Vision for H3Africa and Historical Perspective

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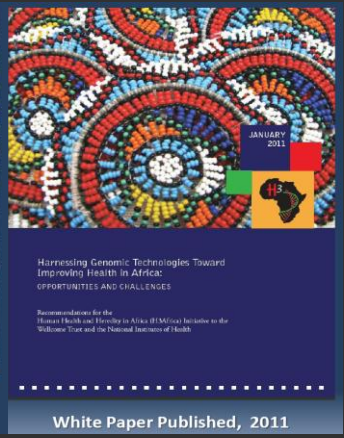
- Director: Center for Research on Genomics and Global Health
- Senior Investigator: Inherited Disease Research Branch, National Human Genome Research Institute, NIH

Annual meeting of the AfSHG – Nov 2007, Cairo, Egypt

Press Release, 2010

Working Group Meeting, 2010



White Paper Published, 2011

In response to discussion in Cairo regarding genomics in Africa, the AfSHG, NIH and WT convened a Frontiers Meeting in Yaoundé, Cameroon in March 2009 to discuss a research agenda to study genetic diversity in health and disease in Africans.

High Level Working Group:

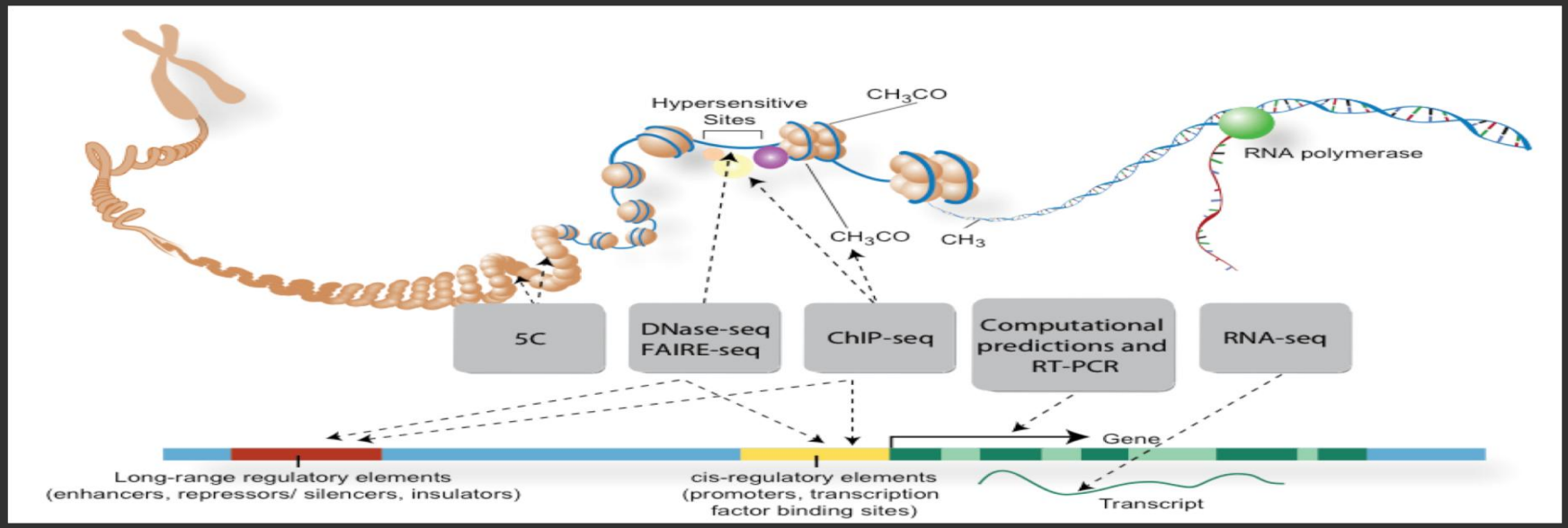
Kay Davies; Eric Green; Pat Goodwin Thomas Egwang; Barry Bloom; C Rotimi

Cape Town Meeting, 2011

Encode - Encyclopedia of DNA Elements

Over 440 researchers in 32 labs around the world applied high-throughput approaches to detect all sequence elements that confer biological function in the human genome

Findings calls into question our gene-centric view of the genome
Example: there are many "genes" in which DNA codes for RNA, not a protein; 76% of the bases in the genome is transcribed



HaploReg

HaploReg is a tool for exploring annotations of the noncoding genome at variants on haplotype blocks, such as candidate regulatory SNPs at disease-associated loci. Using LD information from the 1000 Genomes Project, linked SNPs and small indels can be visualized along with their predicted chromatin state in nine cell types, conservation across mammals, and their effect on regulatory motifs. HaploReg is designed for researchers developing mechanistic hypotheses of the impact of non-coding variants on clinical phenotypes and normal variation.

