Attenuation of cardiac hypertrophy by G-CSF is associated with enhanced migration of bone marrow-derived cells.

Granulocyte-colony stimulating factor (G-CSF) has been shown to promote mobilization of bone marrow-derived stem cells (BMCs) into the bloodstream associated with improved survival and cardiac function after myocardial infarction. Therefore, the aim of the present study was to investigate whether G-CSF is able to attenuate cardiac remodelling in a mouse model of pressure-induced LV hypertrophy focusing on mobilization and migration of BMCs. LV hypertrophy was induced by transverse aortic constriction (TAC) in C57BL/6J mice. Four weeks after TAC procedure, mice were treated with G-CSF (100 μg/kg/day; Amgen Biologicals) for 2 weeks. The number of migrated BMCs in the heart was analysed by flow cytometry. mRNA expression and protein level of different growth factors in the myocardium were investigated by RT-PCR and ELISA. Functional analyses assessed by echocardiography and immunohistochemical analysis were performed 8 weeks after TAC procedure. G-CSF-treated animals revealed enhanced homing of VLA-4(+) and c-kit(+) BMCs associated with increased mRNA expression and protein level of the corresponding homing factors Vascular cell adhesion protein 1 and Stem cell factor in the
hypertrophic myocardium. Functionally, G-CSF significantly preserved LV function after TAC procedure, which was associated with a significantly reduced area of fibrosis compared to control animals. Furthermore, G-CSF-treated animals revealed a significant improvement of survival after TAC procedure. In summary, G-CSF treatment preserves cardiac function and is able to diminish cardiac fibrosis after induction of LV hypertrophy associated with increased homing of VLA-4(+) and c-kit(+) BMCs and enhanced expression of their respective homing factors VCAM-1 and SCF.