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Perspective

Quantitative Holistic Medicine Algorithms in Quantum Vaccinomics

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ABSTRACT

In the context of the challenges associated with ticks and tick-borne diseases (TBD) for human and animal health worldwide, the collaboration between art and science contributes to advance in biomedicine. Art is interconnected with science and has played an important role in both biological and phenomenological factors during human evolution. Holism and reductionism are involved in both medicine and arts as illustrated here by Wifredo Lam pieces and signatures. Art representations are interconnected, and message can be explained only by referring to the whole piece in accordance with a holistic approach. However, art pieces may be also subjected to reductionist approaches with iconic representations providing large messages in simple images and signatures as shown here by phylogenetic analysis of Lam signatures translated into DNA and protein sequences. Medicine evolved from holistic to reductionist or mechanistic approaches to recent quantitative holistic approaches to face medical challenges. An example of the connection between art and quantitative holistic medicine is through quantum vaccinomics, which provides another perspective of the impact of art to advance in the development of innovative effective preventive and control interventions.

Keywords: Art, Infectious disease, Medicine, Quantitative holistic, Quantum vaccinomics, Vaccine

1. Introduction

Anti-tick vaccines are the most effective, environmentally friendly and sustainable alternative to chemical acaricides for the control of ticks and ticks and tick-borne diseases (TBD) within a One Health perspective.^{1,2} The evolution of anti-tick vaccines progressed from the only registered and commercialized formulations based on *Rhipicephalus microplus* BM86 recombinant antigen to the identification and characterization of new tick protective antigens to "personalized medicine" approach and innovative formulations for the

control of tick infestations¹⁻⁴. However, the control of TBD is still a major challenge that requires innovative approaches to produce effective and efficacious vaccine formulations. Within this context, quantitative holistic medicine algorithms with the collaboration between science and art may provide new tools for designing and combining tick and pathogen derived antigens for vaccines.

2. ART and Human Evolution

Art has been involved in human evolution with promoting

better human well-being as proposed by Charles Darwin in 1885⁵. More recently, Chaplin indicated that art evolutionary role involved both biological and phenomenological factors⁶. He proposed that "some biologically based theories have drawn legitimate attention to the potential role of art in human evolution, their reductive tendencies need to be corrected and complemented by both a phenomenological and a 'symbolic' approach, which situates art in a web of culturally mediated affective encounters with the world in the context of a broader horizon that lends it its meaning", and concluded that "both biological and phenomenological theories can make a significant contribution to a better understanding of the embodied nature of art on the following two conditions: First, even if art contributes not only to general human well-being but also to sexual and natural selection and thus to the biological continuation of the species, its role and importance in life should never be reduced to meeting biological needs. Second, even though the making of and responding to art can involve habitually embodied actions and reactions, nevertheless these should always be recognized as symbolic practices and therefore as open to human interpretation and metaphoric understanding within the context of a broader horizon that lends them their meaning. With those two provisos, I suggest that both biological and phenomenological philosophies of art can continue to open up promising new avenues for a deeper understanding of the embodied nature of art".

3. Holism and Reductionism in Medicine and ART

From the genomic point of view, evolutionary reduction and expansion events resulted in the rise of Bacteria and Eukarya partitioning and homogenizing the architectural diversity within species, respectively⁷. For intracellular symbionts and infectious organisms, host specialization was associated with the inactivation of genes with unnecessary function mostly through small and possibly reversible indels followed by larger genome deletions^{8,9}. However, genome reduction has been also observed in free-living marine cyanobacteria with large populations⁹. In some organisms such as Candidate Phyla Radiation bacteria *Vampirococcus lugosii*, gene loss has been compensated by gene acquisition through horizontal gene transfer and *de novo* evolution¹⁰.

Furthermore, genomic reductive evolution may be also associated with protein-protein interaction networks and increased virulence^{11,12}. Despite these evidence, controversy of reductionism is associated with considering that not all genomic modifications are powered by natural selection and not all phenotypes are adaptive evolution with constrains driven by physics, chemistry, and structure.¹³

Medicine evolved from holistic (treatment of the whole individual considering mental and social factors rather than only illness symptomatology) to reductionist or mechanistic (when body is interpreted as a machine in which individual parts can be studied independently to identify and treat specific diseases or conditions with personalized drugs and other interventions) approaches.¹⁴

Science and art are interconnected with interactions in multiple ways (e.g., ¹⁵⁻¹⁸), and reductionism is another link

between art and science with approaches applied to research and art creations.¹⁹ In art, the different representations are interconnected, and message can be explained only by referring to the whole piece in accordance with a holistic approach. However, art pieces may be also subjected to reductionist approaches by using artist's iconic representations with large messages provided in simple images (**Figure 1**). Additionally, reductionism is also illustrated by artist signature, which may also become part of the artistic representation (**Figures 2A** and **Figure 2B**). An example of this process is found in pieces made by Wifredo Oscar de la Concepción Lam y Castilla (Sagua La Grande, Cuba, 1902 – Paris, France, 1982), better known as Wifredo Lam or just Lam (**Figures 1** and **Figure 2**).

Lam is a reference in Afro-Cuban art with a unique style influenced by movements such as surrealism (https:// en.wikipedia.org/wiki/Wifredo Lam). Lam was born in 1902 in Sagua La Grande, Cuba with childhood in Sagua La Grande and Havana. From 1923 to 1938 he lived in Spain and searched for Spanish art. During 1938-1941 he lived in Paris with initiation in Surrealism and the forced exodus to Cuba (1941-1945) with stopovers in Martinique and Santo Domingo. In the period between 1945 and 1951 he stayed in Haiti, New York, and Cuba with initiation in ceramics in Santiago de Las Vegas. Then, in 1951-1962 returned to Paris with visits to Venezuela, Brazil, Italy, Mexico, Cuba, and the United States. From 1962-1977 he shared stay between Paris and Albisola with passion for ceramics and triumphant reception in Cuba in 1963 with visit to Moscow. In the last years (1977-1982), Lam shared stay between Paris and Havana where he experienced nostalgia for the native country. Lam died in 1982 and as requested by him, his wife Lou Laurin Lam placed the ashes in a burial vault at the Colón cemetery in Havana in the presence of Fidel Castro.

For example, in Figure 1, representations of Elegua, an Orisha deity of roads in Yorùbá religion (https://en.wikipedia. org/wiki/Elegua; panel A), maternity (panel B), and animal metaphors²⁰ such as horse (panel C), bird (panel D), and dog (panel E) provide relevant and multidimensional messages with simple images reproduced in multiple Lam pieces.

3. Translation of Lam Signatures into Dna/Protein Sequences and Phylogenetic Analysis

Lam signatures were derived from pieces produced between 1933 and 1982 (Table 1). All pieces were obtained from the KGJ Collection, Ciudad Real, Spain. Lam signatures from different pieces were translated into DNA shown in FASTA format as used for alignment and analysis (Table 1). DNA and protein sequences with amino acids and DNA codons for each signature letter are W: His, H, CAT; I: Ile, I, ATT; F: Phe, F, TTC; R: Arg, R, CGT; E: Glu, E, GAA; D: Asp, D, GAT; O: Cys, C, TGC; L: Leu, L, CTG; A: Ala, A, GCT; M: Met, M, ATG (Table 1). CLUSTAL FORMAT: MUSCLE (3.8) was used for multiple sequence alignment (http://www.phylogeny. fr).²¹ Phylogenetic tree was made with Neighbor Joining (NJ) method and a F84 distance model with equal site rate, 12 sequences and 5 characters including insertions and gaps stripped (www.hiv.lan.gov). The sum of all branches was calculated using the Neighbor TreeMaker (https://www.hiv. lanl.gov/components/sequence/HIV/treemaker/treemaker.html).



