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Pacific Populations, Metabolic Disease and 'Just-So Stories': A Critique of the 'Thrifty Genotype' Hypothesis in Oceania

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Summary

Pacific populations have long been observed to suffer a high burden of metabolic disease, including obesity, type 2 diabetes and gout. The 'Thrifty Genotype' hypothesis has frequently been used to explain this high prevalence of disease. Here, the 'Thrifty Genotype' hypothesis and the evolutionary background of Pacific populations are examined. We question its relevance not only in the Pacific region but more generally. Not only has the hypothesis not been explicitly tested, but most archaeological and anthropological data from the Pacific fundamentally do not support its application.

Keywords: Obesity, type 2 diabetes, metabolic disease, polynesians, thrifty genes

Introduction

In 1962, the American geneticist, James Neel, put forth a revolutionary hypothesis that the increasing prevalence of type 2 diabetes among many indigenous populations was a result of an evolutionary adaptation to periods of famine (Neel, 1962). Thus, the 'Thrifty Genotype' hypothesis, which also relates to other metabolic conditions, was born. The hypothesis was an important first step in employing evolutionary explanations for differences in disease prevalence between populations. Over the following 50 years, the hypothesis was modified in conjunction with advances in understanding of the complexity of metabolic disease and the anthropology of hunter-gatherer and early Neolithic cultures and their subsistence patterns (Neel, 1982, 1999; Corbett et al., 2009).

The premise of the original hypothesis was that contemporary type 2 diabetes was caused by a disjunction between genes and environment. Specifically, variation in genes which facilitated survival during periods of famine in preindustrialised societies, by allowing for the more efficient storage of energy during periods of plenty, were at odds with a modern, industrialised environment of plenty (Neel, 1962). Consequent to the replacement of traditional diets with a Westernised diet, these so-called 'thrifty genes' were proposed to contribute to the onset of diabetic symptoms. Following the publication of the hypothesis, other possible explanations relating to reasons for metabolic disease were discussed in the literature. These include the 'Thrifty Phenotype' hypothesis wherein inadequate nutrition early in life predisposes an individual to type 2 diabetes (Hales & Barker, 1992), and the 'Drifty Genotype' hypothesis which postulates that the removal of heavy predation pressure resulting from increased social behaviour, the use of fire and invention of weapons removed selective pressures permitting genetic drift which has allowed for genetic variants causal of obesity and type 2 diabetes to accumulate (Speakman, 2008).

Despite many critiques of the hypothesis (Benyshek & Watson, 2006; Speakman, 2006; Paradies et al., 2007; Beil, 2014; Sellayah et al., 2014), and a general lack of genetic evidence, for instance, the detection of selection signatures in metabolic genes (Helgason et al., 2007; Ayub et al., 2014; Steinthorsdottir et al., 2014), the 'Thrifty Genotype' hypothesis continues to be cited as a reason for disparities in metabolic health between populations. In their seminal paper, Gould and Lewontin (1979) warned against the acceptance of evolutionary narratives without due testing and critical thought, and this sentiment remains as true now as it did in 1979 (Nielsen, 2009).

Here, we argue that the 'Thrifty Genotype' hypothesis is another 'Just-So Story' (to borrow the analogy used by

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Gould and Lewontin in their critique of the 'adaptationist programme' (Lewontin, 1991; Gould, 1997), or 'how the human got his fat' as Speakman (2013: 305) put it, referring to the fantastical fables of Rudyard Kipling). It is a possible explanation but one for which there are little or no supporting data. This is particularly true for Pacific Island populations, for whom the 'Thrifty Genotype' hypothesis has been a recurring theme in describing reasons for the high rates of type 2 diabetes, obesity and other metabolic disorders; Pacific Island populations, along with Pima Indians, have long been considered archetypal examples of a 'Thrifty Genotype' in action (Zimmet et al., 1990; Bindon & Baker, 1997; Diamond, 2003; Myles et al., 2007). Other populations, such as Australian aborigines (O'Dea, 1992), Asian Indians (Mohan et al., 2007), sub-Saharan Africans (Van Der Sande, 2003) and Latin Americans (Filozof et al., 2001), have also been subject to the hypothesis. It seems that the 'Thrifty Genotype' hypothesis has been applied in such a way that one of the few populations that seems exempt from these 'thrifty genes' are European-derived populations. As Allen and Cheer (1996) pointed out, it may be that the Europeans themselves were subject to some selection process which caused this discrepancy. But does the 'Thrifty Genotype' hypothesis fit the genetic and anthropological data?

Perhaps a place to begin is the observation that there are indeed high rates of obesity, type 2 diabetes (Fig. 1) and hyperuricaemia (Gosling et al., 2014) among many populations throughout the Pacific both among those still living in their ancestral homelands, and those who have migrated to urban centres in places such as New Zealand, the United States and Australia. While the prevalence of disease is higher among those living in more westernised contexts, the occurrence of metabolic disease in those living a more traditional lifestyle (pre-mid-twentieth century and prehistoric) suggests a genetic contribution to disease. This is supported by skeletal indicators of metabolic disorders (gout and diffuse idiopathic skeletal hyperostosis in particular) in bioarchaeological assemblages from the region (Buckley, 2007, 2011; Buckley et al., 2010) and the epidemiological evidence from the 1950s through to the 1970s (Prior, 1981; Prior et al., 1966). Although it is reasonable to expect that indigenous Pacific populations will have diabetes and obesity risk alleles at a higher prevalence and penetrance, we note that there are currently no systematic genome-wide association studies on genetics of diabetes and obesity in any Pacific population that could illuminate this possibility. More importantly, the theory that this is due to selection as a result of food deprivation is not supported when one considers the population history, settlement process and environment of the Pacific in more depth.

The Migratory History of the Pacific

Understanding the evolutionary history of the region and the colonisation process is instrumental to place the 'Thrifty Genotype' hypothesis in a better context when applied to Oceanic populations. There have been multiple movements of people into the Pacific region throughout the 50,000-year history of human occupation. Given this time depth and population diversity, it might be expected to see significant differences in the metabolic disease frequencies in various populations. People first arrived on the continent of Sahul, which became New Guinea and Australia with subsequent sea-level changes, at least 49,000 years ago (Summerhayes, Leavesley et al., 2010). Genetic analyses have shown that there were probably multiple populations involved in these Late Pleistocene and Early Holocene migrations out into New Guinea and the Solomon Islands, a region known as Near Oceania (Rasmussen et al., 2011). Subsequently, there have been several influxes of people from the Island Southeast Asia region into the islands of the Bismarck Archipelago and beyond as early as 5000 years ago but certainly by some 3350 years ago (Kirch et al., 1989; Summerhayes, Matisoo-Smith et al., 2010). These people, often referred as Austronesians based on their linguistic affiliations, mixed with resident coastal populations prior to expanding out into the wider Pacific where they were the initial colonists on the previously unoccupied islands of Remote Oceania. Thus, Polynesians and Micronesians have been found to be more genetically similar to certain Asian populations than to the general Near Oceanic populations which are highly heterogeneous (Friedlaender et al., 2008). Because of these differences in ancestry, there are both genetic and phenotypic differences between Pacific populations, even those within a reasonably close geographical distance to one another. The implication of this is that population history should be a major consideration when discussing differences in disease prevalence in the Pacific. For instance, while rates of type 2 diabetes and obesity are high among Polynesian and Micronesian populations, the rates are much lower in Papua New Guinea (Fig. 1), whose general population has a larger proportion of their ancestry being derived from the earliest inhabitants of the region than the later Austronesian-speaking colonists. Some of this disparity between prevalence of obesity and type 2 diabetes in Polynesia and Micronesia and populations in Papua New Guinea could be explained by the differential penetrance of western nutritional influences in this region. A proponent of the 'Thrifty Genotype' hypothesis might suggest other explanations for this phenomenon – for instance, the selection for 'thrifty genes' occurred after moving through this region, but these arguments are inconsistent when examined in context of the Pacific archaeology and anthropology.