Build Query | Set Options | Documentation

Use one of the three methods below to enter a set of variants. If an r^2 threshold is specified (see the Set Options tab), results for each variant will be shown in a separate table along with other variants in LD. If r^2 is set to NA, only queried variants will be shown, together in one table.

Query (refSNP ID(s), comma-delimited): rs17125401,rs12582592

or, upload a text file (one refSNP ID per line): Browse...

or, select a GWAS:

Submit Query

Query SNP: rs17125401 and variants with r^2 >= 1

chr	pos (hg19)	LD	variant	Ref	Alt	ASN freq	CEU freq	YRI freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	eQTL tissues	Motifs changed	GENCODE genes	RefSeq genes	dbSNP func annot
12	51454210	1	rs17125286	T	C	0.51	0.13	0.04					HBMEC			Pou3f3,Bach1,AP-1	2bp 3' of LETMD1	2bp 5' of LETMD1	
12	51471152	1	rs17125346	A	G	0.54	0.13	0.03									CSRNP2	CSRNP2	intronic
12	51490334	1	rs55864652	C	T	0.48	0.13	0.04								Pou2f1	TFCP2	TFCP2	intronic
12	51513608	1	rs12582592	G	A	0.51	0.13	0				NHEK	Monocytes-CD14+				TFCP2	TFCP2	intronic
12	51514352	1	rs17125401	T	C	0.51	0.13	0.05								Pou2f1	TFCP2	TFCP2	intronic

Query SNP: rs12582592 and variants with r^2 >= 1

chr	pos (hg19)	LD	variant	Ref	Alt	ASN freq	CEU freq	YRI freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	eQTL tissues	Motifs changed	GENCODE genes	RefSeq genes	dbSNP func annot
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12	51513608	1	rs12582592	G	A	0.51	0.13	0				NHEK	Monocytes-CD14+				TFCP2	TFCP2	intronic
12	51514352	1	rs17125401	T	C	0.51	0.13	0.05								Pou2f1	TFCP2	TFCP2	intronic

http://www.broadinstitute.org/mammals/haploreg/haploreg.php

Why the Encode Example

1. 32 labs: none in Africa

2. Forced the development of computational and high throughput strategies for the analysis of the human genome – possible because there were existing "good" labs

3. International collaboration – Scientists in diverse labs used the same protocol and delivered high quality data

4. Training of next-generation of scientists

5. Encode is a "global good" (H3Africa – promises to generate a global good that will be housed on the continent of Africa)

The NEW ENGLAND JOURNAL of MEDICINE

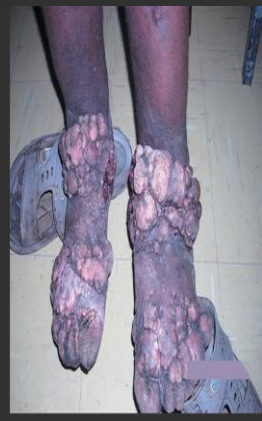
ORIGINAL ARTICLE

HLA Class II Locus and Susceptibility to Podoconiosis

Fasil Tekola Ayele, Ph.D., M.P.H., Adebowale Adeyemo, M.D., Chris Finan, Ph.D., Elena Hailu, M.Sc., Paul Sinnott, Ph.D., Natalia Diaz Burlinson, M.Sc., Abraham Aseffa, M.D., Ph.D., Charles N. Rotimi, Ph.D., M.P.H., Melanie J. Newport, M.D., Ph.D., and Gail Davey, M.D.

