

2. Of mice and monkeys: Quantitative genetic analyses of size variation along the dental arcade

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Abstract

We present preliminary results from quantitative genetic analyses of tooth size variation in two outbred pedigreed populations, baboons and mice. These analyses were designed to test the dental field theory as proposed by Butler (1939), that there are three fields within the dentition: incisor, canine, and molar. Specifically we estimated the genetic correlation between pairs of linear size measurements. Results from the baboon analyses suggest that there may also be a premolar field that is only partially independent of the molar field proposed by Butler (1939). Analyses of the mouse data indicate that for mice, size variation in the incisors appears to be genetically independent of molar size. If the field theory is correct, future analyses on incisor data for the baboons will return similar results of genetic independence. Circumstantial evidence from the fossil record suggests that there will be at least some degree of independence between the anterior and postcanine dentitions of primates.

Introduction

Huxley and de Beer (1934) were among the first embryologists to formalize the concept of the gradient-field in relation to the

development of the animal body plan. They defined it as:

“...a region throughout which some agency is at work in a co-ordinated way, resulting in the establishment of an equilibrium within the area of the field.

A quantitative alteration in the intensity of operations of the agency in any one part of the field will alter the equilibrium as a whole. A field is thus a unitary system, which can be altered or deformed as a whole; it is not a mosaic in which single portions can be removed or substituted by other without exerting any effect on the rest of the system.” (1934: 276).

In 1939, Butler evoked this concept to explain the dental pattern of mammals, i.e., the number and morphology of incisors, canines, premolars, and molars. In his morphogenic field theory of dental development, Butler suggests that each tooth primordium is equivalently pluripotent, possessing the potential to develop into any type of tooth in the dentition. Determination of the ultimate form of each tooth is a function of the tooth primordium's exposure to morphogens and the nature and concentration of these morphogen(s), both of which are related to the tooth placode's location within a developmental field. Butler infers that morphogenic fields are distinct: each perfused with a characteristic combination of morphogens and, consequently, one should be able to identify different morphogenic fields within a dental arch based on tooth morphology. By this logic, Butler identifies three distinct dental morphogenic fields in the mammalian dentition: the molar, canine, and incisor fields. In this scheme, incisor size and shape would be developmentally independent of molar size and shape; however, because premolars are within the molar field, the development of their size and shape is correlated with that of molars but independent of incisors, for example (Butler, 1939).

The last 15 years have seen a dramatic increase in our understanding of the genetic mechanisms needed to form teeth and pattern the overall dentition, primarily in rodent models. From this work we know that the patterning of the mouse dentition, or dental formula, first appears histologically at embryonic day 11 (E11) when a region of the mouse oral epithelium thickens to form the dental lamina (for more details see Weiss

et al., 1998; Jernvall and Thesleff, 2000; Stock, 2001; Tucker and Sharpe, 2004).

At this dental lamina stage of development, tooth position and fate is induced by the oral epithelium. The dental pattern, or formula that is already determined by this stage of development has been hypothesized to result from one of two possible mechanisms. The first is an odontogenetic combinatorial code (Cobourne and Sharpe, 2003). This is similar in concept to the *Hox* gene patterning of the vertebral column, although *Hox* genes are not expressed in tooth development and therefore do not similarly regulate dental patterning (James et al., 2002). Other regulatory genes including members of the *Barx*, *Dlx*, *Msx*, and *Pitx* gene families have been implicated (Cobourne and Sharpe, 2003). Restricted expression of two members of the *Dlx* family to the more caudal region of the developing branchial arch may be important for determining the maxillary versus mandibular jaws (Depew et al., 2002).

The second dental patterning mechanism proposed is that of a reaction diffusion process. Weiss et al. (1998) attribute the periodicity of the dentition to quantitative interactions of diffusible signaling factors. This idea is based on Savart's and Chladni's nineteenth century recognition that different wave lengths mechanically interact to form different interference patterns, easily visualized as patterns formed by sound waves moving through powder on violin plates (see Weiss et al., 1998 for more details). Bateson (1894) applied this concept to serially homologous traits, such as the dentition, and coined the term “meristic variation”. Alan Turing (1952) later proposed that chemical interactions could similarly result in wave-like patterns as substances, or morphogens, interact in a *reaction diffusion* process.

To date, there have been no convincing data that refute or support the validity of either of these models. We have not yet been able to successfully test these hypotheses partly