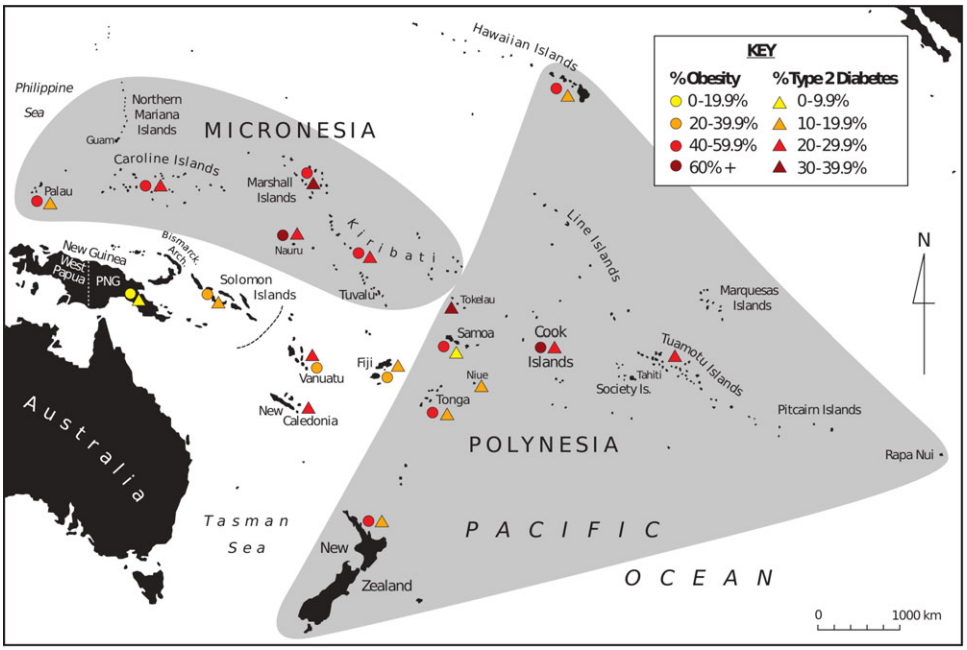

Figure 1 Prevalence of type 2 diabetes and obesity in the Pacific (for references, see Table S1). The dashed line indicates the division between near and remote Oceania.

'Thrifty Genotypes' and Oceanic Voyaging

One of the inherent weaknesses of the 'Thrifty Genotype' hypothesis in the context of the Pacific is the reliance on selective mortality or variation in reproductive success mediated by restricted food supply. A number of mechanisms describing how the hypothesis might operate in the Pacific have been put forth. The scenario laid out by Bindon and Baker (1997) is that the selection for these 'thrifty' traits occurred during the ocean voyages involved in settlement of the Pacific or once people arrived on their new island. This is based on the assumption that the voyaging and island settlement process was perilous and that there was a reasonably high mortality rate. Diamond (2003) takes this a step further by stating that 'in many attested examples of such lengthy voyages, many or most of the canoe occupants died of starvation, and only those who were originally the fattest survived'. No citations were given for this claim. However, given that colonisation voyages are not something that have happened for at least a couple of centuries (Irwin, 1989), it is likely that Diamond is referring to more recent examples of people who have not intentionally ventured out and are not necessarily prepared for long periods in a boat in the middle of the ocean (for instance, fishermen lost at sea). It is certainly not in line with studies which have found that the process of colonising the Pacific is likely to have involved safe, systematic and planned exploration prior to the colonisation (Hiroa, 1954; Irwin, 1994).

Archaeological sites associated with the Lapita culture, the first colonists into islands beyond the Solomon Islands, first appeared in the Bismarck Archipelago approximately 3350 years ago (Summerhayes, Matisoo-Smith et al., 2010). Within a few hundred years, new settlements were established in the Reef Santa Cruz (Southeast Solomon Islands), Vanuatu, Fiji and New Caledonia (Bedford et al., 2006). Lapita expansion halted in Tonga which was settled by 2830–2846 years ago (Burley et al., 2012), and Samoa which was settled at a similar time (Spriggs, 2011). There was an interval close to 2000 years between the settlement of Western and Eastern Polynesia.

The settlement of Eastern Polynesia, from the Samoa/Tonga Polynesian homelands, was similarly rapid, with the occupation of all of the main island groups within a 300-year window between AD 1025 and 1290 (Wilmshurst et al., 2011). The speed at which successful settlement of the wider Pacific region occurred could simply not be sustained if there was great loss of life. While there was some doubt during the 1950s and 1960s about the deliberate nature of Pacific voyaging and navigation, with theorists such as Sharp (1956) arguing for 'accidental voyaging', most scholars now agree that preliminary scouts were sent out on two-way exploratory voyages prior to the departure of a well-provisioned colonisation party who were travelling to a known destination with known resources and for a known period of time (Irwin, 1989; Kirch, 2000; Fitzpatrick, 2007; Montenegro et al., 2014). These colonisation events may have been assisted by

weather patterns such as El Niño (Goodwin et al., 2014), which would have made the voyaging times faster.

Starving at sea is not the only voyaging-related proposal put forth to explain genetic diversity in the Pacific. Houghton (1990, 1996) and Bindon and Baker (1997) have suggested that the increased body mass among New Zealand Māori and other Polynesian populations is a result of selection due to the cold temperatures faced during open ocean voyaging, the premise being that higher body mass would insulate one against wind chill and ocean spray (an adaption of a hypothesis known as Bergmann's rule). This increase in body mass includes a shift in the muscle mass to fat ratio; Polynesians possess less fat per unit weight when compared to Europeans (Swinburn et al., 1999; Rush et al., 2009). More recently, this hypothesis has also been subject to criticism, as the premise that larger mass may be selected for by exposure to cold where a lower surface-to-volume ratio as more heat conserving has been challenged by the fact that larger individuals also need to consume more food; meaning that there is little difference in the absolute energy balance (McNab, 2002). The implication of this observation is that it would be more beneficial to take smaller people voyaging if there was a fixed food supply as their consumptive needs would be lower. To support his hypothesis, Houghton (1996) devised sophisticated calculations to show the likelihood of survival for 10 days voyaging on open ocean at various latitudes and indicated that larger body masses were required for survival under his simulated scenarios.

There are several problems with this hypothesis. First, if selection for large body size was the result of surviving cold temperatures during voyaging, we would expect that populations that inhabit the most southerly or most distant islands (e.g. New Zealand or Rapa Nui) and would have therefore had the longest and coldest voyages, would be the most robust, having the strongest selective pressures – or that East Polynesians would be more robust than Tongans and Samoans, given the greater distances involved in the settlement of East Polynesia. This pattern is not indicated in any data from skeletal or modern populations (Howells, 1970; Houghton, 1996; Pietrusewsky, 1996). Another problem is that Houghton's calculations assume naked bodies that have no cold protection. This does not fit with knowledge of Polynesian voyaging skill and evidence for protective clothing (Hiroa, 1924) or structures in the canoe allowing for some weather protection (Van Dijk, 1991).

Similarly, these simulations are also undermined by the recent reinterpretations of archaeological radiocarbon dates, with the imposition of stricter chronometric hygiene measures, supporting a general shortening of East Polynesian prehistory from the previously accepted dates of AD 410–1270 to AD 1025–1290 (Wilmshurst et al., 2011). For rapid, successive population movements, a larger founding population would be expected, which in turn would require voyaging to have a much reduced mortality rate than this particular application of Bergmann's rule. This is supported by a recent study investigating the cold-induced vasodilation response in a number of populations worldwide, which has indicated that the cold adaptation seen in Polynesian populations is likely an ancestral trait which evolved in Asia prior to the start of the Pacific colonisation process (Wilberfoss, 2012).

