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QUANTITATIVE GENETIC ANALYSES OF POSTCANINE MORPHOLOGICAL CROWN VARIATION

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ABSTRACT

Objectives: This paper presents estimates of narrow-sense heritability and bivariate genetic correlation for 14 tooth crown morphological variants scored on permanent premolars, first molars, and second molars. The objective is to inform data collection and analytical practices in dental biodistance and to provide insights on the development of molar crowns as integrated structures.

Materials and Methods: African American dental casts from the Menegaz-Bock collection were recorded for the Arizona State University Dental Anthropology System (Turner et al., 1991). Estimates of narrow-sense heritability and genetic correlation were generated using SOLAR v.8.1.1, which included assessment of age, sex, and birth year as covariates. Both continuous scale and dichotomized estimates are provided.

Results: Heritability estimates were non-significant for the majority of variables; however, for variables yielding significant estimates, values were moderate to high in magnitude and comparable to previous studies. Comparing left and right side heritability estimates suggests directional asymmetry in the expression of environmental variance, something not seen in anterior tooth traits (Stojanowski et al., 2018). Genetic correlations were moderate among antimeres and metameres and low for different traits scored on the same tooth crown. Although several negative correlations were noted, few reached statistical significance. Results affirm some of the current data cleaning and analytical practices in dental biodistance, but others are

called into question. These include the pooling of males and females and combining left and right side data into a single dataset.

Conclusions: In comparison to anterior tooth crown traits, postcanine heritabilities were more often non-significant; however, those traits with significant heritability also tended to produce higher estimates. Genetic correlations were unremarkable, in part, because they were underpowered. However, M1 results may provide insight into the complex relationship between genes, environment, and development in determining ultimate crown form.

Teeth are used as genetic proxies to reconstruct evolutionary relationships in archaeological and paleontological contexts. Tooth morphology, for example, is used in bioarchaeology to infer population relationships at multiple scales of analysis. The size and morphology of tooth crowns are also used to infer the adaptive niches of extinct species, as heterodonty and the evolution of isomeric occlusion were among the distinct advantages of early mammalian taxa. For this reason, and due to the comparative abundance of tooth crowns in the fossil and archaeological records, understanding the genetic signals manifest in patterns of dental variation is important for a number of fields including anthropology, paleontology, and comparative mammalogy. Researchers have used a combination of experimental, evolutionary-developmental, and quantitative genetic analyses to identify the mechanisms involved in tooth crown differentiation and to reconstruct the developmental processes responsible for the observed range of variation in molar crowns (Gómez-Roblez, & Polly, 2012; Grieco, Rizk, & Hlusko 2013; Hlusko and Mahaney, 2003; Hlusko et al., 2004, 2011; Jernval, Åberg, Kettunen, Keränen, & Thesleff, 1998; Jernvall, Kettunen, Karavanova, Martin, & Thesleff, 1994; Koh, Bates, Broughton, Do, Fletcher, Mahaney & Hlusko, 2010; Polly, 2015; Polly & Mock, 2018; Salazar-Ciudad & Jernvall, 2002, 2010). Developmental origins of crown variants have also been discussed within a quantitative genetic framework, particularly in studies of single species datasets (e.g., *P. hamadryas* –Hlusko, Maas, & Mahaney, 2004; Hlusko, Do, & Mahaney, 2007; *C. parva*—Polly & Mock, 2018). In particular, the work of Hlusko and colleagues has provided critical data on patterns of modularity and integration in the primate dentition, focusing on

features such as interconulid/interconulus presence (Hlusko and Mahaney, 2003), enamel thickness (Hlusko, Suwa, Kono, & Mahaney, 2004a), molar loph/lophid angle (Hlusko et al., 2004b), molar cusp areas (Hlusko et al., 2007; Koh et al., 2010), and geometric morphometric assessments of tooth/arcade form (Hlusko et al., 2011).

By comparison, quantitative genetic analyses of human dental data have been limited, especially concerning crown variation of the postcanine dentition. Most previous studies have focused on overall crown size (e.g., Alvesalo & Tigerstedt, 1974; Dempsey & Townsend, 2001; Stojanowski, Paul, Seidel, Duncan, & Guatelli-Steinberg, 2017; Townsend & Brown, 1978a, 1978b, 1979; Townsend et al., 1986) or specific features such as Carabelli's trait (Alvesalo, Nuutila, & Portin, 1975; Biggerstaff, 1973; Kolakowski, Harris, & Bailit, 1980; Laatikainen & Ranta, 1996; Townsend & Martin, 1992) or cusp 5 of the maxillary molars (Harris & Bailit, 1980; Townsend, Yamada, & Smith, 1986). However, comprehensive assessments of a more complete suite of postcanine crown variants, such as that presented in the ASUDAS (Turner et al., 1991) is lacking (but see Scott & Potter, 1984).

In two previous papers we used quantitative genetic methods to estimate heritability and inter-trait genetic correlations for mesiodistal tooth size and a series of anterior morphological crown variants in a sample of African American individuals from the southeastern US (Stojanowski, Paul, Seidel, Duncan, & Guatelli-Steinberg, 2017, 2018). Results presented in Stojanowski et al. (2017) indicated a high degree of genetic integration of mesiodistal crown size across the dentition. While univariate heritability estimates were lower than those reported for

other human populations, positive estimates of genetic correlation indicated a high degree of dimensional pleiotropy compared to a hypothesized general mammalian pattern based on previous studies of baboons and mice (Hlusko & Mahaney, 2007; Hlusko, Sage, & Mahaney, 2011). In Stojanowski et al. (2018), estimates of narrow sense heritability and inter-trait genetic correlation were presented for anterior tooth crown morphological variants. Results indicated low but statistically significant heritabilities for most traits, strong genetic and phenotypic correlations among antimeres, strong genetic correlations among traits scored across different teeth, and a complex pattern of positive and negative genetic correlations among traits scored on the same tooth crown. As with the odontometric results, heritabilities for tooth crown variants were lower than previously reported estimates, which we interpreted as reflecting the combined effects of reduced additive genetic variation in this population as well as high environmental variance due to the socioeconomic/living conditions of the Gullah (Guatelli-Steinberg, Sciulli, & Edgar, 2006; Stojanowski et al., 2018). Although our interest was in estimating quantitative genetic parameters that speak to the dentition's use as a proxy in evolutionary studies, the lower than expected heritability estimates reported in both papers are consistent with the documented degree of dental asymmetry in the Gullah sample (Guatelli-Steinberg et al., 2006).

Here, we use the same sample of mid-20th century African American individuals living on James Island, South Carolina (ethnic Gullah) to generate estimates of narrow-sense heritability as well as genetic and phenotypic correlations among postcanine crown variants within the Arizona State University Dental Anthropology System (ASUDAS) (Edgar, 2017;

Scott & Irish, 2017; Turner, Nichol, Scott, 1991). This paper has two goals. The first is to present new estimates of narrow-sense heritability and genetic correlation for postcanine morphological crown traits. The second is to use quantitative genetic analyses to assess current assumptions and analytical "best practices" employed in dental biodistance research. The first goal provides foundational knowledge about dental biology, while the second is practical and informs data collection, data cleaning, and statistical methods in dental biodistance research. This work complements previous studies of the same sample (Stojanowski et al., 2017, 2018) and aims to refine the use of postcanine morphological variants for reconstructing biological relationships and microevolutionary processes.

BACKGROUND

Twin and family studies have been essential to exploring the genetic foundations of dental variation. These studies employ documented genealogical information and (typically) casted dentitions of extended pedigree members or kin pairs. For crown morphology, initial efforts focused on determining modes of inheritance, testing simple Mendelian versus complex polygenic trait models. In particular, Carabelli's trait was the focus of intensive, foundational research. Early studies showed Carabelli's trait data to fit either a dominant-recessive or autosomal codominant model, allowing for gene frequency estimation in some cases (Devoto & Perrotto, 1971; Dietz, 1944; Kraus, 1951; Tsuji, 1958; Turner, 1967). These findings were not always corroborated (Goose & Lee, 1971; Lee & Goose, 1972; Sofaer, 1970), suggesting a more complex, polygenic mode of inheritance. The fact that morphological characters like Carabelli's

trait vary widely in their degree of expression has also been viewed as consistent with a multifactorial mode of inheritance (Sofaer, 1970; Scott, Turner, Townsend, Martinón-Torres, 2018). Assuming an underlying polygenic framework, subsequent studies assessed the fit of threshold or quasi-continuous trait models to pedigreed datasets as a means of exploring the variable nature of discrete crown characters (e.g., Bailit, Anderson, & Kolakowski, 1974; Bailit, Brown, & Kolakowski, 1975; Harris, 1977; Scott, 1973). Complex segregation analyses also provided insight into competing genetic effects (i.e., "major genes" and "minor genes") and trait transmissibility (Kolakowski et al., 1980; Nichol, 1989). The results of this work are summarized by Scott and colleagues (2018).

Despite initial searches for major genes and simple modes of inheritance, current perspectives acknowledge that morphological crown traits are likely polygenic and characterized by complex modes of inheritance. As such, dental anthropology has embraced quantitative genetic approaches, which help ground truth the assumptions of biodistance analyses and enhance analytical methods for reconstructing evolutionary processes. Character-specific heritability estimates inform trait selection through quantification of the relative influence of genes on patterns of phenotypic variation; heritability is often seen as a measure of a trait's "utility" for both biodistance and phylogenetic research. It is also a key parameter for reconstructing population structure from quantitative traits via R matrix analysis (e.g., RMET) (Relethford & Blangero, 1990; Relethford, 1994, 1996; Relethford, Crawford, & Blangero, 1997; Williams-Blangero & Blangero, 1989; reviewed in Relethford, 2007, 2016), and can inform trait

weighting in multivariate phenotypic distance calculations (Stojanowski & Schillaci, 2006). Narrow-sense heritability (h^2) is the parameter of interest, because it represents the relative contribution of additive genetic variance alone, as compared to broad-sense heritability (H^2) that does not distinguish between additive and non-additive (e.g., multigene interaction, dominance) genetic effects.

