Supplementary Appendix

I) Mutation Analyses:

We identified the following *ALPL* and *PHEX* mutations in our study patients with HPP and XLH, respectively **(Table S-1)**.

Table S-1
Mutations in *ALPL* and *PHEX* in HPP and XLH, respectively

Diagnosis	Sex	Mutation #1	Mutation #2
Hypophosphatasia	M	c.1432A>T, p.Asn478Tyr*	
"	M	c.1133A>T, p.Asp378Val	
"	F	c.1133A>T, p.Asp378Val	
"	F	c.1172G>A, p.Arg391His	
"	F	c.571G>A, p.Glu191Lys	c.550C>T, p.Arg184Trp
"	F	c.1133A>T, p.Asp378Val	
"	M	c.212G>A, p.Arg71His	
"	M	c.550C>T, p.Arg184Trp	
"	M	c.571G>A, p.Glu191Lys	c.1132G>C, p.Arg378His
"	M	c.129delT, p.Gln44ArgfsX23	c.1307A>G, p.Tyr436Cys
"	M	C.151G>T, p.Ala51Ser	c.400_401AC>CA, p.Thr134His
"	F	C.151G>T, p.Ala51Ser	c.400_401AC>CA, p.Thr134His
"	M	c.1133A>T, p.Asp378Val	
"	M	c.427delC, p.Gln143ArgfsX22	c.1444C>A, p.His482Asn
"	M	c.422C>A, p.Thr141Asn	c.629A>G, p.His210Arg
"	M	c.400_401AC>CA, p.Thr134His	c.571G>A, p.Glu191Lys
"	F	IVS9 c.997+3A>G	c.1181_1182delCT, p.Ser394fsX10
"	F	c.1285G>A, p.Glu429Lys	
"	M	c.1133A>T, p.Asp378Val	
"	M	c.571G>A, p.Glu191Lys	c.881A>C, p.Asp294Ala
"	M	c.1250A>G, p.Asn417Ser	
"	M	c. 346G>A, p. Ala116Thr	
"	F	N.D.	
"	M	c.180T>C, p.Asp60Glu	
"	M	c.1133A>T, p.Asp378Val	
"	M	c.1133A>T, p.Asp378Val	
"	F	c.1133A>T, p.Asp378Val	
"	M	c.526G>A, p.Ala176Thr	c.881A>C, p.Asp294Ala
"	F	c.1133A>T, p.Asp378Val	
"	M	c.571G>A, p.Glu191Lys	c.881A>C, p.Asp294Ala
"	F	N.D.	
"	F	c.1240C>A, p.Leu414Met	
"	F	c.571G>A p.Glu191Lys	c.1001G>A, p.Gly334Asp
"	M	IVS10 c.1189+5 del C	c.1328C>T, p.Ala443Val
"	F	c.931G>A, p.Glu311Lys	c.1363G>A, p.Gly455Ser

Diagnosis	Sex	Mutation #1	Mutation #2
Hypophosphatasia	F	c.931G>A, p.Glu311Lys	c.1363G>A, p.Gly455Ser
“	F	IVS3 c.182-2 A>C	
“	M	c.571G>A, p.Glu191Lys	c.1001G>A, p.Gly334Asp
“	F	c.526G>A, p.Ala176Thr	c.881A>C, p.Asp294Ala
“	M	c.212G>C, p.Arg71Pro	
“	F	c.932A>G, p.Glu311Gly*	
X-Linked Hypophosphatemia	F	c.1520T>C, p.Leu507Pro	
“	F	IVS15 c.1645+1G>A	
“	M	c.*231A>G	
“	M	c.*231A>G	
“	F	c.2102_2102delC, p.Arg702fs	
“	F	c.15_16delAG, p.Gly6fsX44	
“	F	IVS9 c.1080-2A>G	
“	M	none	
“	M	c.*231A>G	
“	F	del of exons 13 thru 22	
“	F	N.D.	
“	M	c.*231A>G	
“	M	c.*231A>G	
“	M	c.*231A>G	
“	M	c.1204C>T,p.Gln402Ter	
“	M	c.163_164ins T, p.Lys56fs	
“	M	none	
“	M	c.*231A>G	
“	M	c.*231A>G	
“	M	c.*231A>G	
“	F	c.830T>A, p.Leu277Ter	
“	F	none	
“	M	c.2078G>A, p.Cys693Tyr	
“	M	c.*231A>G	
“	F	IVS15 c.1645+1G>A	
“	F	c.1645C>T, p.Arg549XTer	
“	M	c.*231A>G	
“	M	N.D.	
“	F	none	
“	M	N.D.	
“	M	c.2250G>C, p.Ter750Tyr	
“	F	c.763_784dup, p.Ala262GlyfsX9	
“	F	c.807delT, p.His269GlnfsX3	
“	M	IVS10 c.1173+2T>C	
“	F	N.D.	
“	M	IVS10 c.1173+2T>C	
“	M	N.D.	
“	M	N.D.	
“	F	IVS5 c.663+2T>A	
“	M	c.2104C>T, p.Arg702Ter	
“	F	none	