There is also archaeological evidence to support extensive sailing between archipelagos (Collerson & Weisler, 2007), at least in the early periods of colonisation, though this interaction dropped off in later prehistory (Irwin, 1994). This reduction in interisland contact may be due to the development of greater sociopolitical complexity in some of these island groups, possibly triggered by climatic change (Field & Lape, 2010). The focus of the island communities turned inwards, rather than maintaining strong links with distant islands. Thus, given this evidence of return voyaging and continued contact within the Polynesian Triangle for at least the first few hundred years, it seems improbable that the voyaging process would be a significant selective pressure. The mortality rates described to select for the postulated 'thrifty' traits indicate a lack of appreciation for the sophistication of sailing technology and expertise of early Pacific Islanders (Hiroa, 1954). Increased mortality rates cannot explain the uniformity of so-called 'thrifty' traits across both Polynesia and Micronesia and are inconsistent with the speed of settlement based on the archaeological record.

Fragile Island Environments

It has been argued that Pacific Island populations might be subject to more famine events than continental populations because of their relative isolation and their susceptibility to cyclonic weather patterns and tsunami (Zimmet et al., 1990; McGarvey, 1994). This might result in the destruction of horticultural crops and impact staple foods such as shellfish and other marine foods, which were mainstays to many prehistoric Pacific Island populations. As evidenced by the devastation caused by these sorts of phenomena in modern times (e.g. the Samoan tsunami in 2009), it is not unreasonable to assume that such occurrences have been persistent but intermittent and relatively localised problems for many island populations since initial colonisation. Indeed, skeletons from archaeological sites in the region show skeletal pathology consistent with nutritional deficiencies (Snow, 1974; Buckley, 2000; Buckley et al., 2014). The palaeopathology record can indicate other skeletal and dental changes reflecting growth disruption for assessing periods of food insufficiency in the past (Goodman et al., 1984). However, these signs of growth disruption may also be a response to infection, especially in a tropical

environment where pathogen loads are high (Buckley, 2006) and they indicate recovery from the stressful event. Therefore, these growth disturbances are generally considered to be a reflection of nonspecific or more generalised stress during growth.

This permutation of the hypothesis does not appreciate the variation in subsistence patterns across the Pacific, partly as a result of the different geological origins of the inhabited islands. Pacific peoples have taken to inhabiting atolls, volcanic and continental islands (Neall & Trewick, 2008), and these different island types offer different subsistence opportunities due to variation in ecological diversity (Kirch, 2000). Factors such as water availability and soil composition alter what horticultural domesticates are likely to grow, and any surpluses which might be produced. As such, different islands are likely to have had different levels of vulnerability when faced with natural disasters. The distribution of obesity-prone populations throughout the Pacific, under this model, would require multiple independent episodes of selection for a 'Thrifty Genotype'. This is unlikely to have occurred. Rather, the broad patterning observed in metabolic disease prevalence among modern Pacific populations is more likely a result of the genetics of founding populations, in addition to differential founder effects and drift.

The high prevalence of obesity throughout the Pacific (Fig. 1) seems indicative of increased body mass index (BMI) being an ancestral trait, which was already present among the colonising population rather than selection for 'thrifty' traits *in situ*. Selective mortality or reproductive success once islands were colonised was unlikely to be a factor that would drive selection or 'thriftiness' uniformly across the broad region and diverse environments of island Polynesia.

Genetic Studies of 'Thrifty Genes' in the Pacific

It seems telling that despite multiple genetic studies (Ohashi et al., 2007; Åberg et al., 2009; Deka et al., 2009; Furusawa et al., 2010; Myles et al., 2011), there is no direct evidence for 'thrifty genes' among Pacific Islanders or other related populations, as manifest by signatures of selection at known diabetes and obesity loci. Furthermore, loci that have been strongly associated with obesity among European populations, for instance, intronic variants in the *FTO* gene (Dina et al., 2007; Frayling et al., 2007), have been found to have allele frequencies consistent with what is seen among Asian populations, so have been argued to be unlikely 'thrifty' candidates (Ohashi et al., 2007). Supporting this assertion, Karns et al. (2012) found that there were no significant associations between common variants in *FTO* with obesity-related phenotypes among Samoans.

The Gln223Arg variant of *LEPR* has also been suggested as a 'thrifty gene' on the basis of differences in allele frequency across Oceania (Furusawa et al., 2010). *LEPR* encodes a protein that is the receptor for the hormone leptin which is released predominantly from fat cells to regulate satiety, and is associated with BMI (Park et al., 2006). An elevated allele frequency, as observed by Furusawa et al. (2010), would be expected in specific populations if the locus had indeed been subject to selection. However, there are other explanations for differences in allele frequency, such as genetic drift. This variation in common allele frequency could very well be related to serial founder effects – as indicated by other genetic markers, for instance, common mitochondrial genome haplogroups which show a similar gradient across the Pacific (Kayser et al., 2006). This, indeed, seems more likely than selection when one considers the lack of evidence for a functional effect of alleles at this particular locus (Stratigopoulos et al., 2009).

Some variants have been associated with metabolic traits in certain populations and not others, for instance, the Gly482Ser variant in *PPARGC1A,* a gene involved in energy metabolism, has been found to associate with high BMI among Tongans but not New Zealand Māori (Myles et al., 2011) although this is not necessarily indicative of this being a 'thrifty gene' *per se*. A recent study has demonstrated no evidence for a selection signature at the *PPARGC1A* locus, nor was the association with BMI in Tongans able to be replicated (Cadzow and Merriman, unpublished data). The higher allele frequency of the *PPARGC1A* variant (Myles et al., 2011) in islands colonised relatively late, such as New Zealand (670–720 BP; Wilmshurst et al., 2011) compared with Tonga (2838 $\pm$ 68 BP; Burley et al., 2012), one of the first Polynesian islands colonised, is consistent with the manifestation of serial founder populations, though inconsistent with a population model of return voyaging and sustained contact between populations which has been suggested through the archaeological evidence.

The higher allele frequency of the Gly482Ser variant in *PPARGC1A* has also been cited as a potential 'thrifty gene' on the basis of its higher allele frequency among Tongans compared with Han Chinese and Papua New Guinean Highlanders (Myles et al., 2007). This same study suggested that this locus has been subject to selection based on the application of F_{ST} analyses on these populations – a rather high F_{ST} value was observed when comparing Highland New Guineans with Tongans (0.703). However, no recognition is given to the fact that these are populations with vastly different ancestral backgrounds. Polynesian populations have been found to have a higher degree of Asian ancestral contribution to their autosomal DNA than Near Oceanic (New Guinea; Wollstein et al., 2010). Given their dissimilar histories, it would therefore be expected to observe genetic differences between these populations – this is made particularly clear in a recent review of genetic diversity in Oceania which emphasises this

need to consider population history (Duggan & Stoneking, 2014). Additionally, the small sample sizes used in this study are unlikely to capture the genetic variation in any of the populations – data from only 23 Polynesians (9 Cook Islanders, 8 Samoans, 4 Tongans and 2 Niueans), 23 Highland New Guineans and 19 Han Chinese were used (Myles et al., 2007). A better approach for detecting more recent selection (i.e. selection consistent with the 'Thrifty Genotype' hypothesis in the Pacific) is probably the haplotype-based extended haplotype heterozygosity concept (Sabeti et al., 2002).