Results of quantitative genetic analyses have shown permanent crown dimensions to be under moderate to strong genetic influence, with additive genetic variance accounting for over half of phenotypic variance on average (e.g., Alvesalo & Tigerstedt, 1974; Dempsey and Townsend, 2001; Dempsey et al., 1995; Lundström, 1948; Stojanowski et al., 2017; Townsend and Brown, 1979). By comparison, morphological characters on adult teeth yield lower heritability estimates, typically falling within the 0.40 to 0.80 range for the mesial-most member of each tooth class (Scott & Turner, 1997:164; for examples see Berry, 1978; Laatikainen & Ranta, 1996; Mizoguchi, 1977; Townsend & Martin, 1992). It is important to note that not all studies employ the same analytical methods and that heritability estimation has improved in statistical rigor over the years. Initial work derived estimates from trait concordance rates among monozygotic and dizygotic twin pairs, familial intra-class correlation coefficients, and analysis of variance. Carabelli's trait, along with certain molar variants, received much attention (Alvesalo et al., 1975; Berry, 1978; Biggerstaff, 1970, 1973; Kaul, Sharma, Sharma, & Corruccini, 1985; Laatikainen & Ranta, 1996; Mizoguchi, 1977; Scott & Potter, 1984; Sofaer, MacLean, & Bailit, 1972). More recently, sophisticated model-fitting approaches have become

the norm, such as path analysis and structural equation modeling (Townsend & Martin, 1992; Townsend et al., 1992; Hughes, Vo, Mihailidis, & Townsend, 2010; Trakinienė et al., 2018), as well as variance components analysis via maximum likelihood estimation (Paul et al., 2018; Stojanowski et al., 2018).

Considering the diversity of these analytical approaches and the population-specificity of heritability, it is not surprising that reported values vary greatly. Molar morphology is no exception. In a recent review of Carabelli's trait research, Scott et al. (2018) summarized the results of several twin concordance studies (e.g., Berry, 1978, Biggerstaff, 1973; Scott & Potter, 1984; Skrinjaric, Sliaj, Lapter, & Muretic, 1985). Heritability estimates ranged from ~0.0 to 0.91 (mean h^2= 0.45) (pp. 143-144). Family-based estimates also varied greatly. While Alvesalo et al., (1975) reported no evidence for correlations among siblings in a sample of rural Finns, Scott (1973) reported intra-class correlations ranging from 0.39 to 0.57 (across sibling and parent-offspring pairs) in Euro-Americans. In a more recent study of South Australian twins, model-fitting approaches yielded heritability estimates of 0.90 for M^1 Carabelli's trait and indicated that a combination of additive genetic effects, shared environmental effects, and unique environmental effects best account for observed phenotypic patterns (Townsend & Martin, 1992). While no single heritability estimate can be applied across populations, research generally indicates a moderate degree of genetic determination for the varying expression of this character, with several twin studies converging upon similar estimates of ~0.40, despite using samples of

diverse bioregional origins (Boraas, Messer, & Till, 1988; Mizoguchi, 1977; Scott & Potter, 1984; Scott et al., 2018; Townsend & Martin, 1992).

Heritability estimates have been reported for select postcanine variants beyond Carabelli's trait. Higgins and colleagues (2009) reported a hypocone heritability estimate of 0.87 for M1 and 0.93 for M2 in a South Australian twin sample. The best-fit model incorporated only additive genetic and unique environmental effects as contributors to hypocone variance (Higgins et al., 2009). Hughes et al. (2010) also reported heritability estimates exceeding 0.75 for several mandibular crown traits in the same sample. With few exceptions, best-fit models included both an additive genetic and unique environmental term (Hughes et al., 2010). The estimates presented in these twin studies exceed all family-based intraclass correlation coefficients reported for postcanine tooth traits by Scott (1973) (M^2 hypocone r=0.40-0.55; M^1 Carabelli's trait r=0.39-0.57; P_1/P_2 lingual cusp number r=0.21-0.61; M_1 cusp 7 r=0.28-0.52). Family studies of M^1 cusp 5 in Solomon Islanders (Harris & Bailit, 1980) and Australian Aboriginals (Townsend, Yamada, & Smith, 1986) yielded fairly low sibling-sibling correlation coefficients (Solomon Islands: M^1 C5 sister-sister ρ=0.32; Australia: M^1 C5 ϕ=0.04). These findings indicated a considerable environmental influence on cusp 5 expression. However, it should be noted that a statistically significant correlation was reported for the deciduous second molar in the Aboriginal sample (m^2 C5 ϕ=0.66) (Townsend et al., 1985), and when Harris and Bailit (1980) pooled data for all Solomon Islander relatives, they obtained cusp 5 heritability estimates of 0.65 and 0.15 for M^1 and M^2, respectively. A more moderate sibling-sibling correlation

coefficient of 0.30 was reported for M_1 cusp 6 in the Australian Aboriginal sample (Townsend et al., 1990).

MATERIALS AND METHODS

Data on 14 morphological molar crown variants were collected using ASUDAS standards (Turner et al., 1991). The trait list includes five maxillary molar traits recorded for both the M1 and M2 (metacone, hypocone, cusp 5, Carabelli's trait, parastyle), one mandibular premolar trait collected for both the P1 and P2 (lingual cusp variation), and eight mandibular molar crown variants, of which six were collected on both the M1 and M2 (cusp 5, cusp 6, cusp 7, cusp number, groove pattern, protostylid) and two were scored only on the M1 (anterior fovea, deflecting wrinkle). Third molar data were infrequent on casted dentitions due to the limitations of the casting protocol. All data were scored by a single investigator (WND) to minimize inter-observer error. We have previously discussed assessment of intra-observer error for this dataset (Stojanowski et al., 2018), which produced estimates within an acceptable range (cf., Marado, 2017; Scott, 1973). Mesiodistal dimensions were recorded by CMS and are used here as markers of crown size.

The study sample consists of ~460 dental casts of African American individuals living in coastal South Carolina during the early to mid-20th century (ethnic Gullah). Casts and genealogical records were collected by Rene Menegaz-Bock during her dissertation research (Menegaz-Bock, 1968); the latter provide information on familial relationships, age at time of casting, sex, and birth year. We used these data to compile genealogies that resulted in the

identification of 22 bilineal families, including one single pedigree that included 313 individuals. The distribution of genealogical relationships is presented in Table S1 and includes 652 individuals inclusive of non-casted founders. All individuals were living on James Island, South Carolina at the onset of Menegaz-Bock's research project. She noted a population of approximately 3,400 individuals living on the island at the time, a number which slightly underestimates the total population size of the island and does not reflect the size of the entire coastal South Carolina Gullah population during the mid-twentieth century. The cast sample represent approximately 13% of the population living on the island at that time. Previous studies using the reconstructed genealogies suggest minimal impact of recording errors (Stojanowski et al., 2017, 2018), although there is the potential for adoptions and other fictive kin relationships (and half sibships) that were not captured in the genealogical recording (Twining and Baird, 1991). Further details on the Gullah sample can be found in Stojanowski et al. (2017, 2018), which summarize the relevant details from initial work among the population (Menegaz-Bock, 1968; Pollitzer, 1958, 1993, 1999; Pollitzer, Menegaz-Bock, Ceppellini, & Dunn, 1964), including prior dental anthropological analyses (Edgar, 2000; Edgar & Sciulli, 2004; Guatelli-Steinberg et al., 2006) and assessments of genetic variation (McLean, Argyropoulos, Page, Shriver, & Garvey, 2005; McLean et al., 2003; Parra et al., 2001; Sale et al., 2009). All research presented in this paper was conducted under the approval of The Ohio State University IRB (2012B0529).

We estimated narrow-sense heritability (h^2) using maximum likelihood variance components analysis. All estimates were derived using SOLAR v.8.1.1 (Almasy & Blangero, 1998; Blangero et al., 2016), which accommodates unbalanced and complex pedigrees and provides more realistic estimates of trait heritability (i.e., free of over-estimation based on sibling, parent-offspring, or twin study designs). Four covariates were screened for significant effects: age, sex, age/sex interaction, and birth year. Significance of covariates was assessed at the $p < 0.10$ level; the total effect of all significant covariates was recorded. All significant covariates were fixed in subsequent bivariate analyses (see Boehnke, Moll, Kottke, & Weidman, 1987; Falconer, 1989; Hopper & Mathews, 1982; Lange, Boehnke, & Opitz, 1983).

Bivariate analyses (SOLAR v.8.1.1) were used to estimate additive genetic (ρ_G) and environmental (ρ_E) correlations between pair-wise combinations of traits (see Almasy, Dyer, & Blangero, 1997; Blangero, Konigsberg, & Vogler, 1991; Hlusko & Mahaney, 2007; Hlusko et al., 2004; Mahaney et al., 1995). Likelihood ratio tests were then used to assess whether the genetic and environmental correlations were significantly different from 0.0 (complete pleiotropy), significantly different from 1.0 (no pleiotropy), or significantly different from both (incomplete pleiotropy). Tests that returned two insignificant results were considered underpowered and interpreted as a non-result. Derived phenotypic correlations (ρ_P) were subsequently estimated using the formula $\rho_P = \sqrt{h_1^2}\sqrt{h_2^2}\,\rho_G + \sqrt{(1-h_1^2)}\sqrt{(1-h_2^2}\,\rho_E$. Because each pair-wise combination of variables could include multiple estimates of heritability

(see below) bivariate analyses included traits dichotomized at expression breakpoints that yielded the highest univaritate heritability estimate.

Narrow-sense heritabilities and estimates of genetic, environmental, and phenotypic correlations were calculated for each variable in two ways. First, the variable was treated as continuous scale in recognition of the fact that ASUDAS morphological scoring applies an ordinal scale to what is an inherently (quasi)continuous variable (see Hlusko & Mahaney, 2003; also Carson, 2006; Cheverud, Buisktra, & Twichell, 1979; Corruccini, 1976; Harris, 1977; Sofaer, Niswander, McLean, & Workman, 1972). Data were transformed using SOLAR's *inorm* function to mitigate the effects of distributional variance (primarily kurtosis) on significance testing. Analyses with kurtosis values beyond the acceptable range were marked in our output and should be interpreted with caution. These results are most comparable to the odontometric heritabilities and correlations previously reported in Stojanowski et al. (2017). Because SOLAR does not accommodate ordinal scale data, we then divided each trait into a number of binary scale variables at different breakpoints as determined by sample frequency. For example, Carabelli's trait was analyzed as a continuous scale variable and as a series of seven binary scale variables with breakpoints for trait presence defined as 1+ = present, 2+ = present, and so forth. The distribution of raw scores is presented in Table S2.

RESULTS

Heritability estimates and results of covariate screening are presented in Table 1. The covariates of birth year and age at time of casting returned significant p-values for some

variables, but these were not consistent across sides or breakpoints and are likely the result of family-wise error. In fact, exactly 9% of tests were statistically significant, which is expected at the $\alpha = 0.10$ level. Birth year may reflect a cohort effect or secular trends in morphological variation due to changing environmental (i.e., lifestyle) conditions. Age, on the other hand, likely indexes scoring error related to dental attrition and the lack of significance for this variable suggests scoring error has been minimized in this sample. For the sex covariate, 17% of p-values were statistically significant at the $\alpha = 0.10$ level, which is beyond the expectations of family-wise error. Many of these significant results were isolated and inconsistent across sides/breakpoints and likely spurious. However, the results for RM^2 hypocone, LM^1 Carabelli's trait, RM_2 cusp 6, and RM_1 cusp 7 suggest a real phenomenon is captured. These results are consistent with previous research documenting sexual dimorphism in Carabelli's trait expression in some populations (Townsend & Brown, 1981; Tsai, Hsu, Lin, & Liu, 1996), and suggest that the expression of other cusp variants is sexually dimorphic. This may require reconsideration of the pooling of sexes in dental biodistance analyses, but even in this sample the effect was not consistent across antimeres.

Heritabilities were moderate in magnitude and generally comparable to previously reported estimates based on analyses of other populations, contrary to results reported for anterior tooth crown data in the Gullah (Stojanowski et al., 2018). The best index of comparison is Carabelli's trait, which returned significant heritability estimates at nearly all breakpoints with the maximum left (0.847) and right (0.691) side estimates comparable to previous studies of

European and Asian samples (reviewed in Scott et al., 2018). Average heritability by tooth type for all statistically significant estimates was: M^1 = 0.621, M^2 = 0.882, M_1 = 0.707, M_2 = 0.870. The average for all statistically significant estimates across tooth types and arcades was 0.748. The M2 (both maxillary and mandibular) heritabilities are likely spuriously high, resulting from small sample sizes. As such, these results should be considered preliminary and provide limited basis for comparing M1 and M2 estimates. We note that all molar averages are considerably higher than those we previously reported for anterior tooth crown variants, which averaged ~0.340 across all statistically significant estimates (Stojanowski et al., 2018). These differences are unlikely to be statistically different given the large standard errors associated with these estimates. A number of molar traits are also characterized by heritabilities that were not significantly different from 0.0 for any breakpoint (M^1 metacone, M^2 Carabelli's trait, M^1 parastyle, M^2 parastyle, P_1 lingual cusp number, P_2 lingual cusp number, M_2 cusp 6*, M_1 cusp 7, M_1 cusp number, M_1 deflecting wrinkle, M_1 groove pattern, M_2 groove pattern, M_1 protostylid*; * indicates kurtosis violation), which is in contrast with the anterior dentition for which only three traits failed to produce statistically significant heritability estimates (Stojanowski et al., 2018). This difference could reflect variation in the way the molar traits are scored and the limited variation that results from the scoring protocol. For example, it is rare to have an M^1 metacone scored less than 4, thus compressing the range of variation to only two scores (4 and 5) for most individuals. Regardless, scoring scale does not explain all traits that returned zero heritability estimates (for example LM_1 cusp 6 and 7).

Another difference between the postcanine morphology and anterior morphology results was the degree of asymmetry in the postcanine heritability estimates. There were many traits for which at least one left side estimate was significantly different from zero and the corresponding right side estimates were not (M^2 metacone*, M^1 cusp 5, M^2 cusp 5, M_1 cusp 5, M_1 cusp 6, M_2 cusp number; * indicates kurtosis violation). For traits for which both sides returned a significant heritability estimate, there was also a tendency for the left side estimate to be higher than the corresponding right side estimate (M^1 hypocone (left higher), M^1 Carabelli's trait (left higher), M_1 anterior fovea (right higher), M_2 cusp 5 (left higher), M_2 cusp 7 (right higher)*; * indicates kurtosis violation). Given that additive genetic variance is held constant for these comparisons, the reduction in heritability on the right side suggests an environmental effect is evident, which represents directional asymmetry in this dataset.

Asymmetry among antimeres is also indicated by estimates of genetic correlation (Table 2), which were not uniformly high and many of which were not significantly different from zero. This is in sharp contrast to the genetic correlations among antimeres for mesiodistal dimensions (Stojanowski et al., 2017) and anterior tooth crown variants (Stojanowski et al., 2018). The same is true for the phenotypic correlations which were, on average, 0.628 for postcanine traits (inclusive of M2s), 0.708 for anterior tooth crown traits (Stojanowski et al., 2018), and 0.799 for mesiodistal dimensions (Stojanowski et al., 2017). That postcanine morphology demonstrates the least antimeric symmetry and overlap in additive genetic contribution might suggest a greater potential effect of environmental variance on trait expression.

Genetic correlations for metameres are presented in Table 3 for those traits scored on both the M1 and M2. The small sample sizes for observable M2s significantly limits the utility of these analyses, however. Significant p-values are infrequent but suggest complete pleiotropy for some hypocone and M^1 cusp 5 comparisons. In general, the correlations are positive, many at or near 1.0, which suggests the same genes are implicated in the formation and size of primary and secondary cusps of the first and second maxillary molar crowns. The lack of consistency across sides and breakpoints indicates caution is needed; results should not be over interpreted. None of the observed negative correlations are significantly different from zero and should be considered spurious until confirmed with additional data.

In Table 4 we present the results of the genetic correlation analyses for traits scored on the same tooth crown. These data test the assumption of trait independence, which is now generally recognized as problematic given our understanding of multicuspid crown development. Following standard protocol, the issue of genetic redundancy is instead ameliorated through the use of key teeth for ASUDAS data collection or through trait omission based on post hoc phenotypic correlations (Scott et al., 2018; Turner et al., 1991). Unfortunately, sample sizes for the M2s were too small to produce interpretable results. In addition, parastyle data were removed, because the trait was extremely infrequent in this dataset, rendering most results meaningless. Comparing left side M^1 crown traits to the mesiodistal dimension indicates that cusp 5 and Carabelli's trait are not genetically correlated with molar crown length; the underpowered metacone results suggest a similar interpretation. Mesiodistal diameter and

hypocone size are incompletely pleiotropic, which is as expected given that mesiodistal length is, in part, determined by hypocone presence and size. In other words, there is some overlap in the genes responsible for mesiodistal tooth size, the size of primary molar cusps, and the presence and size of secondary molar cusps. None of the right side comparisons produced significant p-values, which we interpret as reflecting a higher than expected degree of asymmetry in this sample.

Genetic correlations among maxillary morphological traits returned two significant p-values, indicating complete pleiotropy between metacone and Carabelli's trait and between hypocone and Carabelli's trait. Other trait comparisons returned moderate to high positive genetic correlations; however, p-values were not significant, which in most cases indicated a lack of power. These results call into question the assumption of genetic independence for these traits. Once again, none of the right side comparisons produced a significant p-value.

The greater number of traits scored on mandibular molars makes interpreting these results more challenging. Comparisons involving the M_1 mesiodistal dimension and crown features returned significant p-values only for cusp 5, indicating complete pleiotropy. Results for y groove pattern, anterior fovea, and deflecting wrinkle were also positive, though underpowered. The most surprising result was the consistent finding of negative genetic correlations between tooth size and cusp 6, cusp 7, and cusp number. Although these correlations were also underpowered, the negative correlations suggest the same genes underlie the expression of crown length and the presence of accessory cusps but cause opposing phenotypic effects. In other

words, genes that increase tooth size decrease the presence or size of accessory, but not primary, cusps. Comparison among morphological features affirms this result. All correlations involving cusp 5 (at two different break point values) returned negative genetic correlations, including significantly negative correlations in the case of cusp 6. That is, the same genes that increase the size of cusp 5 work to reduce the size of cusp 6 (and to a lesser extent cusp 7). Remaining comparisons were all underpowered, and any significant p-values are associated with genetic correlations of 1.0, which are suspect.