Diagnosis	Sex	Mutation #1	Mutation #2
X-Linked Hypophosphatemia	F	c.871C>T,p.Arg291Ter	
“	F	c.960_961insGTCATTGA, p.Asp323fsX11	
“	F	none	
“	M	none	
“	F	c.1209G>A, p.Trp403Ter	
“	F	none	
“	F	N.D.	
“	F	c.1522C>T, p.Gln508Ter	
“	M	c.1942G>A, p.Gly648Arg	
“	F	c.587 delG, p.Gly196fs	
“	F	none	
“	F	c.2237G>A, p.Cys746Tyr	
“	F	c.*231A>G	
“	M	c.65_65delC, p.Leu23fs	
“	F	c.1601C>T, p.Pro534Leu	
“	M	c.1601C>T, p.Pro534Leu	
“	M	none	
“	M	N.D.	
“	F	none	
“	M	N.D.	
“	F	c.1735G>A, p.Gly579Arg	
“	F	c.1735G>A, p.Gly579Arg	
“	M	large deletion	
“	M	c.2041_2043delAAC, p.Asn680del	
“	F	c.2041_2043delAAC, p.Asn680del	
“	M	c.*231A>G	
“	F	IVS16 c.1701-2A>C	
“	M	none	
“	F	none	
“	M	c.2104C>T, p.Arg702Ter	
“	F	c.2064, p.Tyr688Ter	
“	M	c.1735G>A, p.Gly579Arg	

*Asterisk at end of mutation = novel *ALPL* mutation.

"none" = no mutation detected by sequencing coding region and mRNA splice sites.

N.D. = sequencing not done.

II) Preteenage Serum Biochemical Findings:

To minimize any impact of puberty on the serum biochemical findings, here we restricted statistical analyses to the preteenage subjects **(Tables S-2 to S-12; Figures S1 to S-11)**.

Table S-2: Study Subject Years-Of-Age & Sex

Group	N	Mean (SD)	Min, Max	Girls	Boys
CTR	9	10.2 (1.7)	7.7, 12.6	7	2
XLH	64	7.7 (2.8)	2.3, 12.6	33	31
HPP	31	6.5 (4.1)	1.2, 12.8	12	19