There is suggested evidence for founder effects in Remote Oceania, in Polynesians in particular (Kayser, 2010), though the sampling of Polynesian populations, in particular East Polynesian populations, is limited. This has significant implications when it comes to impact on genome-wide variation and may complicate the detection of signatures of selection if relying on statistics such as F_{ST} which detect changes in allele frequency. Focused, large-scale genetic studies of populations worldwide with known founder effects, for instance, Ashkenazi Jews and Icelandic populations, have assisted in identification of important susceptibility loci associated with other complex phenotypes (Helgason et al., 2005; Steinthorsdottir et al., 2007; Guha et al., 2012). The only such study, which has been carried out in the Pacific, was a genome-wide association study of a cohort from Kosrae, an isolated island located in the Federated States of Micronesia (Lowe et al., 2009). This study found a relatively genetically homogenous population and showed that a majority of the common variants contributing predisposition to disease in Europeans have little effect on Kosraens. Novel disease associations were identified which further underlines the need for studies focused on populations with well-defined ancestry and population history.

The 'Thrifty Genotype' Hypothesis Worldwide

The lack of support for the 'Thrifty Genotype' hypothesis is a pattern which has emerged from other studies of populations worldwide, including Europeans and Asians (Helgason et al., 2007; Southam et al., 2009; Ayub et al., 2014; Koh et al., 2014; Steinthorsdottir et al., 2014). Ayub et al. (2014) critically evaluated the hypothesis by testing for signatures of selection at type 2 diabetes loci ('thrifty genes'). They examined 65 loci and found no experiment-wide evidence for signatures of selection. Furthermore, Koh et al. (2014) looked for signatures of selection at loci associated with obesity and type 2 diabetes identified in a genome-wide association study of an East Asian cohort and similarly did not find consistent support for the 'Thrifty Genotype' hypothesis. Together, the findings of these studies indicate that the 'Thrifty Genotype' hypothesis should be reassessed as a way of considering evolutionary explanations for higher rates of obesity and type 2 diabetes among various populations.

The 'Thrifty Genotype' hypothesis does not account for the fact that famines are likely to have been a periodic problem for all human populations even before the emergence of our species from other hominins (Prentice, 2005), or that there is little evidence to suggest that famines have ever been a very important mechanism of selection (Speakman, 2013). Mathematical modelling suggests that if 'thrifty genes' did exist, given the number of famine events faced by *Homo sapiens* since the divergence from our hominin ancestors these alleles would likely have reached fixation (where the advantageous allele becomes homozygous; Speakman & Westerterp, 2013). This is in line with the recent suggestion that we should perhaps be looking deeper in human evolution for these 'thrifty genes'. Uricase has been highlighted as a putative 'thrifty gene' (Kratzer et al., 2014), but given that the inactivation of the gene occurred during the Miocene, prior to the divergence of humans from the ape lineage, uricase is also unlikely to account for differences in metabolic health between modern populations – nor is there any direct evidence that the loss of uricase function was driven by periods of famine. In other words, it 'assume[s] rather than demonstrate[s] the operation of natural selection' (Pigliucci & Kaplan, 2000). Given the multiple roles of urate (as an antioxidant, an adjuvant and in maintaining blood pressure; Gosling et al., 2014), there may have been selective forces at work other than nutritional stress.

This is not to say that nutritional exposures have not led to the selection of certain genetic variants (Stover, 2006). Variation in allele frequencies for enzymes involved in the digestion of lactose (Bersaglieri et al., 2004), starch (Perry et al., 2007) and the metabolism of alcohol (Eng et al., 2007) and fructose (Ali et al., 1998) have been detected between populations. That some populations have locally adapted genetically to optimise their nutrient uptake is unsurprising given the role of food in health and well-being, and indeed survival in general. The array of different adaptations is symptomatic of the diversity in subsistence patterns and nutritive resources available in different geographical regions. Some might argue that these variants themselves could be classed as 'thrifty genes', since the ability to digest lactose from cow's milk or to better break down starches from tubers and grains would undoubtedly be advantageous in situations of famine, though being advantageous is not the same as being 'thrifty'.

However, there is also an important distinction to be made between genetic variants which may be potentially advantageous in situations of hypothetical famine, and those actually being advantageous in an actual famine. Given that few famines involve a complete absence of food (Speakman, 2006), an ability to monopolise food resources is likely to be more critical for survival than level of adiposity, for example, via social factors like status and wealth. Certainly, in

a number of Polynesian populations, chiefs are able to restrict access to certain food resources such as fishery stocks by imposing a *rahui* (Best, 1904). It should be noted that *rahui* is not necessarily based on status and wealth, and the purpose of restricting access to food resources is usually to allow the stocks to replenish themselves in order to avoid future food shortages. In such a way, cultural processes may circumvent natural selective forces such as those assumed under the 'Thrifty Genotype' hypothesis. Furthermore, the burden of mortality in famine usually lies among the elderly and the young and both groups are irrelevant as far as the transmission of 'thrifty genes', as the elderly are likely to have already reproduced and the children are usually not variable enough in terms of adiposity for theoretical 'thrifty genes' to confer any particular survival advantage (Speakman, 2007). Therefore, famines may not impose as strong a selective force as assumed by the hypothesis. While beyond the scope of this review, there is growing evidence that individuals with higher BMI can better survive infectious disease (Van Der Sande et al., 2004; Hanrahan et al., 2010; Corrales-Medina et al., 2011). This possibility should be considered in future work on reasons for the increased obesity in modern Pacific populations.

Concluding Remarks

The 'Thrifty Genotype' hypothesis overlooks other important factors that are likely to have had more significant impacts on populations and their genetic diversity, such as migration and disease epidemics (O'Rourke, 2012) or social/cultural selection for particular phenotypes (Van Dijk, 1991). As discussed previously in relation to genetic differences between New Guinean and Tongan populations, genetic ancestry and the specific evolutionary history of a population has a significant impact on the particular variants present within a population and indeed the relative proportions of various alleles. Founder effects are clearly something that require consideration in Oceanic populations, as serial migrations have played a large part in the settlement of the area. Admixture, and the degree and nature of that admixture, is another factor which impacts the genetic variability of a population.

Infectious disease is one of the strongest drivers of genetic change (Karlsson et al., 2014): major human pathogens such as malaria (Kwiatkowski, 2005) and HIV (Schliekelman et al., 2001; Nkenfou et al., 2013) have shaped the genome in exposed populations. Given the links that are increasingly being made between metabolic diseases and innate immunity (Pickup & Crook, 1998; Lumeng & Saltiel, 2011; Robbins et al., 2014), genetic selection resulting from infectious disease exposure may contribute to an underlying susceptibility of certain populations to metabolic diseases. An example of the striking effect that infectious disease can have on a population is the introduction of Western diseases including measles, whooping cough and influenza to the Pacific during the 19th century; it is thought that these introductions caused up to 75% mortality in some East Polynesian populations (Harrison et al., 1988). Clearly this is likely to have had a large impact on the genetic diversity in the modern population.

For its time, the 'Thrifty Genotype' hypothesis was revolutionary. It reflected one of the first efforts to integrate our knowledge of modern epidemiology with human evolution. However, the hypothesis does not recognise other factors that are likely to have a greater impact on the development of genetic traits. In the 53 years since its introduction, contributions by archaeology and biological anthropology to our understanding of colonisation processes and prehistoric demography have remained overlooked in genetic studies and other reviews exploring the possibility of 'thrifty genes' among Pacific Islanders – and indeed, among other populations globally. When the evolutionary and cultural history of Pacific people is considered, the application of the 'Thrifty Genotype' hypothesis is no longer useful; the scenario certainly does not mesh with our current understandings. The continued reiteration of the 'Thrifty Genotype' hypothesis in general and in its application to Pacific populations in particular gets in the way of our formulating alternative, better supported and testable hypotheses based on our knowledge of the context and histories of the populations in question. It is our suggestion that alternative hypotheses, such as selection by infectious disease exposures (Gosling et al., 2014), need to be explored.