Figure 1: Pieces from where Lam signatures were obtained with reduction in the number of letters over time (1930s-1980s). Codes (>No.) refer to entries in Table 1. (>30) Autograph from 1933, "propiedad de Wifredo Lam, Madrid 33". Signed in: Yvan Goll. Pascin. Collection Les Artistes Nouveaux. Paris: Crès & Cie, 1929. (>40a) No title. Wood, paint and bronze. Havana, 1945. Hand signed. From Lydia Cabrera collection. (>40b) Catalog of the Lam exposition. Lyceum, Havana, Cuba, Abril 11-19, 1946. The text includes parts of Cabrera's 1943 article on Lam, with additional statements by Breton, Cesaire, Mabille, Benjamin Peret, Christian Zevros, Georges Besson and Charles Theophile. Signed by Lam in 1946. (>50.1) No title. Dedicated to Swedish poet and essayist Göran Printz-Påhlson. Hand signed by the Lam in Malmö, 1956. (>50.3) Correspondence with Louis Broder. Drawing with tint on paper. Paris, 1959. (>50.2) Autograph letter signed on a note whose upper part is torn, Albisola (Italy), October 8, 1959. One page in-12. Short letter from a Lam trying his hand at French, when he left Cuba in April and was in Italy, in Albisola at Crippa>s and at Jorn's when he wrote this missive undoubtedly intended for Hubert Juin for which he illustrated the book which was to be published in 1960: The Journey of the Tree. Shortly after, Lam went to Chicago where he met several collectors and the art dealer Richard Feigen. (>60.1) From the series, Vingtieme Parallele Suite. Etching and aquatint on Japan paper, XXX/XXXV, 1966. (>60.1) Insolations No. 3. Original hand signed drawing. Editions Fata Morgana, Montpellier, Francia, 9 December 1968. Copy 151/200. Reference: Numbers 6801-6805 of the Catalogue Raisonné Oeuvre Gravé et Lithographié, Ed. Museé de Gravelines 1993, p. 105. (>60.2) Correspondence with Louis Broder. Drawing with tint on paper. New York, 1960. (>60.3) Typed letter to art editor Georges Fall signed by Lam. Paper page (21 x 29.5 cm), Zurich, 17 February 1961. (>70.1) Page of presentation of the book Le Nouveau Monde de Lam. Alain Jouffroy, a cura di Magdalo Mussio, La Nuova Foglio Editrice, Pollenza Macerata, 1975. Edition of 1000 copies. Tint drawing and dedication by Lam. (>70.2) Porcelain crockery (Royal Selb Bavarian, Germany) with serigraph. Factory

Albissola Ceramiche, Albisola, Italy. Hand signed artist proof for the tureen, 15 x 15 cm, P/A, 1970. (>80.2) Conversations. Samuel Feijoo and Wifredo Lam. Ink on paper, Cuba, 1981. (>80.1) L'herbe sous les pavés. Engraving artist poof of his last piece. Milan, 1982. Rare set of 10 original etchings: 3 "Good to print" signed and with the handwritten indications of the artist in pencil for the printer Giorgio Upiglio. 7 Printing trials with the artist's handwritten indications in pencil for the printer Giorgio Upiglio. Hand signed with certificate of authenticity from the printer Giorgio Upiglio. The first print proof announced that the etchings would all be numbered and signed by the artist. A second receipt was printed later below: "The justification for this work was signed by Wifredo Lam in July 1982. Death prevented him from signing, as planned, the six etchings for which he had previously signed the proof. Paris, October 15, 1982". All pieces are from the KGJ Collection, Ciudad Real, Spain.



Figure 2: Reductionism in Lam signatures. (A) Alignment of DNA sequences derived from translation of Lam signatures (Table 1). CLUSTAL FORMAT: MUSCLE (3.8) was used for multiple sequence alignment. (B) Analysis of DNA sequences derived from translation of Lam signatures (**Table 1**). Tree was made with NJ method and a F84 distance model with equal site rate, 12 sequences and 5 characters including insertions and gaps stripped.

