB1 * 04: 07	DRB1 * 13: 01	DQB1 * 06: 04	DQB1 * 06: 04
47	A * 24: 02	A * 24: 02	B * 51: 10	B * 51: 10	C * 15: 02	C * 15: 02	DRB1 * 04: 07	DRB1 * 04: 07	DQB1 * 03: 02	DQB1 * 03: 18

Source: Arnaiz-Villena et al. (2018). In worldwide populations. Open access genotyping data.

Table 6. HLA alleles with the highest frequency found in the population

HLA-A	HLA-B	HLA-C	HLA-DRB1	HLA-DQB1
A*24:02 (48,9%)			DRB1*04:07 (54.2%)	
A*68:01 (10,6%)	B*51:10 (40,4%)	C*15:02 (46,8%)	DRB1*03:02 (9.5%)	DQB1*03:02 (54.2%)
A*24:03 (7,4%)	B*35:43 (13,8%)	C*01:02 (17%)	DRB1*04:17 (6.3%)	DQB1*04:02 (10.6%)
A*02:01 (6,3%)	B*40:09 (4,2%)	C*03:04 (11,7%)	DRB1*15:01 (5.3%)	DQB1*06:02 (10.6%)
A*02:04 (4,2%)	B*78:02 (4,2%)	C*07:01 (7%)	DRB1*04:04 (4.2%)	DQB1*03:01 (7.4%)
A*29:02 (4,2%)				

Source: own elaboration. Percentage based on the 94 alleles of each molecule in the population.

Table 7. Most frequent alleles and their relationship with other populations

Most frequent alleles in Naara Kajmanta	Presence of these alleles in other populations
A*24:02-B*51:10-C*15:02-DRB1*04:07- DQB1*03:02.	Mayos of the Gulf of Mexico and Pacific Ocean
A*24:02, B*35:43, C*01:02, DRB1*04:07, DQB1*03:02.	They are also found in Asia
A*68:01, B*35:43, C*01:02, DRB1*04:07, DQB1*03:02	Mayas, Nahuas (Aztecs) and Uros (Lake Titikaka)
A*24:02, B*35:43, C*01:02, DRB1*04:07, DQB1*03:02.	Maya, Aymara and Quechua (Bolivia), Teeneks (Mexico), Lakota-Sioux (northern and central USA) and Jaidukama (Colombia-Panama border).
A*02:01, B*51:10, C*15:02, DRB1*04:07, BQB1*03:02	Quechua, Jaidukama and Lamas (northern Peru).
HLA-A*24:02 and HLA-C*01:02	High frequency in the Pacific islands.

Source: own elaboration.

The HLA-A24:02 allele was identified in 34 of the 47 Ette individuals (72.3%), including 12 homozygotes. This corresponds to a total of 46 alleles—homozygous and heterozygous—representing 48.93% of all HLA-A alleles in the population. The HLA-B51:10 allele accounted for 40.42% of HLA-B alleles, with 7 homozygotes identified. The HLA-C15:02 allele had a frequency of 46.8% and included 11 homozygotes. For the HLA-DRB104:07 allele, the frequency was 54.25%, with 13 individuals being homozygous. The HLA-DQB103:02

allele also represented 54.25% of HLA-DQB1 alleles, with 15 homozygotes found. The predominant haplotype in this population is: HLA-A24:02, HLA-B51:10, HLA-C15:02, HLA-DRB104:07, and HLA-DQB103:02.

4) Hemogram

The results of the hemogram conducted on the Naara Kajmanta population showed hemoglobin (Hb) levels ranging from 12 to 17.3 g/dL, with a mode of 13.3 g/dL. Hematocrit (Hct) values ranged from 36% to 52%, with a mode of 40%. Eosinophil counts varied significantly, ranging from 1% to 25%, with an average of 5%.

Discussion

The hemogram results indicate that the population does not suffer from anemia, and the values are consistent with the community's altitude relative to sea level. Eosinophils are blood cells associated with intestinal parasites and allergic reactions. During the medical examinations, we observed that many individuals walked barefoot, which facilitates the entry of parasite larvae through the soles and interdigital areas of the feet. Some individuals also presented with skin eruptions suggestive of scabies and/or residual effects of insect bites. During the third visit, we delivered the hemogram results, along with antiparasitic medications (mebendazole tablets and albendazole suspension) for two treatment cycles, scabies treatment lotions (crotamiton), and skin protection lotions (calamine), particularly for children. Preventive guidance was also provided.

The CYP2C19 and NAT2 genes produce enzymes that metabolize substances foreign to the body. Medications are chemical compounds foreign to our organism, so they must be metabolized and eliminated while performing their curative function. Ideally, they should “heal” without adverse reactions. The CYP2C19 gene, whose application in healthcare falls within the field of pharmacogenomics, can code for enzymes that eliminate the drug too quickly. In this case, the person is considered a rapid metabolizer (RM), and the medicine does not fulfill its function. If the person is a slow metabolizer (SM), the drug is not properly eliminated and begins to cause harm to the body—this is known as a secondary reaction. Ideally, a person should be an intermediate metabolizer (IM), allowing for drug elimination within a reasonable timeframe that enables its effect and avoids adverse reactions.