Conflict of Interests Disclosure

The authors declare no conflicts of interest.

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References

Åberg, K., Dai, F., Sun, G., Keighley, E. D., Indugula, S. R., Roberts, S. T., Zhang, Q., Smelser, D., Viali, S., Tuitele, J., Jin, L., Deka, R., Weeks, D. E. & McGarvey, S. T. (2009) Susceptibility loci for adiposity phenotypes on 8p, 9p, and 16q in American Samoa and Samoa. *Obesity* **17**, 518–524.

Ali, M., Rellos, P. & Cox, T. M. (1998) Hereditary fructose intolerance. *J Med Genet* **35**, 353–365.

Allen, J. S. & Cheer, S. M. (1996) The non-thrifty genotype. *Curr Anthropol* **37**, 831–842.

Ayub, Q., Moutsianas, L., Chen, Y., Panoutsopoulou, K., Colonna, V., Pagani, L., Prokopenko, I., Ritchie, G. R. S., Tyler-Smith, C.,

McCarthy, M. I., Zeggini, E. & Xue, Y. (2014) Revisiting the thrifty gene hypothesis via 65 Loci associated with susceptibility to type 2 diabetes. *Am J Hum Genet* **94**, 176–185.

Bedford, S., Spriggs, M. & Regenvanu, R. (2006) The teouma lapita site and the early human settlement of the Pacific Islands. *Antiquity* **80**, 812–828.

Beil, L. (2014) Ancient genes, modern meals: Poking holes in the thrifty gene hypothesis. *Sci News* **186**, 18–22.

Benyshek, D. C. & Watson, J. T. (2006) Exploring the thrifty genotype's food-shortage assumptions: A cross-cultural comparison of ethnographic accounts of food security among foraging and agricultural societies. *Am J Phys Anthropol* **131**, 120–126.

Bersaglieri, T., Sabeti, P. C., Patterson, N., Vanderploeg, T., Schaffner, S. F., Drake, J. A., Rhodes, M., Reich, D. E. & Hirschhorn, J. N. (2004) Genetic signatures of strong recent positive selection at the lactase gene. *Am J Med Genet* **74**, 1111–1120.

Best, E. (1904) Notes on the custom of Rahui: Its application and manipulation, as also its supposed powers, its rites, invocations and superstitions. *J Polyn Soc* **13**, 83–88.

Bindon, J. R. & Baker, P. T. (1997) Bergmann's rule and the thrifty genotype. *Am J Phys Anthropol* **104**, 201–210.

Buckley, H. R. (2000) Subadult health and disease in prehistoric Tonga, Polynesia. *Am J Phys Anthropol* **113**, 481–505.

Buckley, H. R. (2006) 'The predators within': Investigating the relationship between malaria and health in the prehistoric Pacific Islands. In: *Bioarchaeology of Southeast Asia (*eds. M. Oxenham & N. Tayles). Cambridge: Cambridge University Press.

Buckley, H. R. (2007) Possible gouty arthritis in lapita-associated skeletons from Teouma, Efate Island, Central Vanuatu. *Curr Anthropol* **48**, 741–749.

Buckley, H. R. (2011) Epidemiology of gout: Perspectives from the past. *Curr Rheumatol Rev* **7**, 106–113.

Buckley, H. R., Tayles, N., Halcrow, S. E., Robb, K. & Fyfe, R. (2010) The people of Wairau Bar: A re-examination. *J Pacific Archaeol* **1**, 1–20.

Buckley, H. R., Kinaston, R., Halcrow, S. E., Foster, A., Spriggs, M. & Bedford, S. (2014) Scurvy in a tropical paradise? Evaluating the possibility of infant and adult vitamin C deficiency in the Lapita skeletal sample of Teouma, Vanuatu, Pacific islands. *Int J Paleopathol* **5**, 72–85.

Burley, D., Weisler, M. I. & Zhao, J.-X. (2012) High precision U/Th dating of first Polynesian settlement. *PLoS ONE* **7**, e48769.

Collerson, K. D. & Weisler, M. I. (2007) Stone adze compositions and the extent of ancient Polynesian voyaging and trade. *Science* **317**, 1907–1911.

Corbett, S. J., McMichael, A. J. & Prentice, A. M. (2009) Type 2 diabetes, cardiovascular disease, and the evolutionary paradox of the polycystic ovary syndrome: A fertility first hypothesis. *Am J Hum Biol* **21**, 587–598.

Corrales-Medina, V. F., Valayam, J., Serpa, J. A., Rueda, A. M. & Musher, D. M. (2011) The obesity paradox in community-acquired bacterial pneumonia. *Int J Infect Dis* **15**, e54–e57.

Deka, R., Xu, L., Pal, P., Toelupe, P., Laumoli, T., Xi, H., Zhang, G., Weeks, D. & McGarvey, S. (2009) A tagging SNP in INSIG2 is associated with obesity-related phenotypes among Samoans. *BMC Med Genet* **10**, 143.

Diamond, J. (2003) The double puzzle of diabetes. *Nature* **423**, 599–602.

Dina, C., Meyre, D., Gallina, S., Durand, E., Korner, A., Jacobson, P., Carlsson, L. M. S., Kiess, W., Vatin, V., Lecoeur, C., Delplanque, J., Vaillant, E., Pattou, F., Ruiz, J., Weill, J., Levy-Marchal, C., Horber, F., Potoczna, N., Hercberg, S., LeStunff, C., Bougneres, P., Kovacs, P., Marre, M., Balkau, B., Cauchi, S., Chevre, J.-C. & Froguel, P. (2007). Variation in FTO contributes to childhood obesity and severe adult obesity. *Nat Genet* **39**, 724–726.

Duggan, A. T. & Stoneking, M. 2014. Recent developments in the genetic history of East Asia and Oceania. *Curr Opin Genetics Dev* **29**, 9–14.

Eng, M. Y., Luczak, S. E. & Wall, T. L. 2007. ALDH2, ADH1B, and ADH1C genotypes in Asians: A literature review. *Alcohol Res Health* **30**, 22–27.

Field, J. S. & Lape, P. V. 2010. Paleoclimates and the emergence of fortifications in the tropical Pacific islands. *J Anthropol Archaeol* **29**, 113–124.

Filozof, C., Gonzalez, C., Sereday, M., Mazza, C. & Braguinsky, J. 2001. Obesity prevalence and trends in Latin-American countries. *Obes Rev* **2**, 99–106.

Fitzpatrick, S. M. (2007) Archaeology's contribution to island studies. *Isl Stud J* **2**, 77–100.

Frayling, T. M., Timpson, N. J., Weedon, M. N., Zeggini, E., Freathy, R. M., Lindgren, C. M., Perry, J. R. B., Elliott, K. S., Lango, H., Rayner, N. W., Shields, B., Harries, L. W., Barrett, J. C., Ellard, S., Groves, C. J., Knight, B., Patch, A.-M., Ness, A. R., Ebrahim, S., Lawlor, D. A., Ring, S. M., Ben-Shlomo, Y., Jarvelin, M.-R., Sovio, U., Bennett, A. J., Melzer, D., Ferrucci, L., Loos, R. J. F., Barroso, I., Wareham, N. J., Karpe, F., Owen, K. R., Cardon, L. R., Walker, M., Hitman, G. A., Palmer, C. N. A., Doney, A. S. F., Morris, A. D., Smith, G. D., Consortium, T. W. T. C. C., Hattersley, A. T. & McCarthy, M. I. (2007) A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. *Science* **316**, 889–894.