Figure S-1: Serum Alkaline Phosphatase

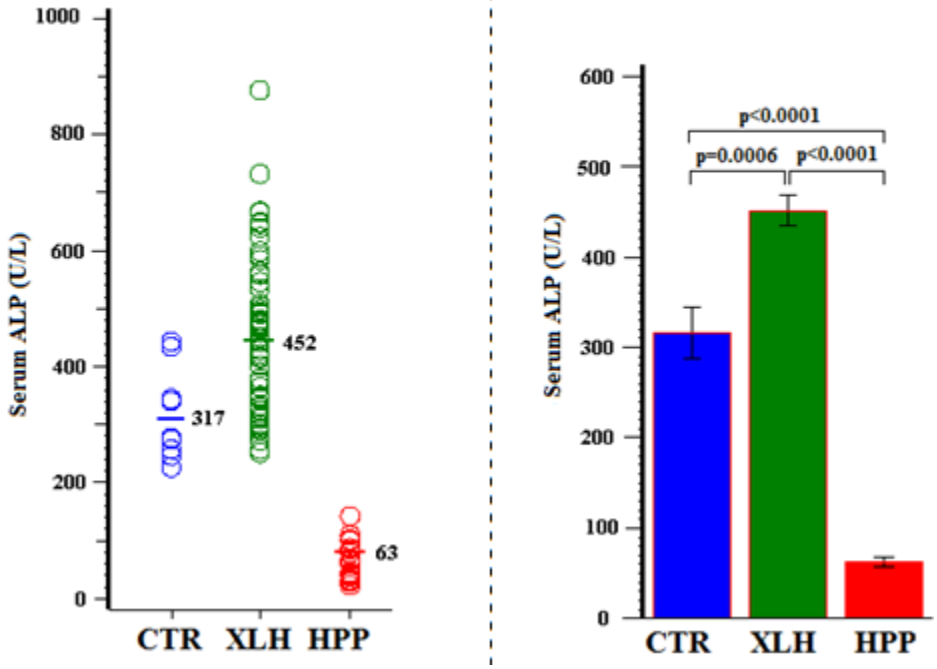

Table S-3: Serum Alkaline Phosphatase

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	317 (80)	227, 444	255, 378	0.0006 (XLH vs CTR)
XLH	64	452 (132)	252, 877	416, 479	<0.0001 (HPP vs CTR)
HPP	31	63 (29)	23, 143	52, 74	<0.0001 (XLH vs HPP)

Figure S-2: Serum Phosphate

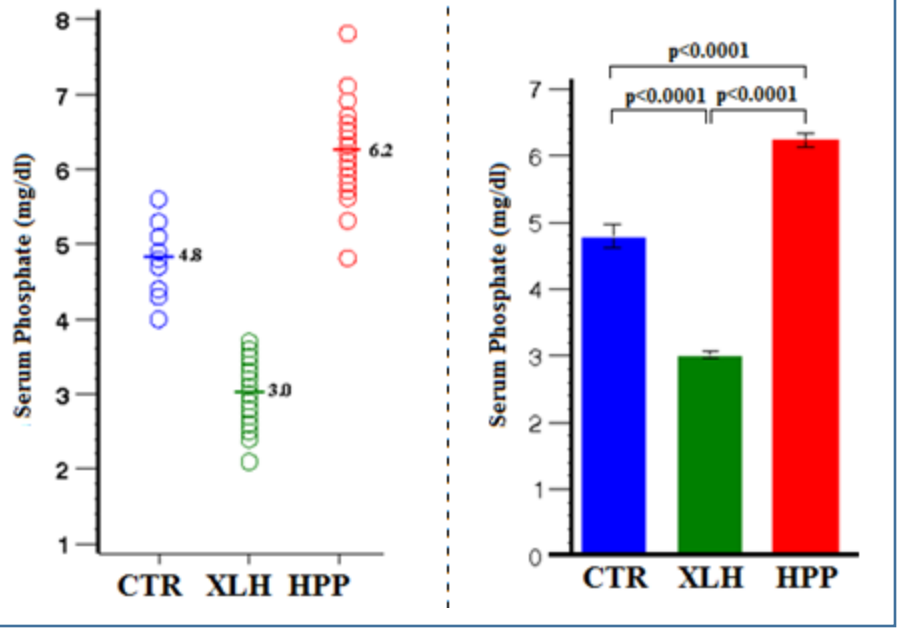

Table S-4: Serum Phosphate

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	4.8 (0.5)	4.0, 5.6	4.4, 5.2	<0.0001 (XLH vs CTR)
XLH	64	3.0 (0.4)	2.1, 3.7	2.9, 3.2	<0.0001 (HPP vs CTR)
HPP	31	6.2 (0.6)	4.8, 7.8	6.0, 6.5	<0.0001 (XLH vs HPP)

Table S-5:[23]

Serum Phosphate (age<13)	N	Mean/Median (SD)	95%CI of Mean	Range (min, max)	P-value (compare to control)
Normal	43	4.9 / 4.9 (0.4)	4.8, 5.0	3.8, 5.9	
Odonto	63	6.0 / 6.1 (0.5)	5.8, 6.1	4.4, 7.0	<0.0001
Mild childhood	37	6.2 / 6.2 (0.4)	6.0, 6.3	5.0, 7.2	<0.0001
Severe Childhood	53	6.1 / 6.2 (0.7)	5.9, 6.3	4.3, 7.1	<0.0001
Infantile	12	6.1 / 6.1 (0.5)	5.8, 6.4	5.5, 6.9	<0.0001
Cohort	165	6.1 / 6.1 (0.5)	6.0, 6.2	4.3, 7.2	<0.0001

