

Left Pulmonary Artery in 22q11 deletion syndrome: echocardiographic findings, role and expression of Tbx1 in human and knockout mice.

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Introduction and Hypothesis: Patients with 22q11 deletion syndrome (del22q11.DS) present typical patterns of cardiac defects, with a particular involvement on the ventricular outflow tract and pulmonary arteries (PAs). Mutation of Tbx1 gene is reported in more than 90% of them. We measured both PAs diameter in patients with and without del22q11.DS during routine echocardiographic evaluation. Our data were also compared to PAs measurement in Tbx1 mutant mice. Finally, a Cell Fate Mapping in Tbx1 was used to understand the expression of this gene mutation in the morphogenesis of PAs.

Methods: We evaluated 49 patients with del22q11.DS without cardiac defects. The control group consisted of 49 healthy patients, matched for age and sex. All patients underwent a complete transthoracic echocardiography. Subsequently, we crossed Tbx1^{+/-} mice and harvested fetuses, genotyped by PCR. We examined the cardiovascular phenotype of 8 wild type (WT), 37 heterozygous (Tbx1^{+/-}) and 6 null fetuses (Tbx1^{-/-}). Finally, we crossed Tbx1^{Cre/+} mice with Cre reporter mice R26^{RmT-mG} to reveal Cre recombinase activity. We studied the Fate Map of Tbx1 to evaluate the expression of this gene on the PAs.

Results: Ninety-eight percent of patients with del22q11 showed a smaller left PA (LPA) diameter compared to the right PA (RPA). Seventy-one percent of controls showed the diameter of the LPA smaller than that of the right one. The mean of the LPA/RPA ratio in del22q11 was 0.80 ± 0.12 vs 0.97 ± 0.08 in the controls with a significant p value ($p < 0.0001$).

In WT, heterozygous and null, the average of LPA/RPA ratio were 0.9, 0.77, 0.6, respectively. Finally we confirmed the expression of Tbx1 on the pulmonary trunk and particularly of the origin of LPA.
Conclusions. Patients with 22q11.DS without cardiac defects show smaller PA compared with healthy patients, and particularly if LPA was compared. The localization of the expression of Tbx1 on LPA, could explain these results considering its significant role on the PAs formation and growth.