

**Transgenic overexpression of the  
secreted;extracellular EGF-CUB  
domain-containing protein SCUBE3 induces  
cardiac hypertrophy in mice**

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**摘要**

**Abstract**

**OBJECTIVE:** The aim of this study was to investigate in a transgenic animal model the cardiac expression and function of a novel extracellular protein SCUBE3 [signal peptide-CUB (complement proteins C1r/C1s, Uegf, and Bmp1)-EGF (epidermal growth factor)-like domain-containing protein 3]. **METHODS AND RESULTS:** Real-time quantitative reverse transcriptase (RT)-PCR analysis showed that SCUBE3 is expressed in the ventricular myocardium. Male transgenic (TG) mice overexpressing SCUBE3 appeared normal during development, from birth to adulthood. However, echocardiography and histopathological examination revealed significant cardiac hypertrophy in TG animals as they aged, at 8 months. Interestingly, left-ventricle hypertrophy occurred more rapidly and more severely under pressure overload in TG mice, as compared to age-matched wild-type littermates. Induced SCUBE3 expression, together with elevated transforming growth factor (TGF)-beta1 level under pressure overload, may account for the accelerated onset and progression of cardiac hypertrophy in TG mice. Furthermore, biochemical and molecular studies revealed that the carboxyl-terminal portion of SCUBE3 could physically interact with TGF-beta1 and promote the TGF-beta1-mediated transcriptional activation. **CONCLUSION:** This report is the first demonstration that SCUBE3 may play a role in the regulation of cardiac growth and remodeling responses, possibly through the stabilization of the TGF-beta1 signaling pathway.