Figure S-3[23]: Serum Phosphate vs HPP Severity

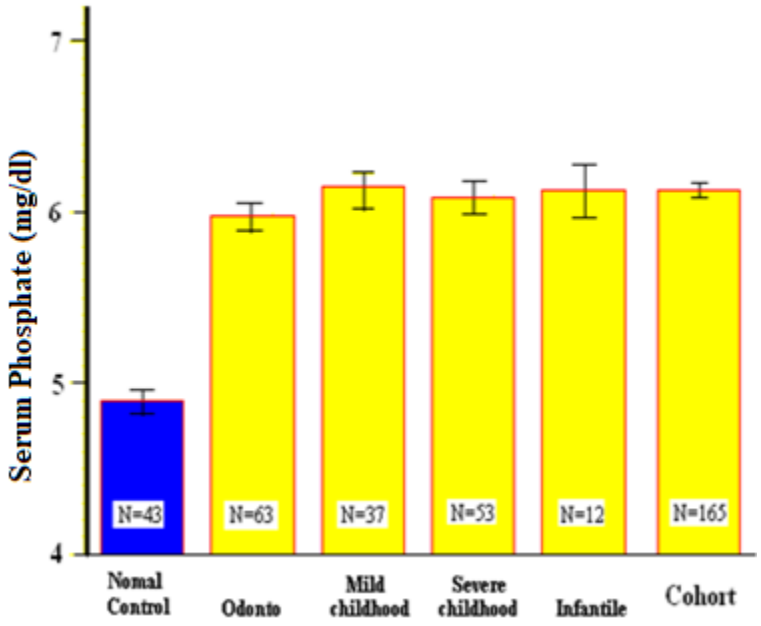

Figure S-4: Serum Calcium (Total)

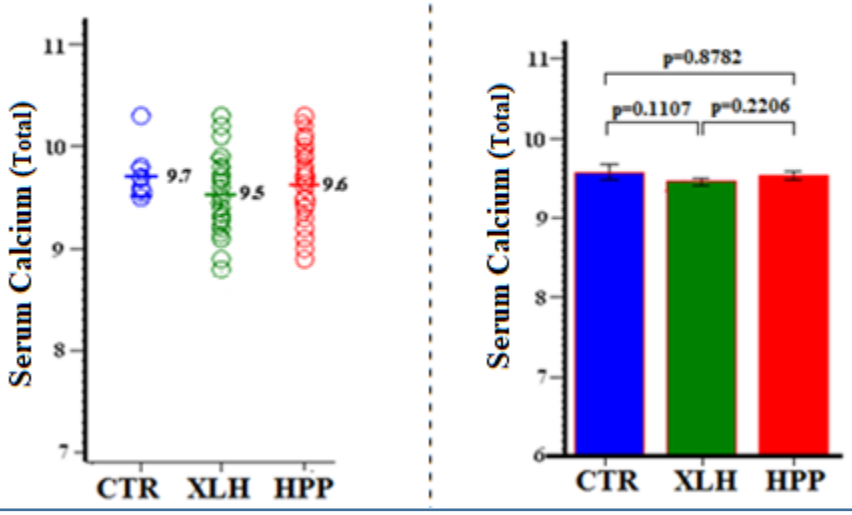

Table S-6: Serum Calcium (Total)

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	9.7 (0.2)	9.5, 10.3	9.5, 9.9	0.1107 (XLH vs CTR)
XLH	64	9.5 (0.3)	8.7, 10.3	9.4, 9.6	0.8782 (HPP vs CTR)
HPP	31	9.6 (0.3)	9.0, 10.3	9.6, 9.8	0.2206 (XLH vs HPP)

Figure S-5 : Serum Calcium (Ionized)