The enzymes encoded by the NAT2 gene function by acetylation; therefore, in this context, individuals are referred to as fast, intermediate, or slow acetylators.

In medical practice, the standard dosage is designed for IMs; dosages must be increased for RMs and decreased for SMs. In the human species, the main CYP2C19 genes are CYP2C19₁, *2, and *3; the principal NAT2 genes are NAT2₄, *5, *6, and *7. The CYP2C19₁ and NAT2₄ alleles are those that perform normal enzymatic functions. An RM has two normal-function alleles, while an SM has two alleles with impaired function. Therefore, the ideal scenario is to have one normal-function allele and one altered-function allele.

All 47 individuals from the Naara Kajmanta Ette population carry the CYP2C19₁ / CYP2C19₂ genotype and are classified as intermediate metabolizers (IM). This allows us to hypothesize that they can receive medications at standard dosages, with a low probability of adverse reactions. Some of the drugs metabolized by this gene are used in the treatment of gastritis, ulcers, convulsions, depression, malaria, cancer, and include certain antibiotics (Lazalde-Ramos, 2012). The frequency of the CYP2C19*2 allele in this Indigenous population is notably high (50%) compared to mestizo individuals (24%) and Afro-descendants (13%) in the Colombian Caribbean (Hernández et al., 2013). This allele has also been reported at a high frequency (31%) in the Tarahumara of Chihuahua, Mexico, who likewise exhibit the **CYP2C19₁/2 genotype with a frequency of 40.5%, indicating a possible genetic relationship in the distribution of CYP2C19 between the Ette of Colombia and the Tarahumara of Mexico (Salazar-Flores et al., 2012).

The NAT2 gene encodes the enzyme N-acetyltransferase 2, which is responsible for eliminating certain drugs from the human body, including Isoniazid, a first-line treatment for tuberculosis (TB). In humans, more than 100 variants (polymorphisms) of this gene have been identified, which result in enzymes with either normal or abnormal function. The most frequent normal-function allele is NAT2₄*, while the most common abnormal-function alleles are NAT2₅*, NAT2₆*, and NAT2₇*. With respect to the NAT2 enzyme, fast acetylators (FA) may eliminate the drug too quickly, reducing its therapeutic effect; slow acetylators (SA) are more susceptible to drug toxicity. Therefore, intermediate acetylation (IA) is considered optimal.

Tuberculosis disproportionately affects Indigenous populations, and one of the objectives of this study was to contribute to the understanding of genetic pharmacology in the Naara Kajmanta Ette population. The results showed that 29.5% of the Ette are fast acetylators, 40.9% are intermediate acetylators, and 29.5% are slow acetylators. In the event of TB treatment in this population, the likelihood of successful treatment with standard protocols is estimated at 41%, while 30% may

develop resistance, and another 30% may suffer adverse drug reactions (Arias et al., 2014; Hernández, 2016).

Table 6 shows the most frequent HLA alleles, while Table 7 presents a homology between the HLA alleles found in the Naara Kajmanta population and those identified in other populations, revealing a strong genetic (ancestral) relationship with other Amerindian groups. These include the Mayos from the Gulf of Mexico and the Pacific Ocean; the Nahuas of Mexico and Central America (Arnaiz-Villena et al., 2020a); the Uros, Aymaras, and Quechuas of Bolivia; and the Lamas from northern Peru (Arnaiz-Villena et al., 2020b). There is also a documented relationship with the Jaidukama people on the border between Colombia and Panama, as well as a strong genetic link between HLA-A24:02 and HLA-C01:02 and the Indigenous peoples of the Pacific Islands (Arnaiz-Villena et al., 2019; Arnaiz-Villena et al., 2020c). Bolinder, who visited the Ette in 1920, was thus correct in suggesting that they were related to the Indigenous peoples of Central America.

Reichel-Dolmatoff, in one of his articles, states that the Kogui do not acknowledge the Sierra Nevada de Santa Marta as their place of origin. Instead, they claim that 52 generations ago, their ancestors came from a land called *Mulkuaba*, located on the other side of the sea. This land caught fire, forcing them to flee between rivers of flame toward the ocean. They set out in nine canoes, led by *Xukulyexa* (“jaguar lord”), the son of *Kaxsata* (“lord of the earthquakes”), and after a long journey, they reached the Caribbean coast (Reichel-Dolmatoff, 1954). Physician Arturo Bermúdez (1977) reports the following:

The Kogui founded the town of *Kukulmeizi*, now known as Hukumeizi, and later expanded into the San Miguel Valley, where they established *Takina*. From their place of origin, they may have brought with them gold, coca, and knowledge of the textile arts. *Kuku* is the root of *Kukulkan*, the name given to the Aztec hero Quetzalcoatl in the Mayan language, which suggests that Aztec influence may have reached the Kogui indirectly—through mythical narratives.

