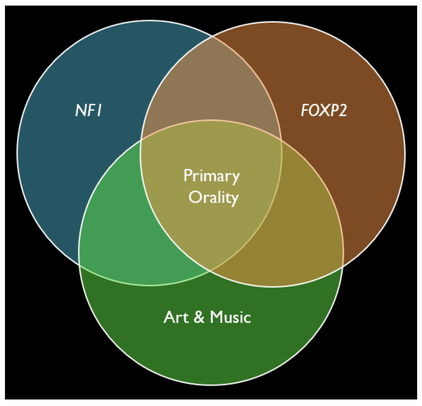

Art, Orality, and Migration

The roles of *NF1*, mnemonics, and somatic adaptation in the hominin biocultural toolkit

Andrea J. Alveshere[a]* Lynne Kelly[b], and Vincent M. Riccardi[c]

[a]Department of Sociology and Anthropology, Western Illinois University, Macomb, IL, USA;
[b]La Trobe University, Melbourne, Australia; [c]The Neurofibromatosis Institute, La Crescenta, CA, USA

Introduction: Two decades have passed since the discovery of the hominin *FOXP2* language gene.[1] Recent identification of the unique, hominin *NF1* gene, and revelations about the importance of art, music, dance, story, and place in the knowledge systems of non-literate societies, have exposed how genetic, somatic, and cultural elements combined to form the extraordinary biocultural toolkit that enabled non-literate humans to populate or traverse every biome on Earth.

***NF1* Background:** In 2020, we reported a unique wild-type human variant of the neurofibromin protein, which is the protein product of the *NF1* gene.[2] The human *NF1* allele varies from chimps by a single point mutation (Figure 1). Other primates share the chimp residue at that locus. No codon producing a chimp-like residue has ever been documented among modern humans; therefore, the human wild-type *NF1* allele is derived (*i.e.,* new) compared to the *NF1* alleles of other primates, and is fixed in the modern human population.[2] Based on available ancient genomes, Neanderthals, Denisovans and early modern humans all share the human *NF1* allele, dating the emergence of this hominin variant to sometime before 300,000 BP.[2]

The *NF1* gene is a massive, high-mutation-rate gene.[3] Pathogenic germline or early embryonic mutations cause the Neurofibromatosis, or NF1, disorder. NF1 is autosomal dominant and affects 1:3,000 births worldwide.[3] Fifty percent (50%) of probands have *de novo* mutations, and the disorder is characterized by benign, proliferative lesions of the nerve sheath.[3] It has never been documented in non-human primates.[2] The NF1 syndrome has highly-variable presentation and progressive phenotype development.[3] Debilitating or disfiguring symptoms are rare before puberty and then often accumulate slowly.[3] Many NF1 patients find mates and have offspring.[3]

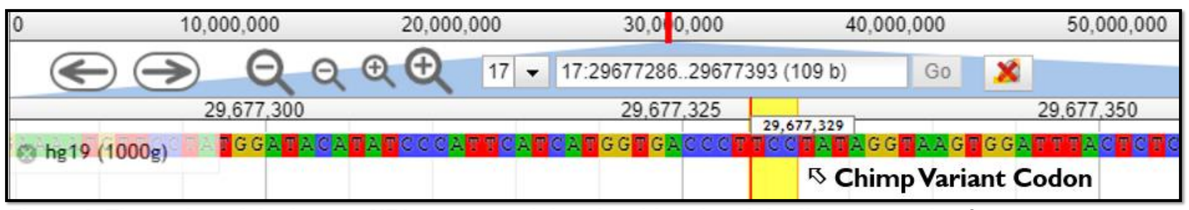

Figure 1. The region of the human *NF1* gene containing the chimp-hominin divergent codon.[2]

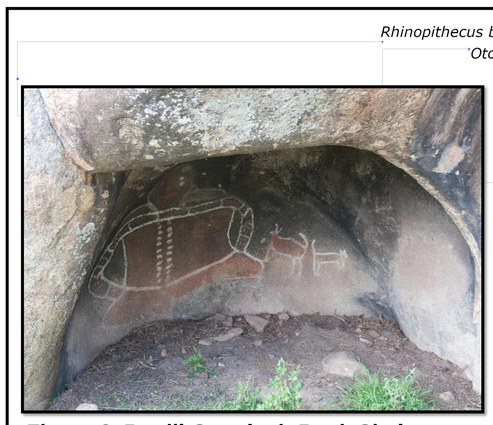

Figure 2. Bunjil Geoglyph Rock Shelter, Victoria, Australia. Photo by Lynne Kelly.

Figure 3. Distance tree of primate neurofibromin protein BLAST.[2] https://www.ncbi.nlm.nih.gov/projects/treeview/

NF1 is a supergene. It has at least ten functional domains and three other genes are embedded on the complementary strand. Most *NF1* research has focused on the GTPase-activating protein-related domain (GRD). Neurofibromin limits the activity of the RAS-controlled cell proliferation, growth, and cell cycle pathways; and stimulates cAMP activity. In this way, *NF1* regulates the availability of ATP (*i.e.,* energy) for use by RAS-modulated pathways and, potentially, for use by other systems, through reducing its availability to RAS.

The human wild-type *NF1* allele makes more ATP available for RAS pathways than is available in other primates, and slightly inhibits cAMP signaling.[2] In humans with only one functional copy of the *NF1* allele, an even higher quantity of ATP is available for RAS, further limiting what is available for other systems. This shift is responsible for the NF1 syndrome and its variable, progressive symptoms. Modulation of ATP, cyclic AMP and RAS can also recruit or repurpose other existing genes or proteins to meet changing needs.

Phenotype differences typical of individuals with the NF1 syndrome, as compared to those with two functional *NF1* alleles have revealed that *NF1* function is associated with a number of evolutionarily-relevant traits.[2] Multiple characteristics of the *NF1* gene invite comparison to the *FOXP2* gene, which was first recognized in 2002, as having a similarly-unique wild-type human language-associated allele (Table 1).[1]

Table 1. Comparison of the *NF1* and *FOXP2* genes and their protein products.[1,3,4,5,6,7,8,9,10]

Gene	*NF1*	*FOXP2*
Length	300,000 bp	600,000 bp
Amino acid diff. vs. chimps	1	2
Chromosome	17	7
Divergence from chimps	>300,000 BP	>300,000 BP
Orthologs in other taxa	Social amoeboids, fruit flies, zebrafish, mice	Vertebrates: Fish, reptiles, birds, rodents
Loss-of-function (LOF) in other taxa	• *NF1* -/- live births in no mice nor humans • Mouse LOF affects memory and spatial learning	• *FOXP2* -/- live births in mice, not humans • LOF affects vocalizations in mice and birds
Primate variation	• No successful primate NF1 models • Fixed amino acid variation between nearly all primate taxa, suggesting a possible role in speciation	• No successful primate FOXP2 models • Only one fixed amino acid variation between mice and most primates • One additional fixed variant in orangutans
Associated Human Traits (based on loss of function)	• Attention/Behavior issues • Executive Function disorder • Deficits in spatial reasoning • Difficulties with prosodic interpretation • Challenges with speech and musicality	• Difficulties mastering complex sequences of mouth movements underlying speech • Impaired expressive and receptive language

Citations: [1]Fisher 2019; [2]Alveshere & Riccardi 2020; [3]Upadhyaya & Cooper 2012; [4]Silva *et al.* 1997; [5]Watkins *et al.* 2002; [6]Levine *et al.* 2006; [7]Fisher & Scharff 2009; [8]Bloomfield *et al.* 2015; [9]Staes *et al.* 2017; [10]Cota *et al.* 2018; [11]Kelly 2015; [12]Neale & Kelly 2020; [13]Nunn 2018; [14]Kelly 2020; [15]Morley 2006; [16]Strier 2017; [17]Hamacher 2022; [18]Evrony *et al*. 2016; [19]Lodato *et al.* 2016; [20]Formicola 2007; [21]Petru 2019.

Two Questions, One Commonality: Why did both the human wild-type *NF1* allele, and the *FOXP2* human language allele, achieve fixity in hominin populations by the Middle Paleolithic, despite causing debilitating syndromes in heterozygotes? Is there a relationship between these two social-cognitive genes, the relative proliferation in artistic production by Upper Paleolithic humans, and their rapid expansion to – and domination of – even the most remote and hostile environments? At the intersection of these questions lies one crucial, common element: Primary orality.

Figure 4. Lukasa memory board. Luba culture, Democratic Republic of the Congo. Brooklyn Museum. Photo by Lynne Kelly.

Figure 5. Coolamon dual-purpose food dish and mnemonic device. Central Desert, Australia. Photo by Lynne Kelly.

