Vein graft (VG) failure is associated with VG intimal hyperplasia, which is characterized by abnormal accumulation of vascular smooth muscle cells (SMCs). However, precise source of the neointimal SMCs and mechanism of the neointimal SMCs accumulation remain poorly understood. Herein we tracked down the fate of endothelial cells (ECs), vascular SMCs, and vascular stem cells (VSCs) expressing stem cell antigen 1 (SCA1) in VG remodeling and clarified their relative contributions to VG intimal hyperplasia. We demonstrated that after transplantation, most of the donor venous cells including ECs, SMCs, and VSCs die within 3 days, and the recipient arterial SCA1+VSCs are recruited to repopulate mainly the adventitia in VGs. The pre-existing mature SMCs, but not ECs, are the major cellular source of neointima cells. SCA1+VSCs do not differentiate into neointimal SMCs, but paracrine enforce media SMC dedifferentiation into neointimal SMCs. In addition, a unique subset of recipient adventitial SCA1+VSCs expressing cyclin-dependent kinase 8 (CDK8) is activated and migrates to the adventitia of VGs. Activation of CDK8 intensifies ISGylation in the SCA1+VSCs, which drives the VSC-mediated paracrine enforcement of SMC dedifferentiation, resulting in intimal hyperplasia toward VG failure. These findings uncover a novel intercellular communication between adventitial VSCs and medial SMCs in VG remodeling towards VG failure and CDK8 is a promising target for the treatment of VG failure.