Friedlaender, J. S., Friedlaender, F. R., Reed, F. A., Kidd, K. K., Kidd, J. R., Chambers, G. K., Lea, R. A., Loo, J.-H., Koki, G., Hodgson, J. A., Merriwether, D. A. & Weber, J. L. (2008) The genetic structure of Pacific Islanders. *PLoS Genet* **4**, e19.

Furusawa, T., Naka, I., Yamauchi, T., Natsuhara, K., Kimura, R., Nakazawa, M., Ishida, T., Inaoka, T., Matsumura, Y., Ataka, Y., Nishida, N., Tsuchiya, N., Ohtsuka, R. & Ohashi, J. (2010) The Q223R polymorphism in LEPR is associated with obesity in Pacific Islanders. *Hum Genet* **127**, 287–294.

Goodman, A., Martin, D., Armelagos, G. & Clark, G. (1984) Indications of stress from bones and teeth. In: *Paleopathology at the origins of agriculture (*eds. M. Cohen & G. Armelagos). Orlando: Academic Press.

Goodwin, I. D., Browning, S. A. & Anderson, A. J. (2014) Climate windows for Polynesian voyaging to New Zealand and Easter Island. *Proc Natl Acad Sci USA* **111**, 14716–14721.

Gosling, A. L., Matisoo-Smith, E. & Merriman, T. R. (2014) Hyperuricaemia in the Pacific: Why the elevated serum urate levels? *Rheumatol Int* **34**, 743–757.

Gould, S. J. (1997). The exaptive excellence of spandrels as a term and prototype. *Proc Natl Acad Sci USA* **94**, 10750–10755.

Gould, S. J. & Lewontin, R. C. (1979). The spandrels of San Marco and the Panglossian paradigm: A critique of the adaptationist programme. *P Roy Soc Lond B Bio* **205**, 581–598.

Guha, S., Rosenfeld, J., Malhotra, A., Lee, A., Gregersen, P., Kane, J., Pe'er, I., Darvasi, A. & Lencz, T. (2012) Implications for health and disease in the genetic signature of the Ashkenazi Jewish population. *Genome Biol* **13**, 1–16.

Hales, C. N. & Barker, D. J. P. (1992) Type 2 (non-insulin-dependent) diabetes mellitus: The thrifty phenotype hypothesis. *Diabetologia* **35**, 595–601.

Hanrahan, C. F., Golub, J. E., Mohapi, L., Tshabangu, N., Modisenyane, T., Chaisson, R. E., Gray, G. E., McIntyre, J. A. & Martinson, N. A. (2010) Body mass index and risk of tuberculosis and death. *AIDS (London, UK)* **24**, 1501–1508.

Harrison, G. A., Tanner, J. M., Pilbeam, D. R. & Baker, D. T. (1988) *Human biology: An introduction to human evolution, variation, growth and adaptability*. Oxford: Oxford University Press.

Helgason, A., Yngvadottir, B., Hrafnkelsson, B., Gulcher, J. & Stefansson, K. (2005) An Icelandic example of the impact of population structure on association studies. *Nat Genet* **37**, 90–95.

Helgason, A., Palsson, S., Thorleifsson, G., Grant, S. F. A., Emilsson, V., Gunnarsdottir, S., Adeyemo, A., Chen, Y., Chen, G., Reynisdottir, I., Benediktsson, R., Hinney, A., Hansen, T., Andersen, G., Borch-Johnsen, K., Jorgensen, T., Schafer, H., Faruque, M., Doumatey, A., Zhou, J., Wilensky, R. L., Reilly, M. P., Rader, D. J., Bagger, Y., Christiansen, C., Sigurdsson, G., Hebebrand, J., Pedersen, O., Thorsteinsdottir, U., Gulcher, J. R., Kong, A., Rotimi, C. & Stefansson, K. (2007) Refining the impact of TCF7L2 gene variants on type 2 diabetes and adaptive evolution. *Nat Genet* **39**, 218–225.

Hiroa, T. R. (1924) The evolution of Maori clothing. *J Polyn Soc* **33**, 293–316.

Hiroa, T. R. (1954) *Vikings of the sunrise*. Christchurch: Whitcoulls.

Houghton, P. (1990) The adaptive significance of Polynesian body form. *Ann Hum Biol* **17**, 19–32.

Houghton, P. (1996) *People of the Great Ocean: Aspects of human biology of the early Pacific*. Cambridge: Cambridge University Press.

Howells, W. W. (1970) Anthropometric grouping analysis of Pacific peoples. *Archaeol Phys Anthropol Oceania* **5**, 192–217.

Irwin, G. (1989) Against, across and down the wind: a case for the systematic exploration of the remote Pacific Islands. *J Polyn Soc* **98**, 167–206.

Irwin, G. (1994) *The prehistoric exploration and colonisation of the Pacific*. Cambridge: Cambridge University Press.

Karlsson, E. K., Kwiatkowski, D. P. & Sabeti, P. C. (2014) Natural selection and infectious disease in human populations. *Nat Rev Genet* **15**, 379–393.

Karns, R., Viali, S., Tuitele, J., Sun, G., Cheng, H., Weeks, D. E., McGarvey, S. T. & Deka, R. (2012) Common variants in FTO are not significantly associated with obesity-related phenotypes among Samoans of Polynesia. *Ann Hum Genet* **76**, 17–24.

Kayser, M. (2010) The human genetic history of Oceania: Near and remote views of dispersal. *Curr Biol* **20**, R194–R201.

Kayser, M., Brauer, S., Cordaux, R., Casto, A., Lao, O., Zhivotovsky, L. A., Moyse-Faurie, C., Rutledge, R. B., Schiefenhoevel, W., Gil, D., Lin, A. A., Underhill, P. A., Oefner, P. J., Trent, R. J. & Stoneking, M. (2006) Melanesian and Asian origins of Polynesians: mtDNA and Y chromosome gradients across the Pacific. *Mol Biol Evol* **23**, 2234–2244.

Kirch, P. 2000. *On the road of the winds: An archaeological history of the Pacific Islands before European contact*. Berkley: University of California Press.

Kirch, P. V., Swindler, D. R. & Turner, C. G. (1989) Human skeletal and dental remains from Lapita sites (1600–500 B.C.) in the Mussau Islands, Melanesia. *Am J Phys Anthropol* **79**, 63–76.

Koh, X.-H., Liu, X. & Teo, Y.-Y. (2014). Can evidence from genome-wide association studies and positive natural selection surveys be used to evaluate the thrifty gene hypothesis in East Asians? *PLoS ONE* **9**, e110974.

Kratzer, J. T., Lanaspa, M. A., Murphy, M. N., Cicerchi, C., Graves, C. L., Tipton, P. A., Ortlund, E. A., Johnson, R. J. & Gaucher, E. A. (2014) Evolutionary history and metabolic insights of ancient mammalian uricases. *Proc Natl Acad Sci USA* **111**, 3763–3768.

Kwiatkowski, D. P. (2005) How malaria has affected the human genome and what human genetics can teach us about malaria. *Am J Med Genet* **77**, 171–192.

Lewontin, R. C. (1991) Facts and the factitious in natural sciences. *Crit Inquiry* **18**, 140–153.

Lowe, J. K., Maller, J. B., Pe'er, I., Neale, B. M., Salit, J., Kenny, E. E., Shea, J. L., Burkhardt, R., Smith, J. G., Ji, W., Noel, M., Foo, J. N., Blundell, M. L., Skilling, V., Garcia, L., Sullivan, M. L., Lee, H. E., Labek, A., Ferdowsian, H., Auerbach, S. B., Lifton, R. P., Newton-Cheh, C., Breslow, J. L., Stoffel, M., Daly, M. J., Altshuler, D. M. & Friedman, J. M. (2009) Genome-wide association studies in an isolated founder population from the Pacific Island of Kosrae. *PLoS Genet* **5**, e1000365.

