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Ancient Health Landscape: foundations and perspectives

Christiana L. Scheib

Estonian Biocentre, Institute of Genomics, University of Tartu, Riia 23B, 51010, Estonia;
St John's College, University of Cambridge, St John's Street, CB2 1TP, United Kingdom
e-mail: cls83@ut.ee

Public health researchers understand that disease research cannot exist in a vacuum. Rather, it must be collaborative, multisectoral, transdisciplinary, and take into account the inescapable interconnection between humans and their environment (One Health 2021). The next stage of development for the field of ancient pathogen research is to follow this lead. We have answered the question, "what caused the 'Black Death'?" The next questions are, "how did the environmental and socio-cultural factors culminate to produce such a deadly effect and what impact did it have on the human genome?" To answer these questions, we must integrate as many variables as possible to understand not only the victims of past diseases, but the range of susceptibility within the population as a whole.

Public health researchers would use the term 'health landscape' to describe such an integrated picture that uses statistical information to build a population-scale picture of 'health' in a region. For example: *The Social and Health Landscape of Urban and Suburban America* (Andrulis and Goodman 1999). The most common use of the phrase (according to Google's Ngram viewer tool) is in conjunction with 'public' (since the early 1980s) and 'global' (since the mid 1990s) (Michel et al. 2011). The search term 'ancient health landscape;' however, produces no results, so I will define it here.

I define an 'ancient health landscape' as the culmination of all the features of a particular geospatial region in the past that influenced individual and population-level health status. This also requires us to define what we mean by 'health,' which is tricky because it is not easily definable nor quantifiable. The term itself comes from the Old English *hǣlth* simply meaning 'whole,' while 'disease' comes from Old French *desaise*, meaning 'lack of ease; inconvenience' (Simpson et al. 1989). Disease is easy to identify and measure, thus the foundation for the entire modern medical establishment; while health is, in the most straightforward sense, the absence of disease.

Disease can be of two types: infectious and non-infectious (though we are learning more and more about the complex interaction between microbes and lifestyle diseases). In the simplest terms, we are looking at a balance between the human immune system / cellular repair machinery and the onslaught of infectious pathogens / breakdown of cellular systems. If the balance shifts too far toward the pathogens or the person's own immune system, there is a reduction in fitness. A state of 'health' lies in the middle. As long as the cellular repair machinery is functioning properly, the body will not fall into a state of 'disease' such as diabetes or cancer. These are two examples of diseases that result in the breakdown of a biological system, in the former the body can no longer cope with producing the amount of insulin needed to process and store the glucose from the diet and in the latter, the clean-up system is no longer able to identify and remove out-of-control cells.

Thus, of interest are all the factors that affect an individual's ability to build the cellular machinery necessary to successfully fight off infection and regulate the body. The main factors (Fig. 1) that affect the strength of these systems are: 1) underlying genes, 2) availability of building blocks (essential nutrients), and 3) energy expenditure / stress. The genome of an individual codes for over 4,000 immune-related genes (Breuer et al. 2013)

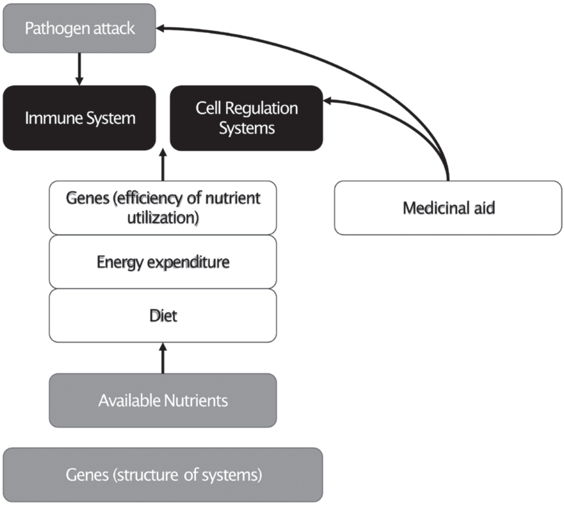

***Fig. 1** - Schematic of elements of an ancient health landscape. The foundation of an individual's health is his/her genetic blueprint. The interaction between the genetic code and nutrients available in the environment are filtered through socio-cultural factors including diet, physical activity and medicinal aid. Medicinal aid can both directly attack pathogens or boost cell regulation systems. Biologically, the innate efficiency or ability of the person to process certain nutrients also plays a role in how well the immune system and cell regulatory systems are able to retain a state of homeostasis under pathogen pressure.*

including those of the major histocompatibility complex (MHC), the region that codes the cell surface proteins foundational to the adaptive immune system and the toll-like receptor family, one key element of the innate immune system. Some individuals have hereditary immunodeficiencies and others may have variation that, in the right moment, gives them the edge over a given pathogen pressure. Some have genes that impede their cell regulatory systems, making them more susceptible to cancers. An individual could also have hereditary or *de novo* variation that affects their ability to convert essential nutrients from their diet into the building blocks necessary to mount a robust immune defense. This then leads to the next layer of influence: the diet and cultural factors that affect the intake of nutrients from the environment. An individual may be a part of a certain social group that has rules regarding diet (e.g. vegans) or are deprived of nutrients due to their place in the social hierarchy (e.g. urban poor). If an individual must expend more energy than they can take in, this physiological stress also affects their immune system. Again, socio-cultural factors are influential as the level of physical labor required to survive depends greatly on the environment an individual is a part of.