There is, however, a potentially significant relationship between groove pattern and other crown features. Because we used the variant that yielded the highest univariate heritability estimate for subsequent genetic correlation analyses, left M_1 comparisons were made between the presence of a y configuration and other crown traits, while right M_1 comparisons were made between the presence of a + configuration and other crown traits. For the left side comparisons, all minor crown variants, including accessory cusps, returned negative genetic correlations. The magnitudes varied considerably. Some were quite low and unlikely to achieve statistical significance with increased sample size (anterior fovea and, to some extent, cusp 7 and protostylid). However, the negative correlations between y groove pattern and both cusp 6 and deflecting wrinkle were large in magnitude and likely to be significant with a larger sample size. Interestingly, the right side comparisons against + groove pattern were all positive and mostly large in magnitude. This suggests a relationship between overall crown form, reflected in a y or + cusp configuration among the four earliest forming cusps, and the presence of most accessory

crown features. That is, the genes responsible for a y configuration work to *reduce* the presence of all other minor anatomical variants, including accessory cusps, while the genes responsible for a + configuration work in concert to produce a more *architecturally complex, cuspidate* molar crown. Though under-powered, univariate tests support this interpretation, with y form crowns exhibiting significantly lower cusp number ($p = 0.011$) and smaller cusp 6s ($p = 0.053$) when compared to + and x form crowns, as well as + form crowns exhibiting significantly higher cusp number ($p = 0.019$) and larger cusp 6s ($p = 0.001$) when compared to y and x form crowns. Comparisons for cusp 5, cusp 7, and protostylid generally followed the same patterns, although p-values were not significant.

DISCUSSION

In this paper we have presented new estimates of heritability and genetic correlation for a series of dental morphological traits scored in the postcanine dentition using ASUDAS standards. Despite decades of prior work on the heritability of specific postcanine crown features (for a recent review see Scott et al., 2018), we believe this is the first paper to present heritability estimates for a nearly complete series of postcanine crown features using maximum likelihood variance components analysis, a statistically robust, model-fitting approach. Limitations of the paper include the small sample size for second molars and the high degree of asymmetry in the results. As such, we focus our discussion primarily on the first molar data from the left side only (except where asymmetry is the focus). We interpret the results with respect to two distinct, yet overlapping areas of inquiry: 1) the implications of these quantitative genetic analyses for the

practice of dental biodistance, and 2) the implications of these analyses for understanding patterns of variation and development in the human dentition. The latter directly relates to existing dental developmental models (i.e., the patterning cascade model- Jernvall (2000), Jernvall & Thesleff (2000)) and previous research using other primates and mammalian model organisms (Hlusko and Mahaney, 2003; Hlusko, et al., 2004a, 2004b, 2007, 2011; Koh et al., 2010).

Implications for Dental Biodistance

Many postcanine traits scored in the Gullah sample were not heritable. In fact, more than half (12 of 21) of the features typically recorded in the ASUDAS returned heritabilities not significantly different from 0.0 (including premolar traits—cf., Ludwig, 1957; Lundström, 1963; Wood and Green, 1969) (Table 1). Some of these results can be explained by small sample size (most of the M2 traits) and some can be explained by low sample frequency. However, low frequencies cannot explain all of the non-significant results. For the maxillary M^1, Carabelli's trait (sample frequency = 20-63%), hypocone (14-69%) and cusp 5 (27%) all returned positive heritabilities (see Tables 1 and S2). However, metacone and parastyle did not, and while the low frequency of parastyles (1%) in this sample likely explains the trait's lack of observed heritability, metacone frequencies varied between 4 and 25% across different breakpoints. The upper range matches frequencies of molar traits that returned positive heritabilities, and we suspect the metacone results reflect an issue with the compressed scoring scale with respect to this feature's range of variation. The same pattern was evident for the mandibular first molar.

Traits with positive heritability included hypoconulid (sample frequency = 84%), cusp 6 (9-20%), and anterior fovea (17%), while traits that returned 0.0 heritability included cusp 7 (sample frequency = 40%), protostylid (8%), and groove pattern (4-84%). As such, there is no clear relationship between trait frequency and heritability that might reflect an analytical artifact.

We previously attributed low heritabilities in the Gullah sample to both reduced genetic variance due to isolation and endogamy, as well as increased environmental variance due to suboptimal socioeconomic conditions (Guatelli-Steinberg et al., 2006; Stojanowski et al., 2017, 2018). As such, the results reported for the Gullah may not reflect broader patterns among human populations. That is, while previous twin studies may over-estimate heritability due to study design, our results may under-estimate heritability due to the demographic and socioeconomic history of the study sample. However, we may have over-stated the case for reduced trait heritability in our previous papers. It is widely recognized that the Gullah were isolated from surrounding communities for an extended period of time after the Civil War and abolition of slavery (Opala, 1987; Pollitzer, 1999; Twining and Baird, 1991), with little reported out- or in-migration for the Sea Island communities of the South Carolina coast until very recently (but see Matory, 2008). As such, the cultural and linguistic ties to West Africa are still apparent, leading some to conclude that the Gullah are the least acculturated African American ethnic group. This is also reflected in patterns of genetic variation. The Gullah show the lowest levels of Euro-American admixture among African American communities (but not Afro-Caribbeans/South Americans) (Parra et al., 1998, 2001). Estimates of Euro-American admixture

average around 3-4% and Native American admixture around 2-3% (Maclean et al., 2003, 2005; Parra et al., 2001; Pollitzer, 1999). Even within South Carolina African American communities, the low level of European admixture is noteworthy with 80% of ethnic Gullah exhibiting < 10% European admixture as compared with ~50% of African Americans from the surrounding Low Country and Columbia environs (Parra et al., 2001).

However, a low level of admixture is not necessarily the same as reduced additive genetic variance. The Gullah are clearly linked to West African populations, specifically to those in Sierra Leone and populations living along the "rice coast" of West Africa (McClean et al., 2003, 2005; Stefflova et al., 2011). Therefore, as an African-derived population, internal genetic variation is actually considerably higher in the Gullah than in European populations (mtDNA haplotype diversity: Gullah = 0.8768, European American = 0.6280 per MacLean et al., 2005). Observed levels of haplotype diversity in the Gullah are also comparable to other African and African American populations. How patterns of mtDNA or Y chromosome haplotype diversity map onto dental phenotypes is difficult to predict. We note, however, that previous quantitative genetic studies of Gullah biomedical data failed to find evidence of bias due to population structure (Divers et al., 2010). Thus, there is no clear rationale for assuming a causal relationship between the isolation and endogamy of the Gullah and the low heritability estimates reported here and in our previous papers. Furthermore, we argue the pedigree structure of this sample better represents the realities of research on phenotypic variation using the archaeological record, as compared with single-generation twin or sibling studies.

Effect of breakpoints on heritability estimates. Dental morphological data are typically dichotomized in a distance analysis. There are two reasons for this. Dichotomization minimizes observer error allows for the calculation of sample frequencies and the Mean Measure of Divergence, the most commonly used population-level distance statistic in dental biodistance research. While trait dichotomization reduces the observed range of variation in a dataset, results presented here justify the approach. For example, treating the traits as continuous variables almost always produced lower heritability estimates than treating the traits as binary (presence/absence) variables. The average heritability for continuous scale analyses was ~0.38, while the average heritability for binary traits was nearly double that when the maximum dichotomization breakpoint was used (~0.69). Whether this reflects the effects of observer error or a real biological phenomenon is difficult to determine.

A related question is whether the standard breakpoints identified in Scott and Irish (2017), which are used widely in the dental biodistance literature, are optimized for evolutionary inferences. Table 5 summarizes heritabilities presented here and in Stojanowski et al. (2018) at the breakpoints specified by Scott and Irish (2017). Of note, the final column presents additional data for those traits with non-significant estimates, in particular, the breakpoint and sample frequency at which a statistically significant heritability is observed in the Gullah sample (if any). For example, I^1 double shoveling returned a 0.0 heritability using a breakpoint of 2. Reducing the breakpoint to 1 produces a significant heritability estimate of 0.34 and the sample frequency of expression increases from 20.9% to 57.5%. Data in Table 5 indicate that any

analysis of the Gullah sample using the breakpoints specified in Scott and Irish (2017) would include nine traits with significant positive heritability and 12 traits with 0.0 heritability. Shifting the breakpoint scale does little to ameliorate this; there is almost no correlation between positive heritability and sample frequency. For example, traits with positive heritability at the Scott and Irish (2017) breakpoint varied in frequency from 7.0 to 76.2%, while traits with 0.0 heritability varied from 0.7 to 73.7%. Therefore, it does not seem possible to use trait frequency as a guide toward generating project-specific breakpoints based on regional patterns of dental morphological trait expression. Rather, adjustments during the data collection phase may be required if ASUDAS standards fail to capture underlying genetic signals.

Selecting between antimeres for analysis. Although data may be collected for both antimeres, the estimation of distances based on dental morphological variables does not use data from both sides of the dentition. Most often the side with the maximum degree of expression is used; however, other options include using left or right side data only with antimere substitution in the case of missing data. Here we provide genetic correlations for antimeres that were generally significantly positive (Table 2), which indicates that antimeres are highly genetically correlated and should not be double counted. However, further complicating the issue is the degree of asymmetry noted in postcanine trait heritabilities and genetic correlations. Right side estimates of heritability were inconsistent and more often non-significant than left side estimates. This is difficult to explain in any other way than to assume that environmental variance components were higher for the right side of the dentition, although a biological explanation for this is

unknown. Additionally, antimere genetic correlations were much lower than those observed for odontometric (Stojanowski et al., 2017) and anterior morphological variables (Stojanowski et al., 2018), with derived phenotypic correlations being lower than expected based on previous studies of dental asymmetry (Baume & Crawford, 1979, 1980; Bollini, Rodriguez-Florez, & Colantonio, 2009; Mayhall & Saunders, 1986; Marado, Silva, & Irish, 2017; Mizoguchi, 1990; Moskona, Vainder, Herschkovitz, & Kobyliansky, 1996; Noss, Scott, Potter, & Dahlberg, 1983; Saunders & Mayhall, 1982). Interpreting the entirety of the pattern is difficult, but results seem to suggest that the postcanine dentition experiences greater directional asymmetry in the expression of dental morphological variants. This may be related to differences in developmental timing across antimeres (Harris, 1992), that are potentially exaggerated in later-forming tooth crowns, such as the premolars and second molars. Guatelli-Steinberg et al. (2006) previously documented fluctuating and directional asymmetry for Gullah crown size. Although permanent molars were not included in their study, results presented here are consistent with their findings. Similarly, Riga et al. (2014) documented increased, directional variation in molar cusp number and size in a stressed (vs. non-stressed) sample, indicating that environment can act “non-randomly” on developmental parameters throughout crown formation. Our results suggest caution is needed in selecting which side to use in dental biodistance analyses.

