Magnetic reconnection is a commonly known multi-scale plasma process that quickly converts magnetic energy into kinetic energy in bulk plasma flow, thermal and nonthermal particle distributions. An important problem that remains unsolved is the acceleration of nonthermal charged particles in the reconnection region. In particular, the large-scale theory and 3D extension of this problem are poorly known. To shed more lights to this problem, we utilize a number of tools to resolve this problem. Using LANL’s VPIC code, we study particle acceleration in magnetic reconnection via large-scale 3D kinetic simulations to examine several effects that may be important, including pre-existing fluctuations, kink and secondary tearing instabilities, and open boundary conditions. The results show that particle acceleration in reconnection layers is surprisingly robust despite the development of 3D turbulence and instabilities. Furthermore, the observed particle acceleration in the 3D simulations is sometimes more efficient than the corresponding 2D case, indicating viable new acceleration mechanisms. We then study the large-scale reconnection acceleration by solving the Parker's transport equation in a background reconnecting flow provided by MHD simulations. Due to the compression effect, the simulations suggest fast particle acceleration to high energies in the reconnection layer. This study clarifies the nature of particle acceleration in reconnection layer, and may be important to understand particle acceleration and plasma energization during solar flares and other astrophysical environments.