

## Molecular signaling pathways in right heart failure of adult patients after tetralogy of Fallot repair

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### Introduction:

Right heart failure (RHF) secondary to pressure and/or volume-overload contributes to significant morbidity and mortality in the growing population of adult patients after tetralogy of Fallot (TOF) repair. The goal of this study was to describe signaling pathways contributing to right ventricular (RV) remodeling by analyzing longitudinal over lifetime alteration of RV gene expression in affected patients.

### Methods:

RV tissue was collected at the time of cardiac surgery in 13 patients with a diagnosis of TOF. RNA was isolated and whole transcriptome sequencing was performed. Gene profiles were compared between a group of 6 adults with signs of RHF undergoing RV-PA conduit surgery and a group of 7 infants undergoing elective TOF correction. Definition of RHF was based on clinical symptoms, such as fluid retention, dyspnea and/or arrhythmia, and evidence of RV hypertrophy, dilation, dysfunction or elevated pressure on echocardiographic, cardiovascular magnetic resonance, or catheterization evaluation.

### Results:

Median age was 34 years (range 30 – 62 years) in RHF patients and 5 months (range 4.8 – 5.8 months) in infants. Based on an adjusted p-value of less than 0.001, RNA sequencing of RV specimens identified a total of 1927 differentially expressed genes in adult patients with TOF and RHF as compared to infant patients with TOF and no RHF. Gene Ontology and Kyoto Encyclopedia of Genes (KEGG) databases highlighted pathways involved in cellular metabolism, cell-cell communication, cell cycling and cellular contractility to be dysregulated in adult patients with corrected TOF and chronic RHF. Relevant genes and pathways are depicted in the figure.

### Conclusions:

Right ventricular transcriptome profiling in adult patients with RHF after TOF repair allows identification of signaling pathways contributing to pathologic RV remodeling and helps in the discovery of biomarkers for disease progression and of new therapeutic targets.

### Figure:

