

Genetic Determinants of Orofacial Shape and Relationship to Cleft Lip/Palate



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Specific Aims

1. **Determination of heritable midfacial morphometric variation among 8 mouse strains of the mouse Collaborative Cross**
2. Fine-map major quantitative trait loci (QTLs) responsible for those major heritable midfacial morphometric phenotypes using the mouse Collaborative Cross > Instant mouse models
3. Carry out GWAS of four homologous human midfacial morphometric phenotypes in Tanzanian children. Connect with Weinberg/Marazita project and test association of confirmed loci in USA EUR, USA Hispanic/Latino, (Asian) populations



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Project Collection Sites



Summary of Enrollment



	Opened	Status	Enrollment
Tanzania	5/09	Open	5690
Denver	5/19/10	Open	472
San Francisco	7/27/10	Closed 3/28/12	251

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Planned GWAS for Orofacial Shape Parameters in Tanzania (Bantu)

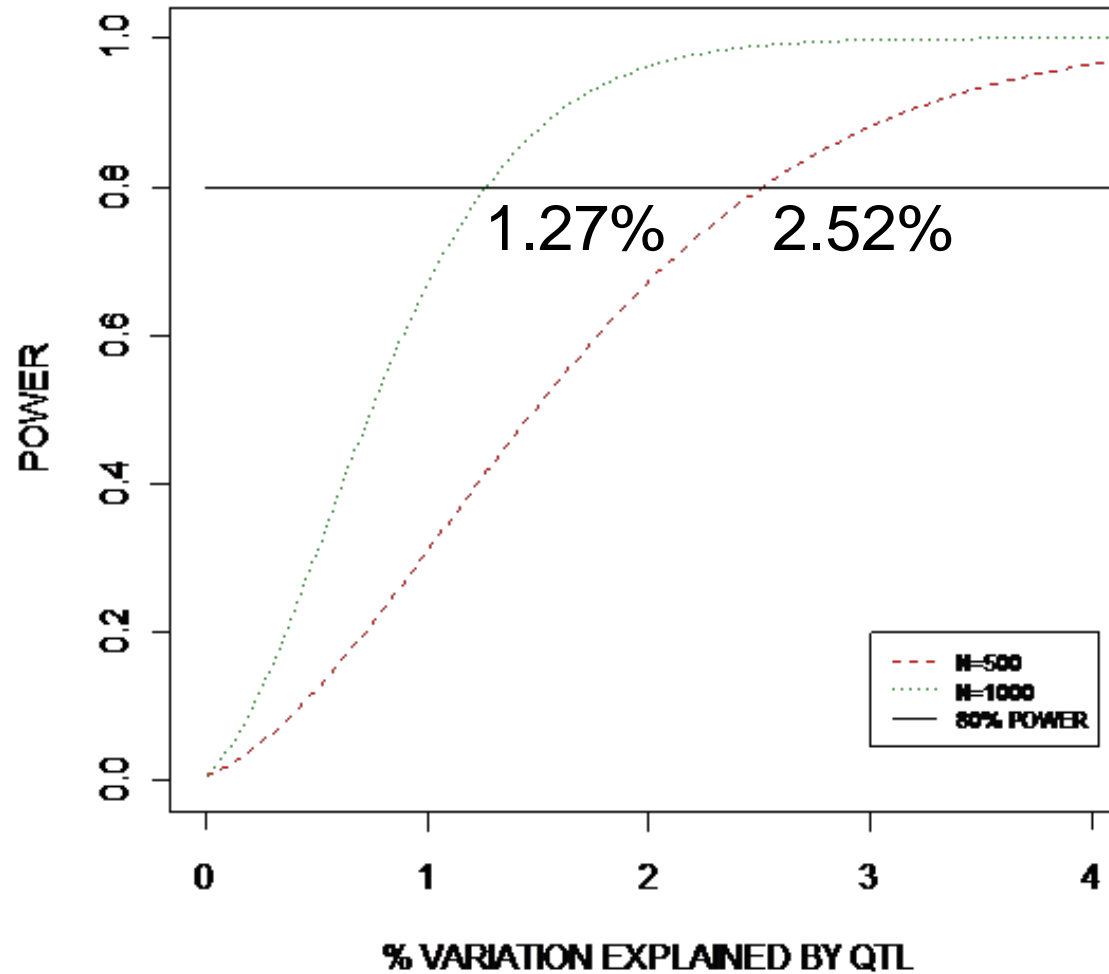


Planned GWAS for Orofacial Shape Parameters in Tanzania (Bantu)

Replication stage; n=2500

Planned GWAS for Orofacial Shape Parameters

EUR & Hispanic extension stage; n=500, 1000



4 measurement traits X 2 loci per trait

Progress on Aim 3

1. Redirection of Aim 3 officially approved by FB Steering Committee, FB SLG, FB CSOC
2. Permission to apply to CIDR given by NIDCR
3. Application to CIDR for Aim 3 genotyping with Illumina 2.5M array; approved by CIDR review and CIDR BOG
4. Tanzanian GWAS approved by NIDCR at this time
5. Request to CIDR to change to Illumina 2.5+Exome array; approved by CIDR and NIDCR
6. Worked w/ CIDR/U Wash to randomize platemaps
7. DNAs sent to CIDR for genomewide genotyping
8. Test array run, problem samples reported
9. Problem samples resolved or being replaced now

Tanzania 3D Photo / Data / Saliva Collection



Summary of Tanzania Enrollment

	2009	2010	2012	Total
Target	1000	2500	2500	6000
Enrolled	979	2680	2031	5690

Summary of Tanzania DNAs

	Problems	Resolution
Subjects enrolled	5690	
Salivas received in Spritz lab	3664	
Salivas prepped to DNA	3664	
DNAs that passed QC	3651 (99.65%)	All 13 wgPCR
Failures subjected to wgPCR	9	4 successful

Summary of CIDR TestArray Outcomes

	Problems	Resolution
Samples approved	3700	
Salivas submitted	3655	
Unexpected duplicates	42 (x2)	5/5 true duplicates; 24 (x2) unresolved
Poor genotyping performance	30	2 wgPCR
Sex switches	59	32 data entry errors

The Root of all Evil



Tanzania 3D Photo / Data / Saliva Collection



Plan to Reduce Future Problems

1. Assign each participant FaceBase ID number, with label to be on consent, sample tube, **shirt**.
2. Engage teachers to **check consent signatures** and **keep track to avoid duplications**.
3. **Carefully observe spitting, collect tubes early.**
4. **Add 2D photo of face and ID# on shirt.**
5. **When taking 3D photos, check ID# on forms versus on shirt.**
6. **In Canada, check consent and intake forms against database fields.**

