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Are Gene Polymorphisms of Fibroblast Growth Factor 10 Associated with Patent Ductus Arteriosus and Bronchopulmonary Dysplasia in Extremely Low Birth Weight Infants?

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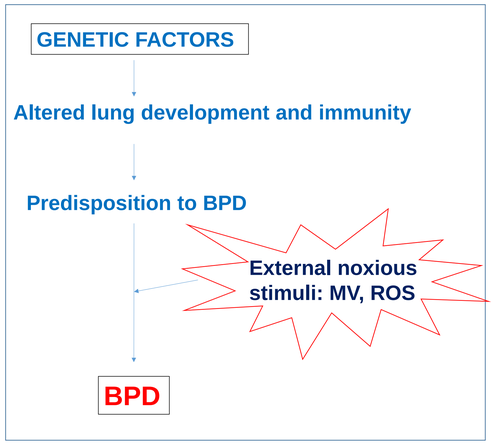
Background



Roles of FGF 10 –

Fibroblast growth factor 10 (FGF10) plays a significant role in cardiac outflow tract formation and possible PDA. Downregulation of the FGF/Ras/Erk pathway are important for the differentiation of the progenitors and colonization of the cardiac outflow tract.

FGF10 is also an integral part of the signaling required for distal lung branching morphogenesis in fetus. It is an alveolar epithelium cell (AEC) mitogen protects against cyclic stretch and oxidant injury via DNA repair. It regulates the mitogen activated protein kinase pathway (MAPK) that, in turn activates the Na-K-ATPase in AEC - protein responsible for fetal lung fluid resorption and β2 receptor mediated actions.

FGF10 SNPs ; rs2973644, rs900379, rs1011814 were chosen as the SNPs were studied in adult collagen disorders.

Patent Ductus Arteriosus

Persistent PDA is defined as requiring medical treatment/surgery

It causes significant morbidity in the ELBW infants

Bronchopulmonary Dysplasia

Defined as an oxygen need at 36 weeks postmenstrual age

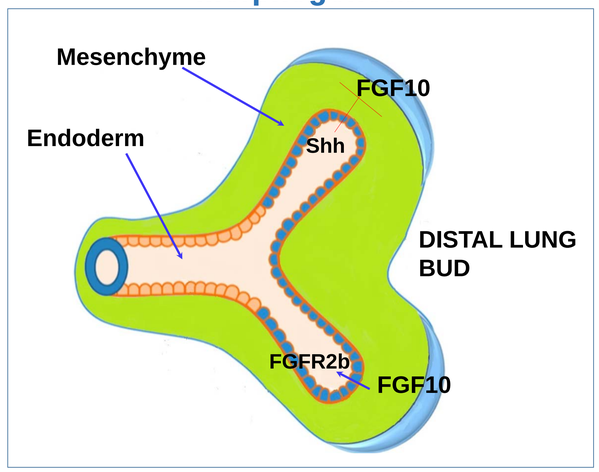
Incidence is about 40% for ELBW infants

Genetic variation may predispose to BPD in preterm infants about 30-80%

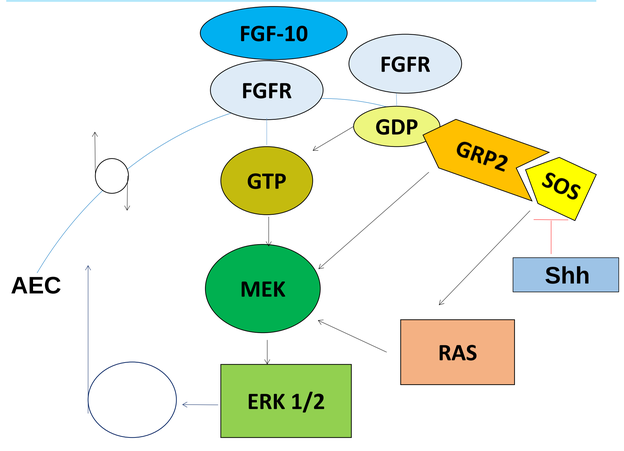
Hypothesis

FGF10 SNP ; rs2973644, rs900379, rs1011814 are associated with susceptibility to PDA and or BPD in ELBW infants.