Sexual dimorphism in trait expression. The influence of sex on the expression of morphological traits is debated. As Scott et al. (2018: 105-106) note, "…given the nature of sampling distributions, reports of significant sex differences for traits vary from one sample to

another….When differences are found, they are usually inconsistent among samples and low-order in magnitude. For this reason crown and root traits…can be pooled to estimate population frequencies." Our results corroborate this, for the most part. We were able to replicate the results of numerous studies suggesting Carabelli's trait expression is sexually dimorphic in certain populations (e.g., Durner, 2013; Kondo and Townsend, 2006; Scott, Potter, Noss, Dahlberg, & Dahlberg, 1983; Townsend and Brown, 1981; Tsai et al., 1996), although here only the left side data produced consistent results (but these were the most consistent for any variable). In addition to Carabelli's trait, sex was a significant covariate for parastyle expression, and in the mandible, cusp 6 and cusp 7 expression. All of these traits are accessory cusps of the molar crown. It is often assumed that dental morphological traits (with the exception of canine distal accessory ridge) are not sexually dimorphic. Although our analyses leave the biological mechanism unexplained, the results suggest that care is needed in ascertaining the sex composition of pooled samples in archaeological contexts. Indeed, targeted association studies of single nucleotide polymorphisms and dental morphology have also documented significant sex effects for several postcanine dental traits (Kimura et al., 2015).

Trait independence. A basic assumption of biological distance analysis is that the traits used to estimate phenotypic similarity are genetically independent of one another. ASUDAS protocol dictates that each trait be represented by data collected on a single tooth, as supported by previous research on phenotypic correlation among metameres (Scott et al., 2018). Based on

thousands of samples, Turner and his students have identified what they call “key teeth” for each trait that best reflect patterns of variation (reviewed in Scott and Irish, 2017).

Quantitative genetic analyses of metameric variation directly assess the independence assumption. While small M2 sample size for the Gullah prevents a comprehensive evaluation, data presented in Table 3 generally support it. Most genetic correlations among metameres demonstrate large, positive correlations that are statistically different from 0.0. Note that even large negative correlations validate using only one tooth per trait in biodistance analyses, because a negative correlation reflects the action of the same genes operating to produce the opposite phenotypic effects. For example, the consistent negative correlations between metameres for mandibular cusp number simply reflects the tendency for cusp number to decrease as one moves distally in the tooth row. Still, many p-values were not significant, and additional data are needed to fully evaluate the metameric correlations.

The assumption of trait independence does not only apply to metameric scoring of morphological traits. A more foundational assumption of the ASUDAS is that each trait itself is genetically independent of all other traits recorded, including those located on the same tooth crown. Here, the results are less conclusive (Table 4), with many comparisons returning non-significant p-values for tests of both complete pleiotropy and complete genetic independence. Many of the significant correlations were also spuriously high, suggesting an issue with model convergence. The one significant maxillary result suggests that hypocone score and Carabelli’s trait are genetically correlated, but this was found only on the left side. None of the right side

correlations were significantly different from 0 or 1, which is interpreted as a non-result. In the mandible, cusps 5, 6, and 7 demonstrate limited evidence for complete pleiotropy (Table 4). Although inconclusive, the results suggest more research with larger sample sizes is warranted, especially in consideration of evolutionary developmental research suggesting integration of molar crown morphology through iterative enamel knot signaling.

Implications for Understanding Dental Variation

Quantitative genetic research has, until recently, failed to explore patterns of pleiotropy in an effort to identify hierarchically-structured morphological modules across the human dentition (but see Stojanowski et al., 2018). Thus, a comprehensive study of postcanine variants in a sample of complex pedigree structure—especially one employing model-fitting approaches to estimate both heritability *and* genetic correlation—is timely. This work complements a rich body of research on Cercopithecoid dental traits (e.g., Hlusko et al., 2004, 2007, 2009, 2011, 2016; Hlusko & Mahaney, 2003, 2007) and evo-devo models of mammalian postcanine tooth form (Jernvall, 2000; Jernvall & Thesleff, 2000; Hunter et al., 2010; Moormann, Guatelli-Steinberg, & Hunter, 2013; Ortiz, Bailey, Schwartz, Hublin, & Skinner, 2018) in an attempt to map genotype—phenotype pathways in the dentition. Unfortunately, given M2 sample size limitations, as well as a dearth of homologous ASUDAS crown features scored across arcades, regions of the dentition, and postcanine tooth classes (premolars and molars), we were unable to evaluate higher-level modularity in the Gullah sample. However, we did elucidate differential

patterns of modularity at the within-crown scale, especially for the later-forming and accessory cusps of the M^1/M_1 crowns.

That a pleiotropic relationship was shared between M^1 Carabelli's trait and a) metacone, and b) hypocone meets expectations outlined by the patterning cascade model, as the size and presence of these three later-forming cusps are (to some degree) governed by the configuration of the earlier forming protocone and paracone. These results suggest an overlap in the genes that regulate distal and accessory cusp expression, which is perhaps complexly related to the activation, inhibition, and protein signaling mechanisms functioning at the level of the molar crown as a "developmental unit." However, the negative genetic correlations between M_1 cusp 5 and a) cusp 6 and b) cusp 7 indicate that the mandibular molar is fundamentally different in its genetic architecture, at least with regards to its later forming cusps. Interestingly, it is hypothesized that negative genetic correlations are the hallmark of resource competition across processes, for example in life history traits (Atchely, 1987; Norry, Vilardi, & Hasson., 2000). Here, the resource in play may be the cellular real estate and developmental energy expended in crown formation, as negative genetic correlations are often expected when characters arise as the result of the subdivision of "developmental precursors" (Norry et al., 2000: 177; see also Atchely, 1987; Riska, 1986). It seems the expression of M_1 cusp 5 and cusp 6, in particular, are impacted by overlapping genes but in opposite directions, as limited biological resources are allocated throughout crown development or epithelial "partitioning" (Bochdanovits & de Jong, 2004). A functional explanation for this relationship is not readily apparent.

It is unclear why the patterns of within-crown genetic correlation were so different for the maxillary and mandibular molars. It is possible that genetic correlations between M1 isomeric cusp areas or crown shape would reveal these distinct morphological patterns to be the residual outcome of higher-level partitioning of the dentition into maxillary and mandibular occlusal units (or modules) (Gómez-Robles & Polly, 2012). Indeed, the functional role of the M1 in mastication makes this scenario plausible (Cheverud, 1996; Gómez-Robles & Polly, 2012; Young & Hallgrímsson, 2005), and analyzing continuous morphological variation between isomeres represents a crucial next step in exploring hierarchical modularity in Gullah dentitions. Importantly, results are specific to this sample and confirmation of these patterns in other populations is required before we can obtain a complete picture of the genetic architecture of the human dentition, as well as the potential contribution of small-scale modularity and negatively (genetically) correlated traits to the exceptional morphological diversity that characterizes our species.

Finally, this research bolsters recent molecular genetic research on the pleiotropic effects of gene variants among the components of ectodermally derived structures such as hair, mammary glands, and teeth (e.g., Hlusko et al., 2018). While the bulk of these studies have examined the correlation between specific *EDAR* and *PAX9* polymorphisms and incisor shoveling (Kimura et al., 2009, Lee et al., 2012; Park et al., 2012), molar morphology has also been examined. For example, Park et al. (2012) reported a marginally significant relationship between the Asian-specific *EDAR* 370A variant and M_2 cusp 5 or *hypoconulid* presence; this,

despite minimal phenotypic correlation between hypoconulid expression and incisor shoveling—another character associated with the *EDAR* genotype. Kimura et al. (2015) also reported associations between a single nucleotide polymorphism in *WNT10A* and variation in a) P_2 distolingual cusps, b) M^1 cusp 5, and c) M_2 cusp 5. These studies inform our understanding of microevolutionary processes and migration histories in *Homo sapiens*, yet their capacity to identify true "causation" and/or targets of selection are limited due to the effects of linkage disequilibrium and pleiotropy. Outlining the genetic architecture of the human dental complex provides insight into the overall potential for morphological characters to be impacted by the same genes or sets of genes, even when they are not phenotypically correlated.

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References Cited

Almasy, L., & Blangero, J. (1998). Multipoint quantitative-trait linkage analysis in general pedigrees. *American Journal of Human Genetics, 62,* 1198-1211.

Almasy, L., Dyer, T. D., & Blangero, J. (1997). Bivariate quantitative trait linkage analysis: Pleiotropy versus co-incident linkages. *Genetic Epidemiology, 14,* 953-958.

Alvesalo, L., Nuutila, M., & Portin, P. (1975). The cusp of Carabelli: Occurrence in first upper molars and evaluation of its heritability. *Acta Odontological Scandinavica, 33,* 191-197.

Alvesalo, L., & Tigerstedt, P. M. A. (1974). Heritabilities of human tooth dimensions. *Hereditas, 77,* 311-318.

Atchely, W. R. (1987). Developmental quantitative genetics and the evolution of ontogenies. *Evolution, 41*, 316-330.

Bailit, H. L., Anderson, S. & Kolakowski, D. (1974). The genetics of tooth morphology. *American Journal of Physical Anthropology, 41,* 468.

Bailit, H. L., Brown, R., & Kolakowski, D. (1975). The heritability of non-metric dental traits. *The American Journal of Physical Anthropoloyg, 42,* 289.

Baume, R. M., & Crawford, M. H. (1979). Discrete dental trait asymmetry in Mexico and Belize. *Journal of Dental Research, 58,* 1811.

Baume, R. M., & Crawford, M. H. (1980). Discrete dental trait asymmetry in Mexican and Belizean groups. *American Journal of Physical Anthropology, 52,* 315-321.

