Austin Journal of Pharmacology and Therapeutics

Open Access

Austin Publishing Group

Rapid Communication

Rapid Genetic and Developmental Morphological Change Following Extreme Celerity

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Received: October 16, 2017; **Accepted:** November 09, 2017; **Published:** November 16, 2017

Abstract

Proximate environmental effects on metamorphosis have been explored in many vertebrate systems, but less attention has been devoted to how the environment affects developmental morphological change in mammals. Understanding proximate environmental effects on mammalian morphological change, particularly changes involving skin replacement, may aid in the design of therapeutic strategies to address severe burn or other debilitating injuries. Here, we specifically explore effects of celerity broadly, and we present results showing rapid change in mammalian morphological development following encountering maximum celerity. Morphological changes were pronounced within 96 hours and included at least partial regeneration of skin and organs as well as an elevated somatic mutation rate. Significantly, this high mutation rate did not result in detectable loss of fertility or viability of offspring. Overall, our findings strongly suggest that extreme celerity, an environmental factor rarely considered, can produce strikingly rapid developmental changes in morphology even in mammalian systems and open the door to future studies on the impact of celerity on genetics and morphology.

Keywords: Celerity; Morphology; Development; Genetic

Introduction

Many studies have shown that environmental features can profoundly affect aspects of iodothyronine-induced metamorphosis in various vertebrate species. For example, [1] classic study demonstrated that mean size at metamorphosis was strongly affected by larval density in the American toad. More recent work has shown that environmental trends anticipated to occur with global climate change are likely to influence various aspects of morphology in various metamorphic frog species [2]. However, such studies have understandably focused on fish and amphibia, since formal metamorphosis does not occur in mammals such as humans or mice.

Nonetheless, some mammals are also capable of developmental transformations or other major morphological change. These changes also have the potential to be influenced by environmental factors. For instance, research on cell lines derived from Chinese hamster treated with dibutyrl adenosine cyclic 3′:5′-monophosphate changes the form from multilayer to a monolayer of elongated cells arranged in parallel within one hour [3]. However, insufficient research has been conducted in experimental mammalian (e.g., mouse) systems *in vivo* to explore proximate environmental effects on major individual developmental transitions.

One environmental factor rarely considered for its impact on development is celerity [4]. Species and individuals can potentially vary in their aided or unaided celerity up to a theoretical maximum, and one might hypothesize that achieving maximum celerity could have a profound effect on various biological functions, potentially triggering cascade morphological changes. In this study, we test this hypothesis *in vivo* in a mammalian system.

Materials and Methods

We employed a replicated design wherein the study organisms were exposed to the theoretical maximum celerity and examined. Physical examinations included non-invasive measures of hypothalamic serum serotonin (5-hydroxytryptamine, specifically seeking deviation from the typical range of 101-283 ng/mL) immediately following exposure and subsequent magnetic resonance imaging and quantification of any alterations in internal structure. MRI measurements were compared across time points using ImageJ [5].

We also conducted serial nucleogenic scans every 24 hours followed via single-molecule real-time whole-genome sequencing (via PacBio). Approximately 100X coverage was achieved for each time-point. DNA sequences from the various time-points were cleaned, assembled, aligned, and analyzed for differences using the Picard command line tools package (http://broadinstitute.github.io/picard/) following GATK Best Practices standard workflow recommendations [6]. Raw or assembled DNA sequences are available from the authors upon request. Mutation rate was calculated as number of mutations per base per cell division.

Results

Immediately following maximum celerity, mammalian subjects exhibited somnolence that was readily terminated with audible stimulation. This somnolence was associated with slightly elevated hypothalamic serum serotonin (350ng/mL). Within a few hours, the subjects began to experience an unspecific general histamine response to normal environmental inputs (e.g., water) and subsequent reduced neural activity. This response lasted no more than 4 hours.