FGF10 expression and lung bud morphogenesis



FGF10 signaling pathway



*Alveolar epithelial cell, fibroblast growth factor 10, extracellular signal regulated kinase, Guanosine triphosphate, Sonic hedgehog, Growth factor receptor-bound protein 2 , Son of sevenless, mitogen extracellular kinase

Methods

Inclusion criteria:

- **ELBW infants (birth weight < 1kg)**
- **Informed parental consent**

FGF10 SNPs Analysis:

DNA was isolated from buccal swabs and real-time PCR was performed using Taqman probes

BPD is defined by the need for oxygen supplementation at 36 weeks post menstrual age.

Statistics: Student's t-test, Chi-square, Mann-Whitney, z-test; *P* <0.05

Results

Demographic Characteristics- PDA

		PDA	No PDA	*p*-value
GA (wk; median;IQR)		25 (24, 26)	25 (24, 26)	0.1
BW (gm; mean± SD)		742±171	737 ±175	0.9
Prenatal Steroid		52(78%)	17 (74%)	0.8
Female Gender		32(49%)	12(50%)	0.6
Race	Non Hispanic White	17(29%)	9(28%)	0.6
	Non Hispanic Black	15(26%)	11(34%)	
	Hispanic	22(38%)	11(34%)	
	Other	4(7%)	1(3%)	

Demographic Characteristics- BPD

		No BPD	BPD	*p*-value
GA (wk; median;IQR)		26 (25, 27)	25 (24, 26)	0.001
BW (gm; mean± SD)		761±143	690 ±157	0.001
Prenatal Steroid		42 (76%)	25(85%)	0.2
Female Gender		18(60%)	24(45%)	0.1
Race	Non Hispanic White	9(30%)	11(19%)	0.4
	Non Hispanic Black	5(16%)	16(28%)	
	Hispanic	11(37%)	13(23%)	
	Other	5(16%)	13(23%)	

Genotype Distribution -PDA

FGF10 SNPs	rs2973644β		rs900379β		rs1011814β	
	No PDA N=29	PDA N=49	No PDA N=31	PDA N=57	No PDA N=30	PDA N=56
Wild allele	9(31%)	7(14%)	15(48%)	26(45%)	10(33%)	25(45%)
Heterozygous	6(20%)	14(28%)	9(29%)	22(38%)	6(20%)	15(27%)
Minor allele	14(48%)	28(57%)	7(22%)	9(15%)	14(47%)	16(28%)
Any variant allele	20(68%)	42(85%)	16(51%)	31(53%)	20(67%)	31(55%)

α: p<0.05 β: NS

Genotype Distribution-BPD

FGF10 SNPs	rs2973644β		rs900379β		rs1011814β	
	BPD N=33	No BPD N=45	BPD N=38	No BPD N=53	BPD N=30	No BPD N=54
Wild allele	19(58%)	22(49%)	17(45%)	25(47%)	15(50%)	20(37%)
Heterozygous	7(21%)	14(31%)	12(31%)	20(37%)	7(24%)	15(28%)
Minor allele	7(21%)	9(20%)	9(24%)	8(15%)	8(26%)	19(35%)
Any variant allele	14(42%)	23(51%)	21(55%)	28(52%)	15(50%)	34(63%)

α: p<0.05 β: NS

Conclusions

- **Low birth weight and gestational age was associated with BPD**
- **FGF10 SNP ; rs2973644, rs900379, rs1011814 were not associated with PDA and or BPD.**
- **Other SNPS may be involved in the susceptibility of PDA or BPD**

References

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