Primary Orality Knowledge Systems: Primary orality knowledge systems utilize art, music, performance, story, and features of the landscape as incredibly powerful mnemonic devices that harness finely-honed memory and communication strategies and maximize humans' abilities to memorize vast quantities of information needed for survival in non-literate societies.[11]

Important elements of stories and songs are often linked to landmarks along familiar routes known in various cultures as "songlines," "pilgrimage trails," "ritual paths," or "ceremonial roads."[12] Once memorized, place-linked information can be recalled by simply envisioning a walk across the landscape, employing the same "memory palace" techniques used by ancient Greeks and modern memory champions.[11] These landscape features can be recreated in miniature on portable memory devices, as well, such as the lukasa (Figure 4).[11] Memorable songs, dances, and stories encode complex, contextual knowledge that enables accurate, detailed information to be transmitted, for up to millennia;[13] and to be recalled, as needed, even if required less than once per generation.[11]

Primary orality is a human universal. Strikingly similar systems have been documented among indigenous societies, worldwide (*e.g.,* Figures 2, 4, 5 and 6).[11] These skills, which gave hominins an unprecedented ability to adapt and survive, are rapidly being lost in literate societies.[14]

Two Hypotheses:

1. Together, the human wild-type *FOXP2* language allele and the human wild-type *NF1* allele optimize the human mind and body for skills crucial to primary orality knowledge systems
2. The proliferation of art and rapid geographic expansion of behaviorally-modern humans in the Upper Paleolithic reflect a cultural mastery of the primary orality knowledge system, the culmination of millennia of hominin experimentation with novel *NF1*- and *FOXP2*-linked traits. Other as-yet-unidentified genetic loci may play important roles, as well.

Primary Orality Skill Set: Based on extensive literature review, decades of NF1 clinical research, and consultations with Indigenous knowledge-keepers, we have identified a set of 85 skills fundamental to oral knowledge systems, worldwide. Next, we've assessed which skills are typically challenge areas, strengths, and unaffected among those with the NF1 disorder. Finally, we assessed which skills are shared with chimpanzees, including bonobos, and which have not been clearly documented in the chimpanzee literature. Table 2 provides a summary of our results.

Figure 6. Kachina doll, Hopi Pueblo. Photo by Brooklyn Museum.

Table 2.
Primary orality skill set summary for human NF1+/+, human NF1+/- and chimp[3,10,11,12,14,15,16,17]

Skill Type	Human NF1 Wild-Type Strengths	Human NF1 +/- Challenge Areas	Human NF1 +/- Strengths	Human *NF1* +/- No change	Chimp Abilities	Not Clearly Documented in Chimps
Art	22	8	3	11	1	21
Music	6	4	1	1	1	5
Performance	8	2	0	6	1	7
Spatial	7	4	0	3	1	6
Cognitive	24	12	4	8	5	19
Social	16	8	8	0	8	8
Language	2	2	0	0	0	2
Total	85	40	16	29	17	68

Implications: The high, survivable mutation rate of the *NF1* gene facilitates the emergence of variation that may be advantageous at somatic, community, species, and interspecies levels.

At the somatic level, mutations in neurons during an individual's lifetime may facilitate the proliferation and culling of neural pathways in real time. This may allow the brain and senses to adjust and adapt as the individual encounters new information and experiences.[18,19] Variation among individuals at both somatic and germline levels provides community-wide diversity in orality skills that enhances the oral knowledge system of the entire community. Other genetic or medical conditions that cause affected individuals to engage differently with the world may also have held great value to early modern human societies. This is possibly reflected by the reportedly high percentage of disfigured skeletal remains in Upper Paleolithic burials.[20,21]

At the species level, variation allows a species to adapt to multiple ecological niches while also retaining the ability to navigate to new areas, and to communicate and interbreed across communities. This creates an increasingly robust species, both in terms of cultural adaptability and genetic diversity.[8] *NF1* is a diversity-generator, likely driving speciation, as suggested by the primate neurofibromin family tree (Figure 3).[2] Speciation arises through some combination of genetic and behavioral changes that cause descendants of a common ancestral population to no longer be able to interbreed. Through its action at the cellular membrane, and broad influence on communication systems, *NF1* provides a strong candidate mechanism for catalyzing much of the robust diversity that has afforded life on Earth the flexibility to adapt to countless cataclysms and environmental transitions. In humans, our *NF1* allele unlocked the full adaptive potential of the hominin biocultural toolkit.

Conclusions: The robust adaptive flexibility of primary orality knowledge systems, enabled by the human *NF1* and *FOXP2* alleles and a lot of ancient ingenuity, is arguably our species' original "superpower." Fortunately, while literate societies may have forgotten, these skills are not yet lost.[11,12,14]

Complete References:

***Contact:**
Dr. Andrea Alveshere
a-alveshere@wiu.edu

alveshere.com