Three-Dimensional Cardiac Reconstructions of GLP and G9a Mutants

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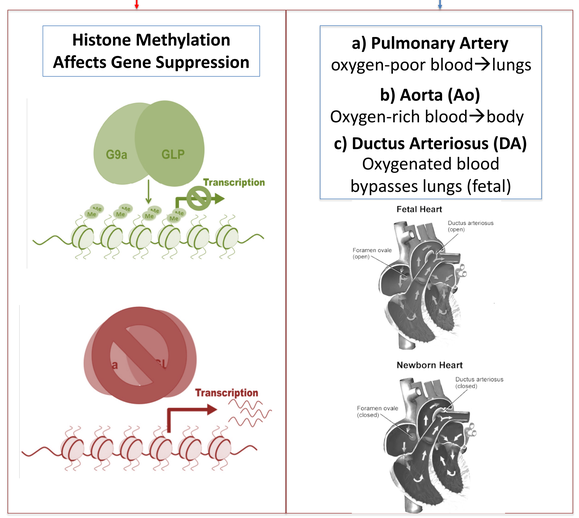
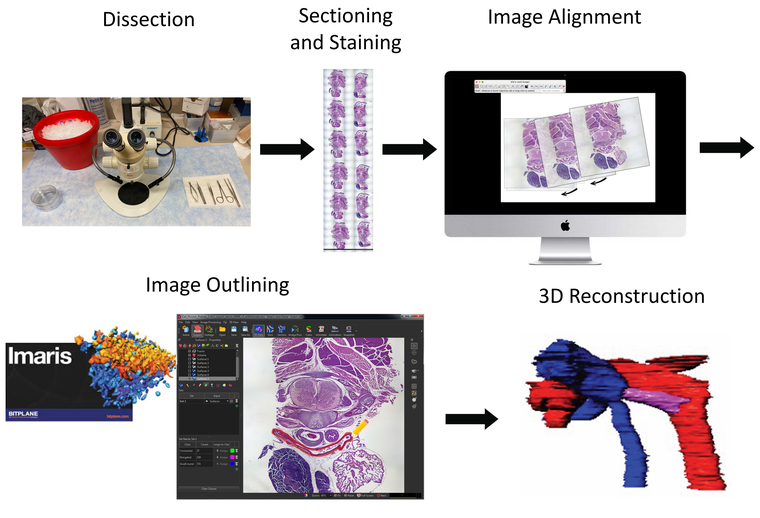
Introduction

GLP and G9a Mutations in Outflow Tracts



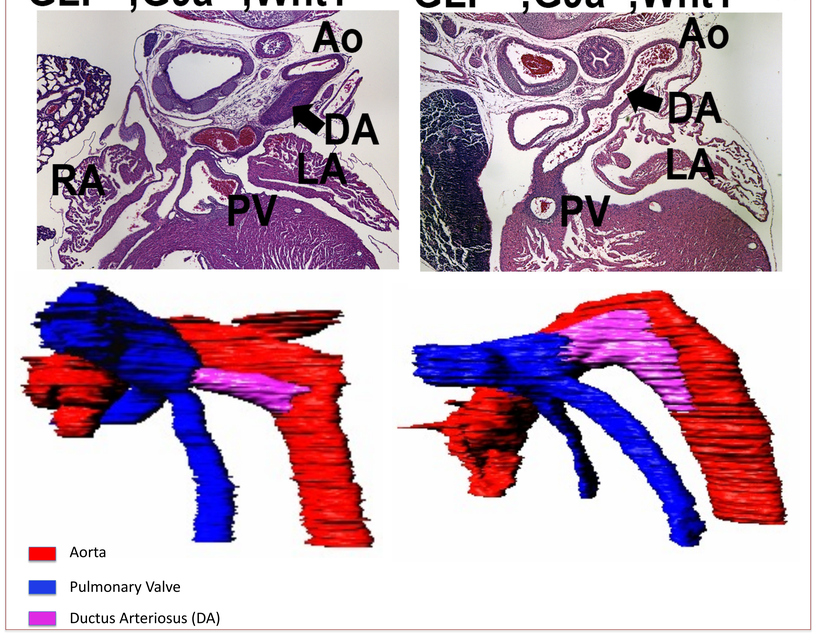
Reconstructing Neonate Outflow Tracts



GLP/G9a Mutants Have Patent Ductus Arteriosus (PDA)

