Age-related macular degeneration (AMD) is the leading cause of blindness among the elderly in developed countries. AMD is classified as either neovascular (NV-AMD) or non-neovascular (NNV-AMD). Cumulative damage to the retinal pigment epithelium, Bruch’s membrane, and choriocapillaris leads to dysfunction and loss of RPE cells. This causes degeneration of the overlying photoreceptors and consequential vision loss in advanced NNV-AMD (Geographic Atrophy). In NV-AMD, abnormal growth of capillaries under the retina and RPE, which leads to hemorrhage and fluid leakage, is the main cause of photoreceptor damage. Although a number of drugs (e.g., anti-VEGF) are in use for NV-AMD, there is currently no treatment for advanced NNV-AMD. However, replacing dead or dysfunctional RPE with healthy RPE has been shown to rescue dying photoreceptors and improve vision in animal models of retinal degeneration and possibly in AMD patients. Differentiation of RPE from human embryonic stem cells (hESC-RPE) and from induced pluripotent stem cells (iPSC-RPE) has created a potentially unlimited source for replacing dead or dying RPE. Such cells have been shown to incorporate into the degenerating retina and result in anatomic and functional improvement. However, major ethical, regulatory, safety, and technical challenges have yet to be overcome before stem cell-based therapies can be used in standard treatments. This review outlines the current knowledge surrounding the application of hESC-RPE and iPSC-RPE in AMD. Following an introduction on the pathogenesis and available treatments of AMD, methods to generate stem cell-derived RPE, immune reaction against such cells, and approaches to deliver desired cells into the eye will be explored along with broader issues of efficacy and safety. Lastly, strategies to improve these stem cell-based treatments will be discussed.