

Contents

1	The Effect of Space	1
2	Sponge	2
3	Animal Generated Seismic Activity	2
	Title	
	Hello. This is how you cite. [1]	
	Another reference [2]	

1 The Effect of Space

1.1 NASA's Twin Study

Identical twins Scott and Mark Kelly

(October 15, 2018) The NASA Twin Study: A multidimensional analysis of a year-long human spaceflight. Presenter Dr. Tejaswin Mishra - Postdoctoral Fellow in Mike Snyder Lab of Department of Genetics Stanford University. Humans have been going to space since the early 1957 - 536 people flown to space. What's next? The future is Mars. Current travel time hours (will be days from Deep Space Gateway and months from Mars.) Space hazards include muscle atrophy, plasma volume contraction, mood, radiation, access to immediate medical care. Risk categories include mitigated and no-go. Human studies needed to identify risks and knowledge gaps. Plenty of opportunity, but low N. Longitudinal multi-omics deep profiling of one person to predict diabetes, effect of lifestyle changes.

NASA One Year Mission Project - sampling before, during and after for both twins.

Results: Gene expression changes during spaceflight - some up and some down, some persist some revert (hypoxia and immune). Methylation levels and methylation entropy - no substantial changes genome wide - some localized changes - immune signaling, environmental adaptation. Cytokine signaling. - immune response and inflammation during spaceflight (IL-10 signalling) - 5 days after return a spike of cytokines. Mark reported skin rash after return. Pattern of complex lipids (metabolomics) Complex lipids containing fatty acids that are metabolized to form pro and anti-inflammation molecules are present at different levels in the twin and increase inflight AA is aa precursor of inflammatory molecules - complex lipids containing fatty acids that are metabolized to form pro- and anti-inflammation Microbiome (stool shotgun metagenome) twins same? no Flight associated loss of diversity? no Come back to "normal": somewhat F/B ratio, Shannon diversity and community structure: changes due to isolation and diet change consistent with ground studies. Products of microbial metabolism Mitochondria-related adaptations during flight (sea horse assay) get oxygen consumption rate. Isolate elements of respiration. Maximal - Basal = Spare reserve capacity to find ATP linked respiration to compare flight to ground. Maximal unchanged. Lower reserve can be stress, ischemia, cell death, heart disease, body mass changes (Scott exercising, lost 7% of body mass). Inflight shift towards anaerobic metabolism - similar results in plasma (could be due to body mass changes) not much evidence for hypoxia based on O2 and CO2 on station. Cardiovascular changes during spaceflight - artery wall thickens, diameter shrinks. Profibrotic markers effect cardiac fibrosis - increase associated with vascular wall dimensions Body mass and nutrition changes - lost urine volume and plasma volume is a dehydration response due to low water intake and low humidity Body mass and nutrition changes - bone go up early in flight, down late in flight. tracks with exercise Summary - low risk - transcriptional and

metabolic changes, telomere changes, microbiome. Neuro-ocular changes - fluid shift in space flattens colloidal folds - space increased Protein LRG1 down regulated in space flight Telomere changes - DNA damage response in flight. Telomere lengthens in space, retracts when back to ground. Distributed differently across different cell populations.

2 Sponge

Animals and sponge have a common ancestor 600 million ago: One that gave both branches of life the genes responsible for multi-cellularity (cell adhesion, metazoan body plans), a recognition of self (allorecognition), and recognition of non-self (innate immunity). Normative physiology relies on these genes to solicit coordinated function from a 3-dimensional collection of individual cells. Cancerous growth can arise when these genes responsible for basic cell processes become defective [3]. These studies were conducted using the *Amphimedon queenslandica* (demosponge from Australia's Great Barrier Reef) [3]. Scientists observed only a fraction of sponge species regenerate functional tissues from dissociated cells. Most sponge species disintegrate before progressing through all four regeneration checkpoints. Two sponge species - *Spongilla lacustris* and *Haliclona cf. permollis* - have adapted to regenerate anatomy comprised of specialized cells with a coordinated function [4]. Sponges feed by heterotrophy, relying on their environment for nutrients, collected by filtering water and hosting a symbiont of bacteria. Water passes through a manifold of interconnected choanocyte chambers lined with specialized cells which capture nutrients - a seemingly metazoan departure from the free-living protozoa they host. Sponge's anatomical architecture throttles the water flow rate to optimize digestion [5]. If ancestral sponge ever had anatomical complexity beyond choanocyte chambers - it has been lost or concealed.

Transcriptome sequences reflect environmental conditions - they also expose phylogenetic relationships.

Sponges (Porifera) are among the earliest evolving metazoans. Their filter-feeding body plan based on choanocyte chambers organized into a complex aquiferous system is so unique among metazoans that it either reflects an early divergence from other animals prior to the evolution of features such as muscles and nerves, or that sponges lost these characters. Analyses of the *Amphimedon* and *Oscarella* genomes support this view of uniqueness?many key metazoan genes are absent in these sponges?but whether this is generally true of other sponges remains unknown. We studied the transcriptomes of eight sponge species in four classes (Hexactinellida, Demospongiae, Homoscleromorpha, and Calcarea) specifically seeking genes and pathways considered to be involved in animal complexity. For reference, we also sought these genes in transcriptomes and genomes of three unicellular opisthokonts, two sponges (*A. queenslandica* and *O. carmela*), and two bilaterian taxa. Our analyses showed that all sponge classes share an unexpectedly large complement of genes with other metazoans. Interestingly, hexactinellid, calcareous, and homoscleromorph sponges share more genes with bilaterians than with nonbilaterian metazoans. We were surprised to find representatives of most molecules involved in cell-cell communication, signaling, complex epithelia, immune recognition, and germ-lineage/sex, with only a few, but potentially key, absences. A noteworthy finding was that some important genes were absent from all demosponges (transcriptomes and the *Amphimedon* genome), which might reflect divergence from main-stem lineages including hexactinellids, calcareous sponges, and homoscleromorphs. Our results suggest that genetic complexity arose early in evolution as shown by the presence of these genes in most of the animal lineages, which suggests sponges either possess cryptic physiological and morphological complexity and/or have lost ancestral cell types or physiological processes.

3 Animal Generated Seismic Activity

The Earth vibrates with information. Wild elephants produce ground-based vibrations during running, vocalization, and stampeding - as caused by poaching threats. Classifying seismic signatures as specific elephant behavior requires deconstruction of geophone measurements - parsing natural vs. anthropogenic, then subtraction of time-varying seismic activity, and accounting for the terrain [6]. The elephant behavior produced a seismic wave. The wave contained information about it was created - time, place, intensity, number of elephants, movements, speed. Seismic vibrations generated by wild elephants were recorded in Kenya (Supplemental Information). We selected a few examples of each observed behaviour type, as well as car noise, which were processed to determine the corresponding source function ? the force strength and pattern generated by the elephant ?at the source? (Supplemental Information). Differences in elephant behaviour caused detectable changes in source function properties, which remained distinguishable during modelled seismic wave propagation up to 1000 metres regardless of the noise level and terrain type (Figure 1; Supplemental Information). Recordings of seismic vibrations can therefore be used to classify elephant behaviours.

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