The factors that affect the strength of pathogen pressure are a similar hierarchy of layers: 1) underlying genes of the pathogen, 2) availability of building blocks (essential nutrients), and 3) exposure (frequency and copy number). The pathogen may have genomically encoded virulence factors that increase its impact on its host. This can be positive or detrimental to the pathogen as, ideally it should strike a balance of replication and spread because death of the host means death of the pathogen in most cases. The pathogen must also have access to the necessary nutrients that it needs to replicate. For example: *Yersinia pestis* bacteria, like many others, need iron to replicate. If there is a lack of iron in the environment, such as the human host, then the bacteria will be unable to thrive (Zauberman et al. 2017). Lastly, the exposure, both in terms of absolute numbers of the pathogen and repeated exposure over time greatly increases the chances of a pathogen overwhelming a host's immune system.

***Tab. 1** - Techniques for measuring the factors of an ancient health landscape. Methodology is categorised as "Well-established" if there is at least a 20 year track record of publications in the area and defined workflows. "Feasible" indicates that the underlying data is generatable and theoretically possible, though very few or no publications have yet to publish on this topic. "Emerging" indicates the technique on specifically ancient remains has less than 20 years of high-impact publications and workflows are still developing.*

FACTOR	TECHNIQUE	MATERIAL	STATE
Genetic ancestry	Ancient DNA	Teeth and bones	Well-established
Immune Genes	Ancient DNA		Feasible
Pathogen presence	Ancient DNA		Well-established
	Ancient proteins		Emerging
	Paleopathology		Well-established
Disease status (inherited)	Ancient DNA		Feasible
Disease status (biomarkers)	Ancient proteins		Emerging
	Ancient metabolites		Emerging
Diet and nutritional status	Isotopes	Teeth and bones	Well-established
	Ancient proteins	Dental calculus, food vessels	Emerging
	Ancient lipids		Well-established
	Ancient metabolomics		Emerging
	Microfossils		Well-established
	Zooarchaeology	Floral and faunal remains	Well-established
Physiological stress	Osteology	Teeth and bones	Well-established
	Morphometrics		Well-established
	Ancient proteins and metabolites		Emerging
Medicinal Use	Ancient metabolomics	Teeth, dental calculus, bone	Emerging
	Archaeology	Material culture	Well-established
	History of Medicine	Historical records	Well-established
Climate	Quaternary Science	Various	Well-established

So, environmental factors that encourage the growth and transmission of pathogens are important to include in our landscape model.

To build up an ancient health landscape we need to utilise all available methods to assess these factors. The current tools at our disposal are listed in Table 1 and include firstly environmental reconstruction: What was the climate, floral and faunal diversity like at this site at this time? What general material culture (manufacture and trade) existed?

How did humans interact with these objects and each other? Secondly, we reconstruct the individual. We sequence his/her genome to answer questions about genetic ancestry and the presence of phenotypes. We reconstruct dietary habits by analysing the proteomic, metabolomic, and metagenomic information from their dental calculus. What do the carbon and nitrogen isotopes say? How did habitual physical stress mark the skeleton? What can we learn about their life from evidence of trauma or pathology? Did they have an infection when they died? Finally, we reconstruct the population by repeating these measures on every individual (or sufficiently large random sample size) within a targeted study area. We ask, what was the level of heterogeneity of the community, mobility and population size? What can we learn about their lifestyles from their collective treatment of the dead? We can then start to tease apart which factors (diet, work patterns, kinship relationships etc.) correlate with health/disease states.

Some of these methodologies, such as the generation of ancient human genomes and bulk carbon and nitrogen isotopes, are well-established. Others, including ancient proteins and metabolites, are just emerging and still require fundamental exploration to determine what can and cannot be inferred by these methods. Even for well-established methodologies, there are some necessary advancements within the field of molecular palaeoanthropology that must occur so that we can definitively answer some of the most pressing questions. The first, and most fundamental, is that we need to understand the mechanism behind the preservation of DNA and proteins in archaeological teeth and bones. At present, it is impossible to differentiate between a non detection due to actual absence versus lack of preservation. At the moment there is still a caveat that negative results are not necessarily negative and we need to be able to remove that hindrance. Related to this point, we need to move beyond 'presence vs. absence' reporting. To do this, we need to be able to quantify ancient biomolecules in a reliable way. These roadblocks can be solved, it's just a matter of someone or some groups putting in the time, money, effort and creative thinking toward the problem.

As evolutionary anthropologists, we are interested in how human genomes have evolved. Pathogen and disease pressures are some of the most important selective factors. In order to answer the questions we have about the function of genomic regions and why they came to be, we must understand the greater picture. Thus, the need for the ancient health landscape. We don't need more samples, we need more data and to contextualise that data in a meaningful way.

References

Andrulis DP, Goodman NJ (1999) The Social and Health Landscape of Urban and Suburban America. Health Forum, AHA Press.

Breuer K, Foroushani AK, Laird MR, et al (2013) InnateDB: systems biology of innate immunity and beyond--recent updates and continuing curation. Nucleic Acids Res 41(Database issue):D1228–D1233. https://doi.org/10.1093/nar/gks1147

Michel J-B, Shen YK, Aiden AP, et al (2011) Quantitative Analysis of Culture Using Millions of Digitized Books. Science 331:176–182. https://doi.org/10.1126/science.1199644

One Health (2001) https://www.cdc.gov/onehealth/index.html

Simpson JA, Weiner ESC (1989) The Oxford English Dictionary, Clarendon Press, Oxford University Press, Oxford.

Zauberman A, Vagima Y, Tidhar A, et al (2017) Host iron nutritional immunity induced by a live Yersinia pestis vaccine strain is associated with immediate protection against plague. Front Cell Infect Microbiol 7:277. https://doi.org/10.3389/fcimb.2017.00277.