Appendix 2

Supplementary data to manuscript
"TBX4 mutations (Small Patella Syndrome) are associated with childhood-onset Pulmonary Arterial Hypertension " by Kerstjens-Frederikse W.S. et al.

Prediction of pathogenicity of missense mutations in *TBX4*

1. *childhood onset PAH patients*
Patient 6: c.1145A>C; p.Y382S
Highly conserved nucleotide (score 1.0, [0-1]), highly conserved amino acid (considering 11 species); Grantham distance 144; Polyphen score 0,531 (possibly damaging); SIFT score 0,00 (not tolerated). Mutation is not detected in 1000 control chromosomes. Conclusion: pathogenic

2. *adult onset PAH patients:*
Patient A1: c.229T>C, p.W77R highly conserved nucleotide (score 1.0, [0-1]); highly conserved amino acid (considering 11 species); Grantham distance 101; Polyphen score 1,00 (probably damaging); SIFT score 0,00 (not tolerated). Mutation is not detected in 1000 control chromosomes. Conclusion: probably disease causing.
Patient A2: c.104C>T, p.A35V: weakly conserved nucleotide (score 0.31, [0-1]); moderately conserved amino acid (considering 11 species); Grantham distance 64; Polyphen score 0,480 (possibly damaging); SIFT score 0,02 (not tolerated). The mutation is not detected in 1000 control chromosomes. Conclusion: unclassified variant
-SIFT algorithm (Sorting Intolerant From Tolerant) is available at http://sift.jcvi.org
-Polyphen-2 (Polymorphism Phenotyping program version 2 is available at http://genetics.bwh.harvard.edu/pph/