Lumeng, C. N. & Saltiel, A. R. (2011) Inflammatory links between obesity and metabolic disease. *J Clin Invest* **121**, 2111–2117.

McGarvey, S. T. (1994) The thrifty gene concept and adiposity studies in biological anthropology. *J Polyn Soc* **103**, 29–42.

McNab, B. K. (2002) *The physiological ecology of vertebrates: A view from energetics*. New York: Cornell University Press.

Mohan, V., Sandeep, S., Deepa, R., Shah, B. & Varghese, C. (2007) Epidemiology of type 2 diabetes: Indian scenario. *Indian J Med Res* **125**, 217–30.

Montenegro, A., Callaghan, R. T. & Fitzpatrick, S. M. (2014) From west to east: Environmental influences on the rate and pathways of Polynesian colonization. *Holocene* **24**, 242–256.

Myles, S., Hradetzky, E., Engelken, J., Lao, O., Nurnberg, P., Trent, R. J., Wang, X., Kayser, M. & Stoneking, M. (2007). Identification of a candidate genetic variant for the high prevalence of type II diabetes in Polynesians. *Eur J Hum Genet* **15**, 584–589.

Myles, S., Lea, R., Ohashi, J., Chambers, G., Weiss, J., Hardouin, E., Engelken, J., Macartney-Coxson, D., Eccles, D., Naka, I., Kimura, R., Inaoka, T., Matsumura, Y. & Stoneking, M. (2011) Testing the thrifty gene hypothesis: The Gly482Ser variant in PPARGC1A is associated with BMI in Tongans. *BMC Med Genet* **12**, 10.

Neall, V. E. & Trewick, S. A. (2008) The age and origin of the Pacific islands: A geological overview. *Philos T Roy Soc B* **363**, 3293–3308.

Neel, J. V. (1962) Diabetes mellitus: A "thrifty" genotype rendered detrimental by "progress"? *Am J Hum Genet* **14**, 353–362.

Neel, J. V. (1982) The thrifty genotype revisited. In: *The genetics of diabetes mellitus* (eds. J. Kobberling & J. Tattersall). New York: Academic Press.

Neel, J. V. (1999) The "thrifty genotype" in 1998. *Nutr Rev* **57**, 2–9.

Nielsen, R. (2009) Adaptionism - 30 years after Gould and Lewontin. *Evolution* **63**, 2487–2490.

Nkenfou, C., Mekue, L., Nana, C. & Kuiate, J. (2013) Distribution of CCR5-Delta32, CCR5 promoter 59029 A/G, CCR2-64I and SDF1-3'A genetic polymorphisms in HIV-1 infected and uninfected patients in the West Region of Cameroon. *BMC Res Notes* **6**, 288.

O'Dea, K. (1992) Diabetes in Australian Aborigines: Impact of the western diet and life style. *J Intern Med* **232**, 103–117.

O'Rourke, D. H. (2012) Why do we migrate? A retrospective. In: *Causes and consequences of human migration* (eds. M. H. Crawford & B. C. Campbell). Cambridge: Cambridge University Press.

Ohashi, J., Naka, I., Kimura, R., Natsuhara, K., Yamauchi, T., Furusawa, T., Nakazawa, M., Ataka, Y., Patarapotikul, J. & Nuchnoi, P. (2007). FTO polymorphisms in Oceanic populations. *J Hum Genet* **52**, 1031–1035.

Paradies, Y., Montoya, M. J. & Fullerton, S. M. (2007) Racialized genetics and the study of complex disease: The thrifty genotype revisited. *Perspect Biol Med* **50**, 203–227.

Park, K., Shin, H., Park, B., Cheong, H., Cho, Y., Lee, H., Lee, J.-Y., Lee, J.-K., Oh, B. & Kimm, K. (2006) Polymorphisms in the leptin receptor (LEPR)—putative association with obesity and T2DM. *J Hum Genet* **51**, 85–91.

Perry, G. H., Dominy, N. J., Claw, K. G., Lee, A. S., Fiegler, H., Redon, R., Werner, J., Villanea, F. A., Mountain, J. L., Misra, R., Carter, N. P., Lee, C. & Stone, A. C. (2007) Diet and the evolution of human amylase gene copy number variation. *Nat Genet* **39**, 1256–1260.

Pickup, J. C. & Crook, M. A. (1998) Is type II diabetes mellitus a disease of the innate immune system? *Diabetologia* **41**, 1241–1248.

Pietrusewsky, M. (1996) The physical anthropology of Polynesia: A review of some cranial and skeletal studies. In: *Oceanic culture history: Essays in honour of Roger Green* (eds. J. Davidson, G. Irwin, B. Leach, A. Pawley & D. Brown). Dunedin: New Zealand Journal of Archaeology Special Publication.

Pigliucci, M. & Kaplan, J. (2000). The fall and rise of Dr Pangloss: Adaptationism and the Spandrels paper 20 years later. *Trends Ecol Evol* **15**, 66–70.

Prentice, A. M. (2005) Early influences on human energy regulation: Thrifty genotypes and thrifty phenotypes. *Physiol Behav* **86**, 640–645.

Prior, I. (1981) Epidemiology of rheumatic disorders in the Pacific with particular emphasis on hyperuricaemia and gout. *Sem Arthritis Rheum* **11**, 213–229.

Prior, I. A., Rose, B. S., Harvey, H. P. B. & Davidson, F. (1966). Hyperuricaemia, gout, and diabetic abnormality in Polynesian people. *Lancet* **1**, 333–338.

Rasmussen, M., Guo, X., Wang, Y., Lohmueller, K. E., Rasmussen, S., Albrechtsen, A., Skotte, L., Lindgreen, S., Metspalu, M., Jombart, T., Kivisild, T., Zhai, W., Eriksson, A., Manica, A., Orlando, L., DeLa Vega, F., Tridico, S., Metspalu, E., Nielsen, K., Ávila-Arcos, M. C., Moreno-Mayar, J. V., Muller, C., Dortch, J., Gilbert, M. T. P., Lund, O., Wesolowska, A., Karmin, M., Weinert, L. A., Wang, B., Li, J., Tai, S., Xiao, F., Hanihara, T., VanDriem, G., Jha, A. R., Ricaut, F.-X., DeKnijff, P., Migliano, A. B., Gallego-Romero, I., Kristiansen, K., Lambert, D. M., Brunak, S., Forster, P., Brinkmann, B., Nehlich, O., Bunce, M., Richards, M., Gupta, R., Bustamante, C. D., Krogh, A., Foley, R. A., Lahr, M. M., Balloux, F., Sicheritz-Pontén, T., Villems, R., Nielsen, R., Jun, W. & Willerslev, E. (2011) An Aboriginal Australian genome reveals separate human dispersals into Asia. *Science* **334**, 94–98.

Robbins, G. R., Wen, H. & Ting, J. P. (2014) Inflammasomes and metabolic disorders: Old genes in modern diseases. *Mol Cell* **54**, 297–308.

Rush, E. C., Freitas, I. & Plank, L. D. (2009) Body size, body composition and fat distribution: Comparative analysis of European, Maori, Pacific Island and Asian Indian adults. *Br J Nutr* **102**, 632–641.

Sabeti, P. C., Reich, D. E., Higgins, J. M., Levine, H. Z. P., Richter, D. J., Schaffner, S. F., Gabriel, S. B., Platko, J. V., Patterson, N. J., McDonald, G. J., Ackerman, H. C., Campbell, S. J., Altshuler, D., Cooper, R., Kwiatkowski, D., Ward, R. & Lander, E. S. (2002) Detecting recent positive selection in the human genome from haplotype structure. *Nature* **419**, 832–837.