Control $GLP^{f/f};G9a^{f/+};Wnt1^{Cre(-)}$

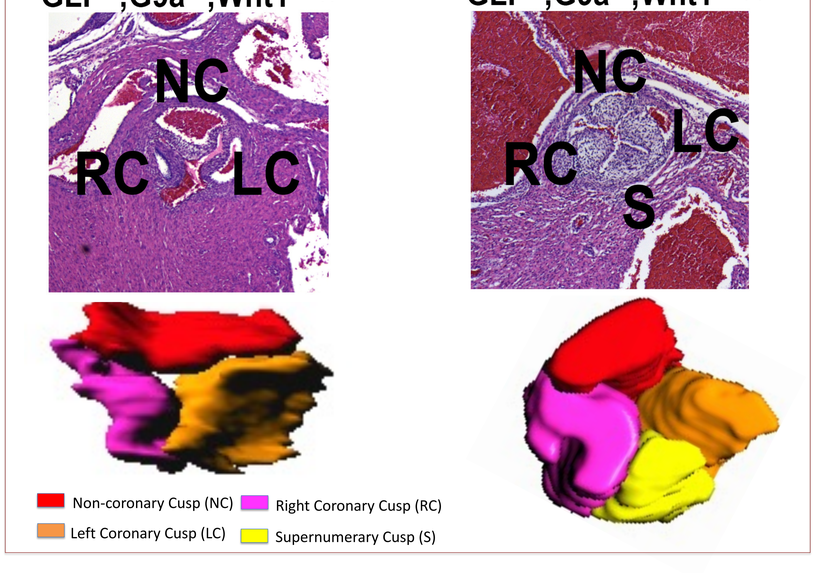
Mutant $GLP^{f/+};G9a^{f/f};Wnt1^{Cre(+)}$



GLP/G9a Mutants Have Abnormal Aortic Valves

Control $GLP^{f/f};G9a^{f/+};Wnt1^{Cre(-)}$

Mutant $GLP^{f/f};G9a^{f/+};Wnt1^{Cre(+)}$

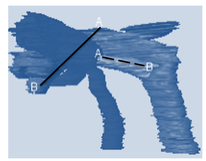


3Ds Allow For Quantitative Analysis

Volume (um^3)

Genotype	Aorta	Pulmonary	DA
$GLP^{f/f};G9a^{f/+};Wnt1^{Cre(-)}$	3.11E+06	2.03E+06	1.87E+05
$GLP^{f/+};G9a^{f/f};Wnt1^{Cre(+)}$	4.94E+06	1.71E+06	6.33E+05

Length (um)



Genotype	Aorta	DA
$GLP^{f/f};G9a^{f/+};Wnt1^{Cre(-)}$	345	154
$GLP^{f/+};G9a^{f/f};Wnt1^{Cre(+)}$	243	133

PDA Penetrance

PDA is a condition that occurs when the ductus arteriosus does not close post-birth; this causes inadequate oxygen supply in the blood running through the body.

Genotype	# with pDA	Total #	Penetrance
$Wnt1^{Cre(-)}$	0	10	0%
$GLP^{f/+};G9a^{f/+};Wnt1^{Cre(+)}$	0	2	0%
$GLP^{f/+};G9a^{f/f};Wnt1^{Cre(+)}$	3	3	100%
$GLP^{f/f};G9a^{f/+};Wnt1^{Cre(+)}$	3	4	75%
$GLP^{f/f};G9a^{f/f};Wnt1^{Cre(+)}$	4	5	80%

Conclusions

Though more analysis must be done, our studies show that GLP/G9a conditional neural crest mutants have a highly penetrant patent ductus arteriosus; measurements from 3D reconstructions show that DA of mutant mice have larger volumes than those of non-mutant mice; histological examination from which these models were derived demonstrate an open DA that did not close after birth in P0 neonate.

Acknowledgements

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