Berry, A. C. (1978). Anthropological and family studies on minor variants of the dental crown. In: P. M. Butler, & K. A. Joysey (Eds.), *Development, function and evolution of teeth* (pp. 81-98). London: Academic Press.

Biggerstaff, R. H. (1970). Morphological variations for the permanent mandibular first moalrs in human monozygotic and dizygotic twins. *Archives of Oral Biology, 15,* 721-730.

Biggerstaff, R. H. (1973). Heritability of the Carabelli cusp in twins. *Journal of Dental Research, 52,* 40-44.

Blangero, J., Konigsberg, L. W., & Vogler, G. P. (1991). Multivariate segregation analysis using the mixed model. *Genetic Epidemiology, 8,* 299-316.

Blangero, J., Lange, K., Almasy, L., Dyer, T., Göring, H., Williams, J., & Peterson, C. (2016). *SOLAR: Sequential oligogenic linkage analysis routine. Versions 8.1.1.* Southwest Foundation of Biomedical Research.

Bochdanovits, Z, & de Jong, G. (2004). Antagonistic pleiotropy for life-history traits at the gene expression level. *Proceedings of the Royal Society B, 271,* S75-S78.

Boehnke, M., Moll, P. P., Kottke, B. A., & Weidman, W. H. (1987). Partitioning the variability of fasting plasma glucose levels in pedigrees. Genetic and environmental factors. *American Journal of Epidemiology, 125,* 679-689.

Bollini, G. A., Rodriguez-Florez, C. D., & Colantonio, S. E. (2009). Bilaterla asymmetry in permanent dentition of 13 pre-conquest samples from Argentica (South America). *Human Biology*, *60,* 127-137.

Boraas, J. C., Messer, L. B., Till, M. J. (1988). A genetic contribution to dental caries, occlusion, and morphology as demonstrated by twins reared apart. *Journal of Dental Research, 67,* 1150-1155.

Carson, E. A. (2006). Maximum likelihood variance components analysis of heritabilities of cranial nonmetric traits. *Human Biology, 78,* 383-402.

Cheverud, J. M. (1996). Developmental integration and the evolution of pleiotropy *American Zoologist, 36,* 44-50.

Cheverud, J. M., Buikstra, J. E., & Twichell, E. (1979). Relationships between non-metric skeletal traits and cranial size and shape. *American Journal of Physical Anthropology, 50,* 191-198.

Corruccini, R. S. (1976). The interaction between nonmetric and metric cranial variation. *American Journal of Physical Anthropology, 44,* 285-294.

Dempsey, P. J., & Townsend, G. C. (1995). Genetic covariance structure of incisor crown size in twins. *Journal of Dental Research, 75,* 1389-1398.

Dempsey, P. J., & Townsend, G. C. (2001). Genetic and environmental contributions to variation in human tooth size. *Heredity, 86,* 685-693.

Devoto, F. C. H., & Perrotto, B. M. (1971). Phenotypes and genotypes of Carabelli's complex in isolated populations of Argentina highlands. *Journal of Dental Research, 50,* 1152-1153.

Dietz, V. (1944). A common dental morphotropic factor, the Carabelli cusp. *Journal of the American Dental Association, 31,* 784-789.

Divers, J., Sale, M.M., Lu, L., Chen, W-M., Lok, K.H., Spruill, I.J., Fernandes, J.K., Langefeld, C.D., & Garvey, W.T. (2010). The genetic architecture of lipoprotein subclasses in Gullah-speaking African American families enriched for type 2 diabetes: The Sea Islands Genetic African American Registry (Project SuGAR). *Journal of Lipid Research, 51,* 586-597.

Durner, R. M. (2011). Understanding Carabelli expression by sex and population through the patterning cascade model of tooth morphogenesis. Senior honors thesis, The Ohio State University, Columbus.

Edgar, H. J. H. (2000). *Biological distance and the African American dentition*. PhD dissertation, The Ohio State University, Columbus.

Edgar, H. J. H., & Sciulli, P. W. (2004). Elongated mandibular premolar: A new morphological variant. *Dental Anthropology, 17,* 24-27.

Edgar, H. J. H. (2017). *Dental morphology for anthropology*. New York: Routledge.

Evans, A. R., Daly, E. S., Catlett, K. K., Paul, K. S., King, S. J., Skinner, M. M., Nesse, H. P., Hublin, J.-J., Townsend, G. C., Schwartz, G. T., & Jernvall, J. (2016). A simple rule governs the evolution and development of hominin tooth size. *Nature, 530,* 477-480.

Falconer, D. S. (1989). *Introduction to quantitative genetics,* 3rd ed. Essex: Longman.

Gómez-Roblez, A., & Polly, P. D. (2012). Hominin dentition: Evolutionary, developmental, and fuctional factors. *Evolution, 66,* 1024-1043.

Goose, D. H., & Lee, G. T. R. (1971). The mode of inheritance of Carabelli's trait. *Human Biology, 43,* 64-69.

Grieco, T.M., Rizk, O.T., & Hlusko, L.J. (2013). A modular framework characterizes micro- and macroevolution of Old World monkey dentitions. *Evolution, 67,* 241-59.

Guatelli-Steinberg, D., Sciulli, P. W., & Edgar H. J. H. (2006). Dental fluctuating asymmetry in the Gullah: Tests of hypotheses regarding developmental stability in deciduous vs. permanent and male vs. female teeth. *American Journal of Physical Anthropology, 129,* 427-434.

Halliday, T. J. D., & Goswami, A. (2013). Testing the inhibitory cascade model in Mesozoic and Cenozoic mammaliaforms. *BMC Evolutionary Biology, 13,* 79.

Harris, E. F. (1977). *Anthropologic and genetic aspects of the dental morphology of Solomon Islanders, Melanesia.* PhD dissertation, Arizona State University, Tempe.

Harris, E. F. (1992). Laterality in human odontometrics: Analysis of a contemporary American white series. In: J. R. Lukacs (Ed.), *Culture, ecology, and dental anthropology* (pp. 157-170). Delhi: Kamla-Raj.

Harris, E. F., Bailit, H. L. (1980). The metaconule: A morphologic and familial analysis of a molar cusp in humans. *American Journal of Physical Anthropology, 53,* 349-358.

Higgins, D., Hughes, T., James, H., & Townsend, G. C. (2009). Strong genetic influence on hypocone expression of permanent maxillary molars in South Australian twins. *Dental Anthropology, 22,* 1-7.

Hlusko, L. J. (2016). Elucidating the evolution of hominid dentition in the age of phenomics, modularity, and quantitative genetics. *Annals of Anatomy, 203,* 3-11.

Hlusko, L. J., Carlson, J. P., Chaplin, G., Elias, S. A., Hoffecker, J. F., Huffman, M., Jablonski, N. G., Monson, T. A., O'Rourke, D. H., Pilloud, M. A, & Scott, G. R. (2018). Environmental selection during the last ice age on the mother-to-infant transmission of vitamin D and fatty acids through breast milk. *Proceedings of the National Academy of Sciences of the United States of America,* 201711788.

Hlusko, L. J., Do., N. & Mahaney, M. C. (2007). Genetic correlations between mandibular molar cusp areas in baboons. *American Journal of Physical Anthropology, 132,* 445-454.

Hlusko, L.J., Suwa, G., Kono, R.T., & Mahaney, M.C. (2004a). Genetics and the evolution of primate enamel thickness: A baboon model. *American Journal of Physical Anthropology, 124,* 223-233.

Hlusko, L. J., Maas, M.-L., & Mahaney, M. C. (2004b). Statistical genetics of molar cusp patterning in pedigreed baboons: Implications for primate development and evolution. *Journal of Experimental Zoology Part B Molecular and Developmental Evolution, 302,* 268-283.

Hlusko, L. J., & Mahaney, M. C. (2003). Genetic contributions to expression of the baboon cingular remnant. *Archives of Oral Biology, 48,* 663-672.

Hlusko, L. J., & Mahaney, M. C. (2007). Of mice and monkeys: Quantitative genetic analyses of size variation along the dental arcade. In: S. E. Bailey & J.-J. Hublin (Eds.), *Dental perspectives on human evolution* (pp. 237-245). New York: Springer.

Hlusko, L. J., & Mahaney, M. C. (2009). Quantitative genetics, pleiotropy, and morphological integration in the dentition of *Papio hamadryas*. *Evolutionary Biology, 36,* 5-18.

Hlusko, L. J., Sage, R. D., & Mahaney, M. C. (2011). Modularity in the mammalian dentition: Mice and monkeys share a common dental genetic architecture. *Journal of Experimental Zoology Part B Molecular and Developmental Evolution, 316,* 21-49.

Hlusko, L. J., Schmitt, C. A., Monson, T. A., Brasil, M. F., & Mahaney, M. C. (2016). The integration of quantitative genetics, paleontology, and neontology reveals genetic underpinnings of primate dental evolution. *Proceedings of the National Academy of Sciences of the United States of America, 113,* 9262-9267.

Hopper, J. L., & Mathews, J. D. (1982). Extensions to multivariate normal models for pedigree analysis. *Annals of Human Genetics, 46,* 373-383.

Hughes, T., Vo, J., Mihailidis, S., & Townsend, G. C. (2010). Twin studies of dental crown morphology: Genetic, epigenetic, and environmental determinants. *American Journal of Physical Anthropology, S50,* 131.

Hughes, T. & Townsend, G. C. (2013). Twin and family studies of human dental crown morphology: Genetic, epigenetic, and environmental determinants of the modern human dentition. In: G. R. Scott, & J. D. Irish (Eds.), *Anthropological perspectives on tooth morphology: Genetics, evolution, variation* (pp. 31-68). Cambridge: Cambridge University Press.