Table 1: Translation of Lam signatures into DNA and protein sequences.

Years	Signature	Amino acids	Sequence ID:DNA codons (5'-3')
1930s	WifredoLamLam	HIFREDCLAMLAM	>30:CATATTTTCCGTGAAGATTGCCTGGCTATGCTGGCTATG
1940s	WifredoLam	HIFREDCLAM	>40a,40b:CATATTTTCCGTGAAGATTGCCTGGCTATG
1950s	WiLa	HILA	>50.1:CATATTCTGGCT
	Wifredo	HIFREDC	>50.2:CATATTTTCCGTGAAGATTGC
	Lam	LAM	>50.3:CTGGCTATG
1960s	WiLa	HILA	>60.1:CATATTCTGGCT
	WiLam	HILAM	>60.2:CATATTCTGGCTATG
	Lam	LAM	>60.3:CTGGCTATG
1970s	WiLa	HILA	>70.1:CATATTCTGGCT
	Lam	LAM	>70.2:CTGGCTATG
1980s	WiLa	HILA	>80.1:CATATTCTGGCT
	Lam	LAM	>80.2:CTGGCTATG

The results showed that signature sequences evolved with reductionism from larger to shorter formats (Figures 1, 2A, and 2B) with corresponding amino acid numbers varying from 13-10 in the 1930s and 1940s to 7 in the 1960s, 5 in the 1960s and 4 in the 1970s and 1980s (Figure 1). Nevertheless, shortest signature, "Lam" (IDs 50.3, 60.3, 70.2, 80.2, 3 amino acids) appeared since the 1950s to 1980s (Figure 1). The phylogenetic analysis showed that the most unique signature was "Wifredo" (ID 50.2, Figure 2B).

4. Perspective: Art is also connected to Quantitative Holistic Medicine

Recently, medicine advanced to a new quantitative holistic (including quantitative, precision, personalized, predictive, and preventive medicine with omics technologies applied to system biology and network analyses) approach.¹⁴ Despite existing challenges and criticisms for holistic and reductionist approaches, the quantitative holism shows the possibility to converge holism and reductionism in medicine as in scientific research to advance in disease prevention and treatment.¹⁴ In this way, quantitative holistic approaches consider the entire system but using quantitative methods to study and analyze its different components considering philosophical and ethical considerations.¹⁴ Accordingly, quantitative holistic approach could also include the study of genetic modifications associated with catastrophic selection and other evolutionary processes to identify novel biomolecules for treatment of different diseases.22-27

Is art also connected to quantitative holistic medicine? Recent advances in quantum vaccinomics do support this connection.¹⁶ The combination of omics technologies for the analysis of tick-host-pathogen interactions and vaccine trials with Big Data analytics including Machine Learning, Random Forest Extension and Hierarchical Clustering guides the identification of tick/pathogen protective antigens. Then, quantum vaccinomics including art, biological and musical algorithms allow the identification of protein protective epitopes or immunological quantum for the design of chimeric antigens for vaccine formulation.^{15,26,28} In this way, candidate vaccine protective antigens identified by intelligent Big Data analytic techniques may be reduced and combined to produce vaccines with potential protection against multiple pathogens and ectoparasite vectors.²⁹

In conclusion, the interconnection between science and art supports quantitative holistic medicine to advance in development of innovative effective preventive and control interventions. Recent results support this approach with the design of new potential protective antigens for the control of tick infestations and pathogen infection/transmission.^{15,30,31} Future projects should evaluate the protective capacity of these and newly designed vaccine chimeric antigens to expand research on quantitative holistic medicine for the control of ticks and TBD.

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6. Conflicts of Interests

The author declares that he has no known competing interests or personal relationships that could have appeared to influence the work reported in this paper.

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8. Ethical Approval

Not required.

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