SUPPLEMENTAL MATERIAL

Supplemental figures

Figure S1. Dual luciferase assay validates two IRF6 binding sites in 2.2kb upstream of zebrafish Klf17. Asterisks indicate siginificant difference between IRF6 overexpression group and control plasmid-transfected group, **: *P<0.01;* plus marks indicate significant difference between Klf17 promoter lacking either IRF6 binding sites and intact promoter, ++: *P*<0.01.

Figure S2. Chromatin Conformation Capture using KLF4-E1 as bait showing KLF4-E2~E5 can physically crosstalk with KLF4-E1.

Figure S3. GFP reporter transgenic fish showing enhancer activity of KLF4-E5 in oral epithelium (lateral and ventral view)

Figure S4. Pedigrees of other families with KLF4 mutation p.R94G. Only proband was sequenced.

Supplemental tables

Table S1. Intersection between NHEK super-enhancers and IRF6 ChIP-seq peaks.

Table S2. Summary of KLF4 variants found in NSCL/P patients.

Table S3 Common variant association statistics in Filipino multiplex families

Marker	Alleles	Minor Allele (Freq)	# Informative Families	Z	P
rs2236599	G/A	A (0.238)	98	0.655	0.512
rs149109998	G/A	A (0.035)	29	1.205	0.228
rs77275043	C/G	C (0.212)	97	0.560	0.575

Table S4. Rare variant statistics for KLF4 (p-values, MAF < 0.01)

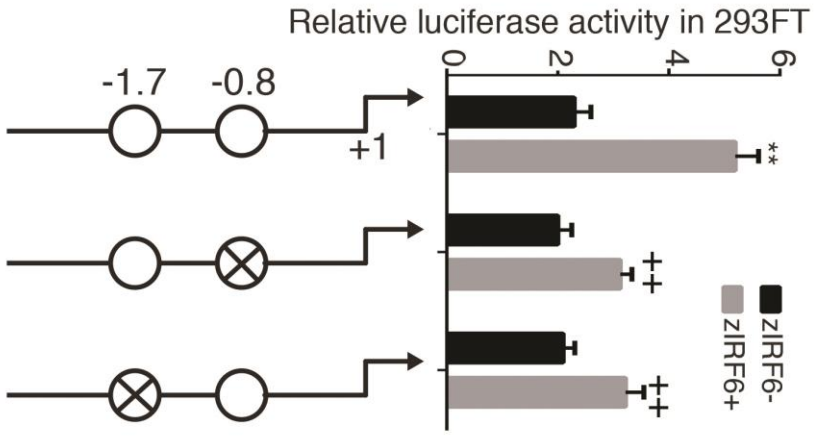
Testing Method	All Coding Variants		All Missense Variants	
	CLP	CLO	CLP	CLO
Burden Tests:				
CAST	0.407	0.636	0.058	0.424
VT	0.074	0.318	0.071	-- [a]
Non-burden Tests:				
RBT	0.152	0.507	**0.026**	0.093
C-alpha	0.525	0.851	0.362	0.591

[a] Insufficient observations

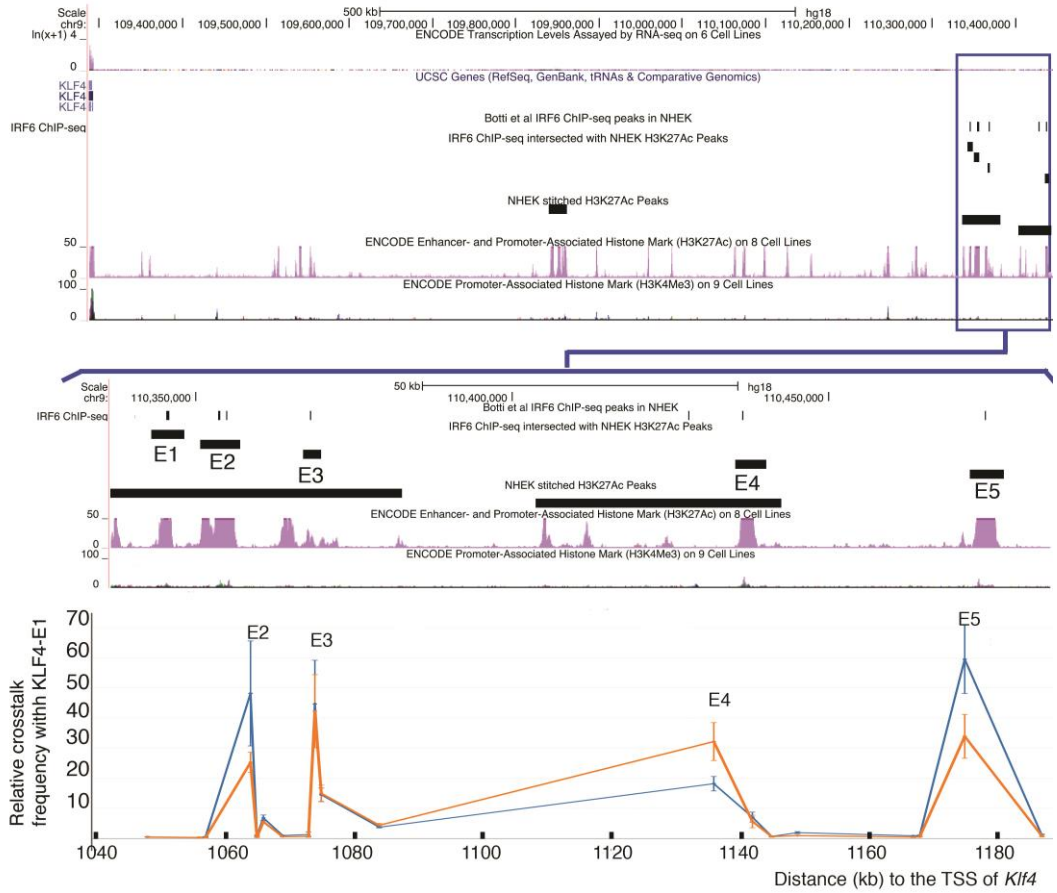
Bold, nominally significant p-value.

Table S5 Sequence of primers used in this study.

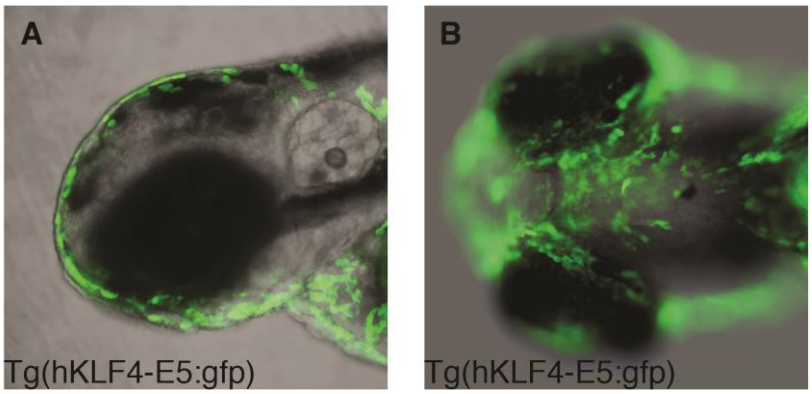
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4