Hunter, J. P., Guatelli-Steinberg, D., Weston, T. C., Durner, R., & Betsinger, T. K. (2010). Model of tooth morphogenesis predicts Carabelli cusp expression, size, and symmetry in humans. *PLoS ONE, 5,* e11844.

Jernvall, J. (2000). Linking development with generation of novelty in mammalian teeth. *Proceedings of the National Academy of Sciences of the United States of America, 97,* 2641-2645.

Jernvall, J., Åberg, T., Kettunen, P., Keränen, S., & Thesleff, I. (1998). The life history of an embryonic signaling center: BMP-4 induces *p21* and is associated with apoptosis in the mouse tooth enamel knot. *Development, 125,* 161-169.

Jernvall, J., Kettunen, P., Karavanova, I., Martin, L. B., & Thesleff, I. (1994). Evidence for the role of the enamel knot as a control center in mammalian tooth cusp formation: Non-dividing cells express growth stimulating *Fgf-4* gene. *International Journal of Developmental Biology, 38,* 463-469.

Jernvall, J., & Thesleff, I. (2000). Reiterative signaling and patterning during mammalian tooth morphogenesis. *Mechanisms of Development, 92,* 19-29.

Kaul, S. S., Sharma, K., Sharma, J. C., & Corruccini, R. S. (1985). Non-metric variances of the permanent dental crown in human monozygous and dizygous twins. In: V. Rami Reddy (Ed.), *Dental anthropology: Application and methods* (pp. 187-193). New Delhi: Inter-India Publications.

Kavanagh, K. D., Evans, A. R., & Jernvall, J. (2007). Predicting evolutionary patterns of mammalian teeth from development. *Nature, 449,* 427-432.

Kimura, K., Yamaguchi, T., Takeda, M., Kondo, O., Toma, T., Haneji, K., Hanihara, T., Matsukusa, H., Kawamura, S., Maki, K., Osawa, M., Ishida, H., & Oota, H. (2009). A common variation in *EDAR* is a genetic determinant of shovel-shaped incisors.

Kimura, R., Watanabe, C., Kawaguchi, A., Kim, Y-I., Park, S-B., Maki, K., Ishida, H., and Yamaguchi, T. (2015). Common polymorphisms in *WNT10A* affect tooth morphology as well as hair shape. *Human Molecular Genetics, 24,* 2673-2680.

Koh, C., Bates, E., Broughton, E., Do, N.T., Fletcher, Z., Mahaney, M.C., & Hlusko, L.J. (2010). Genetic integration of molar cusp size variation in baboons. *American Journal of Physical Anthropology 142*, 246-260.

Kolakowski, D., Harris, E. F., & Bailit, H. L. (1980). Complex segregation analysis of Carabelli's trait in a Melanesian population. *American Journal of Physical Anthropology, 53,* 301-308.

Kondo, S., & Townsend, G. C. (2006). Associations between Carabelli trait and cusp areas in human permanent maxillary first molars. *American Journal of Physical Anthropology*, *129*, 196-203.

Kraus, B. S. (1951). Carabelli's anomaly of the maxillary molar teeth: Observations on Mexican and Papago Indians and an interpretation of the inheritance. *American Journal of Human Genetics, 3,* 348-355.

Laatikainen, T., & Ranta, R. (1996). Occurrence of the Carabelli trait in twins discordant or concordant for cleft lip and/or palate. *Acta Odontologica Scandinavica, 54,* 365-368.

Lange, K., Boehnke, M., & Opitz, J. M. (1983). Extensions to pedigree analysis. IV. Covariance components models for multivariate traits. *American Journal of Medical Genetics, 14,* 513-524.

Lee, G. T. R., & Goose, D. H. (1972). The inheritance of dental traits in a Chinese population in the United Kingdom. *Journal of Medical Genetics, 9,* 336-339.

Lee, W. -C., Yamaguchi, T., Watanabe, C., Kawaguchi, A., Takeda, M., Kim, Y. -I., Haga, S., Tomoyasu, Y., Ishida, H., Maki, K., Park, S. -B., & Kimura, R. Association of common *PAX9*

variants with permanent tooth size variation in non-syndromic East Asian populations. *Journal of Human Genetics, 57,* 654-659.

Ludwig, F. J. (1957). The mandibular second premolars: Morphologic variation and inheritance. *Journal of Dental Research, 36,* 263-273.

Lundström, A. (1963). Tooth morphology as a basis for distinguishing monozygotic and dizygotic twins. *American Journal of Human Genetics, 15,* 34-43.

Mahaney, M. C., Blangero, J., Comuzzie, A. G., VandeBerg, J. L., Stern, M. P., & MacCluer, J. W. (1995). Plasma HDL cholesterol, triglycerides, and adiposity: A quantitative genetic test of the conjoint trait hypothesis in the San Antonio Family Heart Study. *Circulation, 92,* 3240-3248.

Marado, L. M. (2017). Dental nonmetric trait intraobserver precision: Three observations of a large sample. *Anthropologischer Anzeiger: Journal of Biological and Clinical Anthropology, 74,* 15-23.

Marado, L. M., Silva, A. M., & Irish, J. D. (2017). Fluctuating asymmetry in dental and mandibular nonmetric traits as evidence for childcare sex bias in 19th/20th century Portugal. *Homo, Journal of Comparative Human Biology, 68,* 18-29.

Matory, J.L. (2008). The illusion of isolation: The Gullah/Geechees and the political economy of African culture in the Americas. *Comparative Studies in Society and History, 50,* 949-980.

Mayhall, J. T., & Saunders, S. R. (1986). Dimensional and dentral trait asymmetry relationships. *American Journal of Physical Anthropology, 69*, 403-411.

McClean, D. C., Jr., Argyropoulos, G., Page, G. P., Shriver, M. D., & Garvey, W. T. (2005). Mitochondrial DNA (mtDNA) haplotypes reveal maternal population genetic affinities of Sea Island Gullah-speaking African Americans. *American Journal of Physical Anthropology, 127*, 427-438.

McClean, D. C., Jr., Spruill, I., Gevao, S., Morrison, E. Y., Bernard, O. S., Argyropoulos, G., & Garvey, W. T. (2003). Three novel mtDNA restriction site polymorphisms allow exploration of population affinities of African Americans. *Human Biology, 75*, 147-161.

Menegaz-Bock, R. M. (1968). *An investigation of the genetic basis for structural relations in the anterior dentition.* PhD dissertation, The University of Chicago, Chicago.

Mizoguchi, Y. (1977). Genetic variability in tooth crown characters: Analysis by the tetrachoric correlation method. *Bulletin of the National Science Museum, Series D (Anthropology), 3*, 37-62.

Mizoguchi, Y. (1990). Covariation of asymmetries in metric and nonmetric tooth crown characters. *Bulletin of the National Museum of Tokyo, Series D*, *16*, 39-47.s

Moormann, S., & Guatelli-Steinberg, D., & Hunter, J. (2013). Metamerism, morphogenesis, and the expression of Carabelli and other dental traits in humans. *American Journal of Physical Anthropology, 150,* 400-408.

Moskona, D., Vainder, M., Herschkovitz, I., & Kobyliansky, E. (1996). Bilateral asymmetry in dental discrete traits in human isolates: South Sinai Bedouin tribes. *Anthropologischer Anzeiger, 54,* 289-306.

Nichol, C. R. (1989). Complex segregation analysis of dental morphological variants. *American Journal of Physical Anthropology, 78,* 37-59.

Norry, F. M., Vilardi, J. C. & Hasson, E. (2000). Negative genetic correlation between traits of the *Drosophila* head, and interspecific divergence in head shape. *Heredity, 85,* 177-183.

Noss, J. F., Scott, G. R., Potter, R. H. Y., & Dahlberg, A. A. (1983). Fluctuating asymmetry in molar dimensions and discrete morphological traits in Pima Indians. *American Journal of Physical Anthropology, 61,* 437-445.

Opala, J.A. (1987). The Gullah: Rice, slavery, and the Sierra Leone-American connection. United States Information Service, Freetown, Sierra Leone.

Ortiz, A., Bailey, S. E., Schwartz, G. T., Hublin, J.-J., & Skinner, M. M. (2018). Evo-devo models of tooth development and the origin of hominoid molar diversity. *Science Advances, 4,* eaar2334.

Park, J. -H., Yamaguchi, T., Watanabe, C., Kawaguchi, A., Haneji, K., Takeda, M., Kim, Y. -I., Tomoyasu, Y., Watanabe, M., Oota, H., Hanihara, T., Ishida, H., Maki, K., Park, S. -B., & Kimura, R., (2012). Effects of an Asian-specific nonsynonymous *EDAR* variant on multiple dental traits. *Journal of Human Genetics, 57,* 508-514.

Parra, E.J., Marcini, A., Akey, J., Martinson, J., Batzer, M.A., Cooper, R., Forrester, T., Allison, D.B., Deka, R., Ferrell, R.E., & Shriver, M.D. (1998). Estimating African American admixture proportions by use of population-specific alleles. *American Journal of Human Genetics, 63,* 1839-1851.

Parra, E. J., Kittles, R. A., Argyropoulos, G., Pfaff, C. L., Hiester, K., Bonilla, C., Sylvester, N., Parrish-Gause, D., Garvey, W. T., Jin, L., McKeigue, P. M., Kamboh, M. I., Ferrell, R. E., Pollitzer, W. S., & Schriver, M. D. (2001). Ancestral proportions and admixture dynamics in geographically defined African Americans living in South Carolina. *American Journal of Physical Anthropology*, *114,* 18-29.

Paul, K. S., Stojanowski, C. M., Hughes, T., Brook, A., & Townsend, G. C. (2018). Quantitative genetic analyses of human tooth crown morphology: Heritability and genetic integration in a longitudinal Australian twin sample. *American Journal of Physical Anthropology, 165*, 201.

Pollitzer, W. S. (1958). The negroes of Charleston (S.C.). A study of hemoglobin types, serology, and morphology. *American Journal of Physical Anthropology, 16*, 213-234.

