The porcine reproductive and respiratory syndrome virus (PRRSV) is the cause of one of the most economically important diseases affecting swine worldwide. Efforts to develop a next-generation vaccine have largely focused on envelope glycoproteins to target virus-neutralizing antibody responses. However, these approaches have failed to demonstrate the necessary efficacy to progress toward market. T cells are crucial to the control of many viruses through cytolysis and cytokine secretion. Since control of PRRSV infection is not dependent on the development of neutralizing antibodies, it has been proposed that T cell-mediated immunity plays a key role. Therefore, we hypothesized that conserved T cell antigens represent prime candidates for the development a novel PRRS vaccine. Antigens were identified by screening a proteome-wide synthetic peptide library with T cells from cohorts of pigs rendered immune by experimental infections with a closely related (subtype 1) or divergent (subtype 3) PRRSV-1 strain. Dominant T cell IFN-gamma responses were directed against the non-structural protein 5 (NSP5), and to a lesser extent, the matrix (M) protein. The majority of NSP5-specific CD8 T cells and M-specific CD4 T cells expressed a putative effector memory phenotype and were polyfunctional as assessed by coexpression of TNF-alpha and mobilization of the cytotoxic degranulation marker CD107a. Both antigens were generally well conserved among strains of both PRRSV genotypes. Thus, M and NSP5 represent attractive vaccine candidate T cell antigens, which should be evaluated further in the context of PRRSV vaccine development.