Schliekelman, P., Garner, C. & Slatkin, M. (2001) Natural selection and resistance to HIV. *Nature* **411**, 545–546.

Sellayah, D., Cagampang, F. R. & Cox, R. D. (2014) On the evolutionary origins of obesity: A new hypothesis. *Endocrinology* **155**, 1573–1588.

Sharp, A. (1956) *Ancient voyagers in the Pacific* Wellington: Polynesian Society.

Snow, C. E. (1974) *Early Hawaiians: An initial study of skeletal remains from Mokapu. Oahu*, Lexington. University Press of Kentucky.

Southam, L., Soranzo, N., Montgomery, S., Frayling, T., McCarthy, M., Barroso, I. & Zeggini, E. (2009) Is the thrifty genotype hypothesis supported by evidence based on confirmed type 2 diabetes- and obesity-susceptibility variants? *Diabetologia* **52**, 1846–1851.

Speakman, J. R. (2006) Thrifty genes for obesity and the metabolic syndrome — time to call off the search? *Diab Vasc Dis Res* **3**, 7–11.

Speakman, J. R. (2007) A nonadaptive scenario explaining the genetic predisposition to obesity: The "predation release" hypothesis. *Cell Metab* **6**, 5–12.

Speakman, J. R. (2008) Thrifty genes for obesity, an attractive but flawed idea, and an alternative perspective: The 'drifty gene' hypothesis. *Int J Obes* **32**, 1611–1617.

Speakman, J. R. (2013) Evolutionary perspectives on the obesity epidemic: Adaptive, maladaptive, and neutral viewpoints. *Annu Rev Nutr* **33**, 289–317.

Speakman, J. R. & Westerterp, K. R. (2013) A mathematical model of weight loss under total starvation: Evidence against the thrifty-gene hypothesis. *Dis Model Mech* **6**, 236–251.

Spriggs, M. (2011) Archaeology and the Austronesian expansion: Where are we now? *Antiquity* **85**, 510–528.

Steinthorsdottir, V., Thorleifsson, G., Reynisdottir, I., Benediktsson, R., Jonsdottir, T., Walters, G. B., Styrkarsdottir, U., Gretarsdottir, S., Emilsson, V., Ghosh, S., Baker, A., Snorradottir, S., Bjarnason, H., Ng, M. C. Y., Hansen, T., Bagger, Y., Wilensky, R. L., Reilly, M. P., Adeyemo, A., Chen, Y., Zhou, J., Gudnason, V., Chen, G., Huang, H., Lashley, K., Doumatey, A., So, W.-Y., Ma, R. C. Y., Andersen, G., Borch-Johnsen, K., Jorgensen, T., VanVliet-Ostaptchouk, J. V., Hofker, M. H., Wijmenga, C., Christiansen, C., Rader, D. J., Rotimi, C., Gurney, M., Chan, J. C. N., Pedersen, O., Sigurdsson, G., Gulcher, J. R., Thorsteinsdottir, U., Kong, A. & Stefansson, K. (2007) A variant in CDKAL1 influences insulin response and risk of type 2 diabetes. *Nat Genet* **39**, 770–775.

Steinthorsdottir, V., Thorleifsson, G., Sulem, P., Helgason, H., Grarup, N., Sigurdsson, A., Helgadottir, H. T., Johannsdottir, H., Magnusson, O. T., Gudjonsson, S. A., Justesen, J. M., Harder, M. N., Jorgensen, M. E., Christensen, C., Brandslund, I., Sandbaek, A., Lauritzen, T., Vestergaard, H., Linneberg, A., Jorgensen, T., Hansen, T., Daneshpour, M. S., Fallah, M.-S., Hreidarsson, A. B., Sigurdsson, G., Azizi, F., Benediktsson, R., Masson, G., Helgason, A., Kong, A., Gudbjartsson, D. F., Pedersen, O., Thorsteinsdottir, U. & Stefansson, K. (2014). Identification of low-frequency and rare sequence variants associated with elevated or reduced risk of type 2 diabetes. *Nat Genet* **46**, 294–298.

Stover, P. J. (2006) Influence of human genetic variation on nutritional requirements. *Am J Clin Nutr* **83**, 436S–442S.

Stratigopoulos, G., Leduc, C. A., Matsuoka, N., Gutman, R., Rausch, R., Robertson, S. A., Myers, M. G., Chung, W. K., Chua, S. C. & Leibel, R. L. (2009) Functional consequences of the human leptin receptor (LEPR) Q223R transversion. *Obesity* **17**, 126–135.

Summerhayes, G. R., Leavesley, M., Fairbairn, A., Mandui, H., Field, J., Ford, A. & Fullagar, R. (2010) Human adaptation and plant use in Highland New Guinea 49,000 to 44,000 years ago. *Science* **330**, 78–81.

Summerhayes, G., Matisoo-Smith, E., Mandui, H., Allen, J., Specht, J., Hogg, N. & McPherson, S. (2010) Tamuarawai (EQS): An early Lapita site on Emirau, New Ireland, PNG. *J Pacific Archaeol* **1**, 62–75.

Swinburn, B. A., Ley, S. J., Carmichael, H. E. & Plank, L. D. (1999) Body size and composition in Polynesians. *Int J Obesity* **23**, 1178–1183.

Van Der Sande, M. (2003) Cardiovascular disease in sub-Saharan Africa: A disaster waiting to happen. *Neth J Med* **61**, 32–36.

Van Der Sande, M. A., Schim Van Der Loeff, M. F., Aveika, A. A., Sabally, S., Togun, T., Sarge-Njie, R., Alabi, A. S., Jaye, A., Corrah, T. & Whittle, H. C. (2004) Body mass index at time of HIV diagnosis: A strong and independent predictor of survival. *J Acquir Immune Defic Syndr* **37**, 1288–1294.

VanDijk, N. (1991) The Hansel and Gretel syndrome: A critique of Houghton's cold adaptation hypothesis and an alternative model. *NZJA* **13**, 65–89.

Wilberfoss, P. C. R. (2012) *Cold case: Cold induced vasodilation response, and the origins of Polynesian body morphology as an adaptation to a cold environment*. PhD Thesis, University of Auckland.

Wilmshurst, J. M., Hunt, T. L., Lipo, C. P. & Anderson, A. J. 2011. High-precision radiocarbon dating shows recent and rapid initial human colonization of East Polynesia. *Proc Natl Acad Sci USA* **108**, 1815–1820.

Wollstein, A., Lao, O., Becker, C., Brauer, S., Trent, R. J., Nürnberg, P., Stoneking, M. & Kayser, M. 2010. Demographic history of Oceania inferred from genome-wide data. *Curr Biol* **20**, 1983–1992.

Zimmet, P., Dowse, G., Finch, C., Serjeantson, S. & King, H. (1990) The epidemiology and natural history of NIDDM–lessons from the South Pacific. *Diabetes Met Rev* **6**, 91–124.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Type 2 diabetes prevalence estimates for 2013 for Pacific Island populations as reported by the International Diabetes Federation (http://www.idf.org/atlasmap/atlasmap) and age-standardised prevalence of obesity (BMI $\geq$30 kg/m^2) in Pacific Island populations as of 2008 as reported by the WHO (http://apps.who.int/gho/data/view.main.2450?lang=en). New Zealand Māori and Pacific data as reported by NZ Ministry of Health (http://www.health.govt.nz/system/files/documents/publications/health-of-new-zealand-adults-2011-12-v2.pdf). Data for Native Hawaiians as reported by the University of Hawaii (http://www.oha.org/health/downloads/2011NativeHawaiianHealthFactSheet.pdf).

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