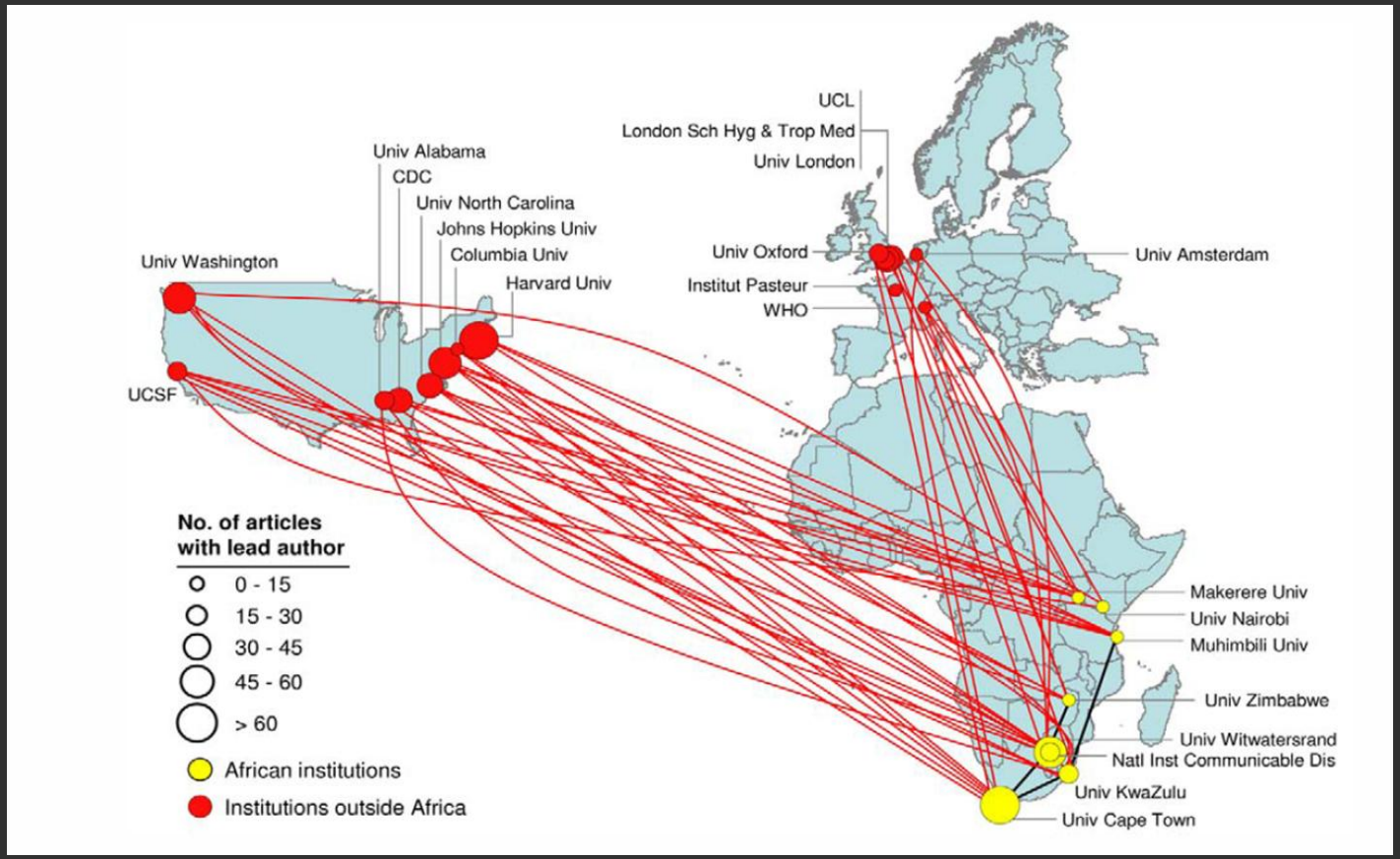
SNP	HLA gene	P	OR
rs17612858	*DQA1*	1.4×10^{-9}	2.4 (1.8–3.3)
rs9273349	*DQB1*	3.5×10^{-7}	2.1 (1.6–2.8)
rs1063355	*DQB1*	3.5×10^{-7}	2.1 (1.6–2.8)
rs17612633	*DQA1*	4.4×10^{-7}	2.1 (1.6–2.8)
rs17843604	*DQA1*	5.4×10^{-7}	2.1 (1.6–2.7)
rs9270856	*DRB1*	1.4×10^{-6}	0.5 (0.4–0.7)

Podoconiosis is a tropical lymphedema (non-filarial elephantiasis) resulting from long-term bare-foot exposure to red clay soil derived from volcanic rock. Not all exposed persons develop podo.



Fasil Tekola Ayele, Ph.D

H3Africa is already succeeding



Thank you