

## Transforming growth factor- $\beta$ 1 T869C gene polymorphism linked to a high serum protein level is associated with non-familial sick sinus syndrome

Jan-Yow Chen, MD, PhD<sup>1,2</sup>, Ying-Ming Liou, PhD<sup>2</sup>,  
Kuo-Hung Lin, MD<sup>1</sup>, Kuan-Cheng Chang, MD, PhD<sup>1</sup>

<sup>1</sup>Division of Cardiology, China Medical University and Hospital, Taichung, Taiwan

<sup>2</sup>Department of Life Sciences, National Chung Hsing University, Taichung, Taiwan

**INTRODUCTION:** Replacement of nodal tissue with fibrosis tissue is known as the pathologic finding of non-familial sick sinus syndrome (SSS). There is a close relationship between the transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) mediated cardiac fibrosis and the acquired arrhythmia. However, it remains to be determined if TGF- $\beta$ 1 involves in the pathogenesis of non-familial SSS.

**METHODS:** Non-familial SSS patients (N=110) and age-/gender-matched controls (N=137) were screened for TGF- $\beta$ 1 gene polymorphisms by gene sequencing method, followed by an association study. Enzyme-linked immunosorbent assay (ELISA) method was used to determine the serum level of TGF  $\beta$ 1 linked to TGF- $\beta$ 1 polymorphism.

**RESULTS:** Two polymorphic sites were identified at -509 and +869 in TGF- $\beta$ 1 gene. The association study further demonstrated that TGF- $\beta$ 1 T869C polymorphism is linked to non-familial SSS. The CC/CT genotype frequency of T869C was significantly higher in non-familial SSS patients than controls (OR = 2.09, 95% CI = 1.16-3.75, P = 0.01). Consistently, the level of serum TGF- $\beta$ 1 measured by ELISA was also significantly greater in the SSS group than in the control (5.3 $\pm$ 3.4 ng/ml vs. 3.7 $\pm$ 2.4 ng/ml, P = 0.01) in the randomly selective patients. In addition, the CC/CT genotypes showed a higher TGF  $\beta$ 1 serum level than the TT genotype (CC/CT vs. TT = 4.25  $\pm$  2.50 ng/ml vs. 2.71 $\pm$  1.76 ng/ml, P = 0.028) in the control group.

**CONCLUSION:** TGF- $\beta$ 1 T869C polymorphism linked to high serum TGF- $\beta$ 1 levels is associated with the susceptibility of non-familial SSS.