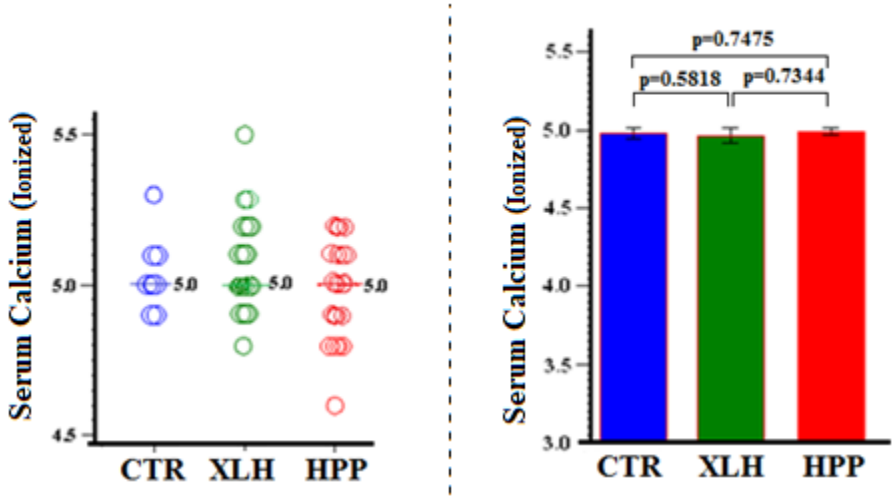

Table S-7: Serum Calcium (Ionized)

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	5.0 (0.12)	4.9, 5.3	4.9, 5.1	0.5818 (XLH vs CTR)
XLH	64	5.0 (0.14)	4.7, 5.5	4.9, 5.1	0.7475 (HPP vs CTR)
HPP	31	5.0 (0.13)	4.6, 5.2	4.9, 5.1	0.7344 (XLH vs HPP)

Figure S-6: Serum Parathyroid Hormone

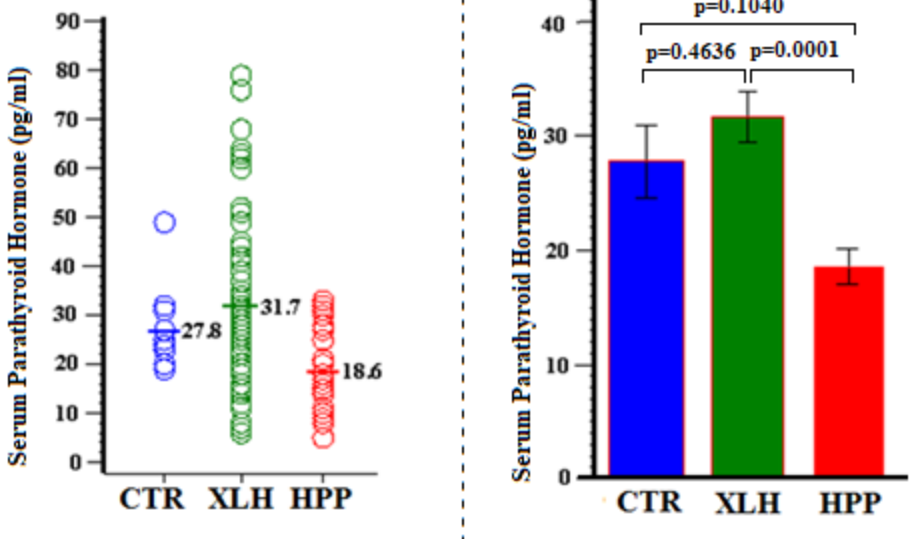

Table S-8: Serum Parathyroid Hormone

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	27.8 (9.1)	19, 49	20.8, 34.8	0.4636 (XLH vs CTR)
XLH	64	31.7 (17.6)	6, 79	27.2, 35.8	0.1040 (HPP vs CTR)
HPP	31	18.6 (8.3)	5, 33	15.5, 21.6	0.0001 (XLH vs HPP)