According to Kogui oral tradition, a natural catastrophe occurred in their original homeland 52 generations ago (approximately 1,300 years ago), possibly involving earthquakes and a volcanic eruption, which forced them to cross the sea. This sea was likely the Atlantic Ocean, as they arrived at the Caribbean islands and the northern region of Colombia. The association of fire followed by only water seems to resonate with the mythical history of the Ette as well. However, analysis of the HLA molecules of the Ette reveals genetic links to Amerindian groups from

Peru, Bolivia, Panama, and Mexico—all located near the Pacific Ocean—and their most frequent HLA alleles are related to those found in Pacific Island populations. Recent DNA studies using modern genomic techniques are confirming this connection. A July 2020 publication in *Nature* (Ioannidis et al., 2020) investigated the genomic relationship between 807 individuals from 17 populations of the Indonesian islands and 15 Indigenous groups from the Pacific coasts of the Americas, and found conclusive evidence of contact between Polynesians and Native American individuals around the year 1200 CE. The authors state the following:

Our analyses strongly suggest that a single contact event occurred in eastern Polynesia, prior to the settlement of Rapa Nui, between Polynesian individuals and a group of Native Americans more closely related to the Indigenous inhabitants of present-day Colombia.

Other recent publications (2020–2021) based on genome analysis are linking contact between Pacific Islander aborigines and Indigenous peoples from northern Ecuador and Colombia.

Based on the ancestral history of the Ette people, it is possible to discern events triggered by natural catastrophes—phenomena that have similarly affected other peoples throughout human history. Yet humanity overcomes the obstacles of the life cycle and begins anew the eternal process of existence. These are not different lands, but rather distinct geographical environments on the same planet, successively inhabited by generations of a community with a specific culture and worldview. The historical significance of the Ette emerges with the arrival of the Spanish, whose pursuit of wealth led to the conquest and near extinction of numerous Amerindian groups. However, this process should not be framed in terms of blame; these were events that formed part of the broader arc of human evolution.

With the Spanish conquest begins the modern history of the Ette—an indomitable people who resisted the brutal onslaught of colonization and who stand today as a powerful example of resilience. Much has been written about their resistance in the face of both human greed and natural disasters. At present, the Ette are gradually regaining control over their ancestral lands with the support of various institutions, all while maintaining their language and cultural traditions. In 2009, Colombia's Constitutional Court declared the Ette people to be "at risk of cultural and physical extinction." In November 2018, a specialized Land Restitution Court in Santa Marta issued Ruling 004, acknowledging the hardships endured by this community. The ruling ordered the symbolic recognition of the

Ette's historical territorial boundaries and the restitution and protection of their fundamental territorial rights.

Sociologist Édgar Rey Sinning notes that the origin of the Ette has long been a subject of debate among anthropologists, historians, and linguists. Some classify this ethnic group within the Arawakan language family, while others link them to the Chibchan family. The HLA gene data obtained in this study support the hypothesis that the Ette have ancestral ties with Indigenous groups from Central America and Mexico along the Pacific coast, as well as with Indigenous populations of Peru and the Pacific Islands. The hypothesis of an ancestral connection to Central American Indigenous peoples was first proposed by the anthropologist Erland Nordenskiöld Bolinder in 1920.

Conclusions

With respect to health, the Naara Kajmanta Indigenous population presents eosinophilia, likely associated with intestinal parasitosis and allergic dermatitis.

With respect to the CYP2C19*1 and 2 alleles, individuals are classified as intermediate metabolizers, which indicates a high likelihood of avoiding adverse reactions to medications commonly used to treat gastritis, gastric ulcers, seizures, depression, and malaria. It is important to note that 100% of the Naara Kajmanta Ette individuals carry the CYP2C191/*2 genotype and exhibit a genetic relationship with the Tarahumara people of Chihuahua, Mexico, among whom this same genotype is found in approximately 41% of individuals.

Regarding the NAT2* genes, there is variability in the population's response to medications: 40% are expected to respond well to treatment, 30% may exhibit resistance, and another 30% may experience adverse side effects. This information is particularly important to consider in the context of tuberculosis treatment.

With respect to the HLA alleles, HLA-A24:02 and HLA-C01:02 show high frequencies in the Naara Kajmanta population and are also found at high proportions among Indigenous groups from the Pacific Islands. Other alleles further link this population to Amerindian groups along the Pacific coast.

The principal haplotype of the Ette from Naara Kajmanta is: HLA-A24:02, HLA-B51:10, HLA-C15:02, HLA-DRB104:07, HLA-DQB1*03:02.

The Ette Ennaka people are a powerful example of the struggle to preserve freedom and uphold democratic values. Despite facing adverse circumstances throughout their history, they have maintained their culture, language, and spiritual principles. Their resilience in the face of life's challenges and their commitment to preserving the unity of their community is truly admirable.

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