Pollitzer, W. S. (1993). The relationship of the Gullah-speaking people of coastal Carolina and Georgia to their African ancestors. *Historical Methods: A Journal of Quantitative and Interdisciplinary History, 26*, 53-67.

Pollitzer, W. S. (1999). *The Gullah people and their African heritage.* Athens: The University of Georgia Press.

Pollitzer, W. S., Menegaz-Bock, R., Ceppellini, R., & Dunn, L. C. (1964). Blood factors and morphology of James Island, Charleston, S. C. *American Journal of Physical Anthropology, 22*, 393-398.

Polly, P. D. (2007). Development with a bite. *Nature, 449*, 413-415.

Polly, P. D. (2015). Gene networks, occlusal clocks, and functional patches: New understanding of pattern and process in the evolution of the dentition. *Odontology, 103*, 117-125.

Polly, P. D., & Mock, O. B. (2018). Heritability: The link between development and the microevolution of molar tooth form. *Historical Biology: An International Journal of Paleobiology, 30,* 53-63.

Relethford, J. H. (1994). Craniometric variation among modern human populations. *American Journal of Physical Anthropology, 95,* 53-62.

Relethford, J. H. (1996). Genetic drift can obscure population history: Problem and solution. *Human Biology, 68,* 29-44.

Relethford, J. H. (2007). The use of quantitative traits in anthropological genetic studies of population structure and history. In: M. H. Crawford (Ed.), *Anthropological genetics theory, methods and applications* (pp. 187-209). Cambridge: Cambridge University Press.

Relethford, J. H. (2016). Biological distances and population genetics in bioarchaeology. In: M. A. Pilloud, & J. T. Hefner (Eds.), *Biological distance analysis: Forensic and bioarchaeological perspectives* (pp. 23-33). Amsterdam: Academic Press.

Relethford, J. H., & Blangero, J. (1990). Detection of differential gene flow from patterns of quantitative variation. *Human Biology, 62,* 5-25.

Relethford, J. H, Crawford, M. H., & Blangero, J. (1997). Genetic drift and gene flow in post-famine Ireland. *Human Biology, 69,* 443-465.

Riska, B. (1986). Some models for development, growth, and morphometric correlation. *Evolution, 40,* 1301-1311.

Renvoisé, E., Evans, A. R., Jebrane, A., Labruère, C., Laffont, R., & Montuire, S. (2009). Evolution of mammal tooth patterns: New insights from a developmental prediction model. *Evolution, 63,* 1327-1340.

Salazar-Ciudad, I., & Jernvall, J. (2002). A gene network model accounting for development and evolution of mammalian teeth. *Proceedings of the National Academy of Sciences of the United Stated of America, 99,* 8116-8120.

Salazar-Ciudad, I., & Jernvall, J. (2010). A computational model of teeth and the developmental origins of morphological variation. *Nature, 464,* 583-586.

Sale, M.M, Lu, L., Spruill, I.J., Fernandez, J.K., Lok, K.H., Divers, J., Langefeld, C.D., & Garvey, W.T. (2009). Genome-wife linkage scan in Gullah-speaking African American families with Type 2 diabetes. *Diabetes, 58,* 260-267.

Saunders, S. R., & Mayhall, J. T. (1982). Fluctuating asymmetry of dental morphological traits : new interpretations. *Human Biology*, *54,* 789-799.

Scott, G. R. (1973). *Dental morphology: A genetic study of American White families and variation in living Southwest Indians.* PhD dissertation, Arizona State University, Tempe.

Scott, G. R., & Irish, J. D. (2017). *Human tooth crown and root morphology*. Cambridge: Cambridge University Press.

Scott, G. R., & Potter, R. H. Y. (1984). An analysis of tooth crown morphology in American white twins. *Anthropologie, 22,* 223-231.

Scott, G. R., & Turner, C. G. II. (1997). The anthropology of modern human teeth: Dental morphology and its variation in recent human populations. Cambridge: Cambridge University Press.

Scott, G. R., Potter, R. H. Y., Noss, J. F., Dahlberg, A. A., & Dahlberg, T. (1983), The dental morphology of Pima Indians. *American Journal of Physical Anthropology, 61,* 13-31.

Scott, G. R., Turner, C. G. II, Townsend, G. C., & Martinón-Torres, M. (2018). The anthropology of modern human teeth: Dental morphology and its variation in recent fossil *Homo sapiens,* 2nd ed. Cambridge: Cambridge Univeristy Press.

Skrinjaric, I., Slaj, M., Lapter, V., & Muretic, Z. (1985). Heritability of Carabelli's trait in twins. *Collegium Anthropologicum, 2,* 177-181.

Sofaer, J. A. (1970). Dental morphologic variation and the Hardy-Weinberg law. *Journal of Dental Research, 49,* 1505-1508.

Sofaer, J. A., MacLean, C. J., & Bailit, H. L. (1972). Heredity and morphological variation in early and late developing human teeth of the same morphological class. *Archives of Oral Biology, 17,* 811-816.

Sofaer, J. A., Niswander, J. D., MacLean, C. J., & Workman, P. L. (1972). Population studies on Southwestern Indian tribers. V. Tooth morphology as an indicator of biological distance. *American Journal of Physical Anthropology, 37,* 357-366.

Stefflova, K., Dulik, M.C., Barnholtz-Sloan, J.S., Pai, A.A., Walker, A.H. & Rebbeck, T.R. (2011). Dissecting the within-Africa ancestry of populations of African descent in the Americas. *PLoS ONE 6(1),* e14495.

Stojanowski, C. M., Paul, K. S., Seidel, A. C., Duncan, W. N., & Guatelli-Steinberg, D. (2017). Heritability and genetic integration of tooth size in the South Carolina Gullah. *American Journal of Physical Anthropology, 164,* 505-521.

Stojanowski, C. M., Paul, K. S., Seidel, A. C., Duncan, W. N., & Guatelli-Steinberg, D. (2018). Heritability and genetic integration of anterior tooth crown variants in the South Carolina Gullah. *American Journal of Physical Anthropology, In Press.*

Stojanowski, C. M., & Schillaci, M. A. (2006). Phenotypic approaches for understanding patterns of intracemetery biological variation. *Yearbook of Physical Anthropology, 49,* 49-88.

Townsend, G. C., & Brown, T. (1978a). Inheritance of tooth size in Australian Aboriginals. *American Journal of Physical Anthropology, 48,* 305-314.

Townsend, G. C., & Brown, T. (1978b). Heritability of permanent tooth size. *American Journal of Physical Anthropology, 49,* 497-504.

Townsend, G. C., & Brown, T. (1979). Family studies of tooth size factors in the permanent dentition. *American Journal of Physical Anthropology, 50,* 183-190.

Townsend, G. C., & Brown, T. (1981). The Carabelli trait in Australian aboriginal dentitions. *Australian Orthodontic Journal, 7,* 3-12.

Townsend, G. C., Brown, T., Richards, L. C., Rogers, J. R., Pinkerton, S. K., Travan, G. R., & Burgess, V. B. (1986). Metric analyses of the teeth and faces of South Australian twins. *Acta Geneticae, Medicae, et Gemellologiae, 35,* 179-192.

Townsend, G. C., & Martin, N. G. (1992). Fitting genetic models to Carabelli trait data in South Australian twins. *Journal of Dental Research, 71,* 403-409.

Townsend, G. C., Richards, L., Brown, T., Burgess, V. B., Travan, G. R., & Rogers, J. R. (1992). Genetic studies of dental morphology in South Australian twins. In: P. Smith, & E. Tchernov (Eds.), *Structure, function, and evolution of teeth* (pp. 501-518). London: Freund Publishing House.

Townsend, G. C., Yamada, H., & Smith, P. (1986). The metaconule in Australian Aboriginals: An accessory tubercle on maxillary molar teeth. *Human Biology, 58,* 851-862.

Townsend, G. C., Yamada, H., & Smith, P. (1990). Expression of the entoconulid (sixth cusp) on mandibular molar teeth of an Australian aboriginal population. *American Journal of Physical Anthropology, 81,* 267-274.

Trakinienė, G., Šidlauskas, A., Andriuškevičiutė, I., Šalomskienė, L., Švalkauskienė, V., Smailienė, D., & Trakinis, T., (2018). Impact of genetics on third molar agenesis. *Scientific Reports, 8,* 8307.

Tsai, P. L., Hsu, J. W., Lin, L. M., Liu, K. M. (1996). Logistic analysis of the effects of shovel trait on Carabelli's trait in a Mongoloid population. *American Journal of Physical Anthropology, 100,* 523-530.

Tsuji, T. (1958). Incidence and inheritance of the Carabelli's cusp in a Japanese population. *Janapese Journal of Human Genetics, 3,* 21-31.

Turner, C. G. II. (1967). Dental genetics and microevolution in prehistoric and living Koniag Eskimo. *Journal of Dental Research, 46,* 911-917.

Turner, C. G. II, Nichol, C. R., & Scott, G. R. (1991). Scoring procedures for key morphological traits of the permanent dentition: The Arizona State University Dental Anthropology System. In:

M. A. Kelley & C. S. Larsen (Eds.), *Advances in dental anthropology* (pp. 13-31). New York: Wiley-Liss.

Twining, M.A., & Baird, K.E. (1991). *Sea Island Roots: African Presence in the Carolinas and Georgia*. Trenton,NJ: Africa World Press, Inc.

Williams-Blangero, S., & Blangero, J. (1989). Anthropometric variation and the genetic structure of the Jirels of Nepal. *Human Biology, 61*, 1-12.

Wood, B, F., & Green, L. J. (1969). Second premolar morphologic similarities in twins. *Journal of Dental Research, 48*, 74-78.

Yound, N. M., & Hallgrímsson, B. (2005). Serial homology and the evolution of mammalian limb covariation structure. *Evolution, 59*, 2691-2704.