Figure S-7: Serum Creatinine

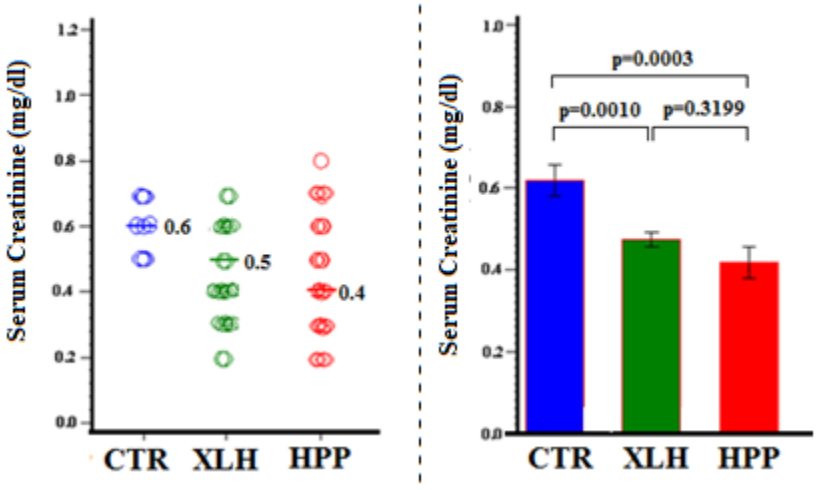

Table S-9: Serum Creatinine

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	0.6 (0.1)	0.5, 0.7	0.6, 0.7	0.0010 (XLH vs CTR)
XLH	64	0.5 (0.1)	0.2, 0.7	0.4, 0.5	0.0003 (HPP vs CTR)
HPP	31	0.4 (0.2)	0.2, 0.8	0.4, 0.5	0.3199 (XLH vs HPP)

Figure S-8: Serum FGF23

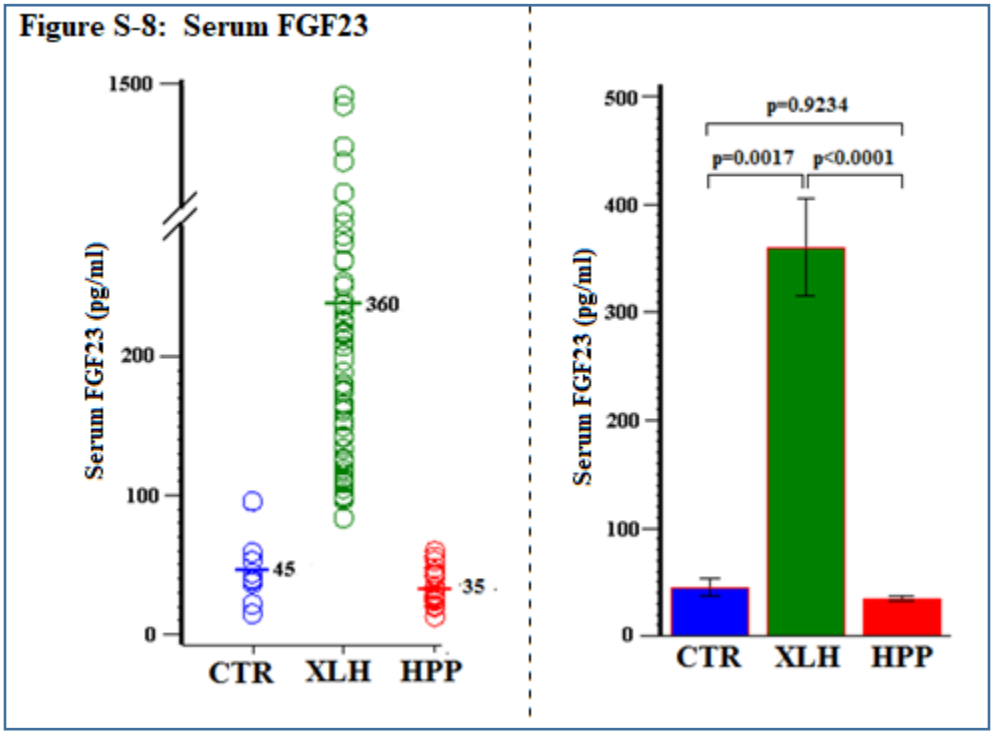

Table S-10: Serum FGF23

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	45 (24)	15, 96	26.9, 63.1	0.0017 (XLH vs CTR)
XLH	58	360 (341)	84, 1442	273, 450	0.9234 (HPP vs CTR)
HPP	26	35 (12)	13, 60	30.0, 39.8	<0.0001 (XLH vs HPP)

Figure S-9: Serum sFRP4

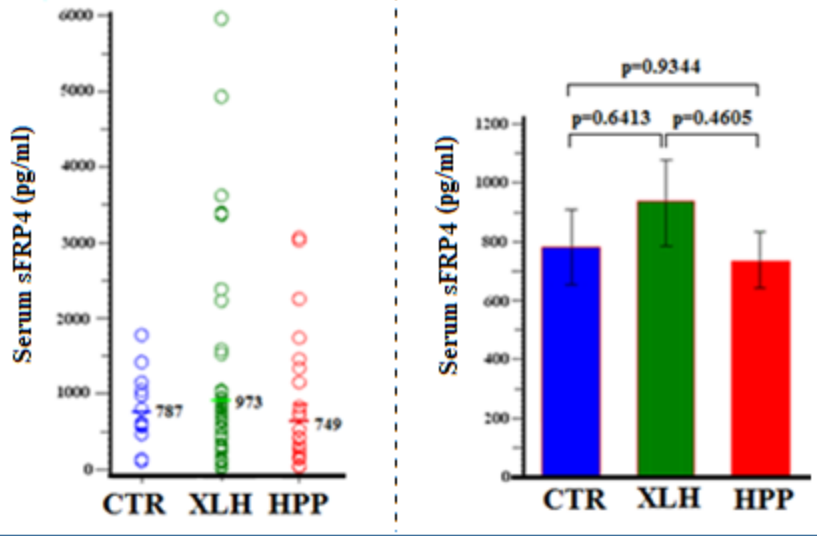

Table S-11: Serum sFRP4

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	787.2 (566.1)	113, 1779	352, 1222	0.6413 (XLH vs CTR)
XLH	53	973.5 (1252.7)	23, 5965	663, 1328	0.9344 (HPP vs CTR)
HPP	18	749.4 (759.9)	52, 3031	372, 1128	0.4605 (XLH vs HPP)

Figure S-10: Serum FGF7

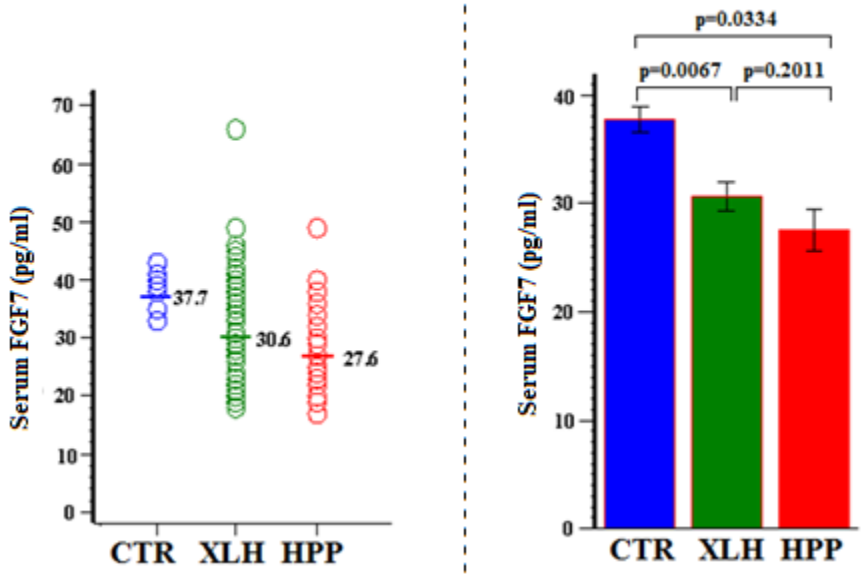

Table S-12: Serum FGF7

Group	N	Mean (SD)	Min, Max	95% CI	P (Group Comparisons)
CTR	9	37.7 (3.4)	33, 43	35.1, 40.2	0.0067 (XLH vs CTR)
XLH	55	30.6 (9.8)	18, 66	28.5, 33.8	0.0334 (HPP vs CTR)
HPP	21	27.6 (8.6)	17, 49	23.6, 31.5	0.2011 (XLH vs HPP)
Odonto	5	34.6 (9.7)	22, 49	22.6, 46.6	P = 0.0404 (regression analysis according to HPPSSC)
Mild childhood	6	27.0 (9.6)	17, 40	16.9, 37.1	
Severe childhood	8	24.6 (6.4)	17, 34	19.2, 30.0	
Infantile	2	23.5 (2.1)	22, 25	4.4, 42.5	

Figure S-11: Serum FGF7 vs HPPSSC