Citation: Paris T, Kim H, Torres B, Ocampa K, Janeway K and Zimmerman L. Rapid Genetic and Developmental Morphological Change Following Extreme Celerity. Austin J Pharmacol Ther. 2017; 5(3).1099.

Physical responses to the celerity became apparent in later observations. Spontaneous exfoliation of skin cells commenced, and a comparably thick intact layer of new skin cells formed within 96 hours. Internal morphological differences were noted via MRI and ImageJ analysis, with measurement of heart number increasing two-fold (statistical $p<0.0001$). External morphological changes were also noted but not quantified directly.

Whole genome sequencing identified an unusually high somatic Single Nucleotide Variant (SNV) mutation rate, which we estimated at 3.1×10^{-5} mutations per cell division and accelerating over the observation period. We were unable to measure the associated germline mutation rate.

Because of the high mutation rate, we sought to examine if fertility was impaired. Two subjects were allowed to breed, and a litter of three viable, motile progeny were produced with no obvious external physical deformity relative to the parents.

Discussion

We sought to explore the effects of extreme celerity on developmental morphological change in a model mammalian system. Replicates were exposed to theoretical maximum celerity and assessed for developmental and genetic alterations as a result. We found that celerity induced major changes in internal and external form as well as an elevated mutation rate. This study is the first to identify celerity as a potentially major force in such developmental changes, arguably increasing the pace of evolution.

While the developmental morphological changes are striking, the somatic mutation rate increase was wholly unexpected. Other studies have found a median somatic mutation frequency of 2.8×10^{-7} and 4.4×10^{-7} per bp per cell mitosis for human and mouse respectively for single nucleotide sites [7], so our observed somatic mutation rate following extreme celerity is roughly 100 times higher. Importantly, we failed to find evidence that this mutation rate increase had severe effects on fertility or offspring viability.

While our results are preliminary at present, these findings have major basic and applied science research implications. From an applied standpoint, induction of such radical turnover of skin and internal morphological change by celerity may lead to therapeutic approaches for patients subjected to extreme burns or other injuries. From a basic science standpoint, such extreme changes, which also appear heritable, provide a physical foundation for how rapid evolution as observed in the fossil record may occur [8]. However, the frequency with which organisms encounter theoretical maximum celerity has not yet been measured definitively.

Acknowledgements

We thank the UFP for financial support. The authors also thank B. Braga for helpful insights.

References

1. Wilbur HM. Density-dependent aspects of growth and metamorphosis in Bufoamericanus. Ecology. 1977; 58: 196-200.
2. Tejedo M, Marangoni F, Pertoldi C, Richter-Boix A, Laurila A, Orizaola G, et al. Contrasting effects of environmental factors during larval stage on morphological plasticity in post-metamorphic frogs. Clim Res. 2010; 43: 31-39.
3. Hsie AW, Puck TT. Morphological transformation of Chinese hamster cells by dibutyryl adenosine cyclic 3′:5′-monophosphate and testosterone. Proc Natl Acad Sci USA. 1971; 68: 358-361.
4. Zimmerman L. Consequences of celerity on developmental morphology and genetics: a review. Austr Res J BioSci. 2017; 3: 219-226.
5. Schindelin J, Rueden CT, Hiner MC, Eliceiri KW. The ImageJ ecosystem: An open platform for biomedical image analysis. MolReprod Dev. 2015; 82: 518-529.
6. DePristo M, Banks E, Poplin R, Garimella K, Maguire J, Hartl C, et al. A framework for variation discovery and genotyping using next-generation DNA sequencing data. Nature Genet. 2011; 43: 491-498.
7. Milholland B, Dong X, Zhang L, Hao X, Vijg J. Differences between germline and somatic mutation rates in humans and mice. Nature Comm. 2017; 8: 15183.
8. Eldredge N, Gould SJ. Punctuated equilibria: An alternative to phyletic gradualism “in” T.J.M. Schopf ed., Models in Paleobiology, Freeman, San Francisco. 1972; 82-115.

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