Effective transplantation of photoreceptors derived from three-dimensional cultures of embryonic stem cells

Summary
Irreversible blindness caused by loss of photoreceptors may be amenable to cell therapy. We have previously demonstrated retinal repair and restoration of vision through transplantation of photoreceptor precursors obtained from postnatal retinas into visually impaired adult mice. Considerable progress has been made in differentiating embryonic stem cells (ESCs) in vitro toward photoreceptor lineages. However, the capability of ESC-derived photoreceptors to integrate after transplantation has not been demonstrated unequivocally. In order to isolate photoreceptor precursors fit for transplantation, we have adapted a recently reported three-dimensional (3D) differentiation protocol that generates neuroretina from mouse ESCs. In this study we show that a pure Rhodopsin::GFP population of rod precursors can integrate within degenerate retinas of adult mice and mature into outer segment–bearing photoreceptors. Notably, ESC-derived precursors at a developmental stage similar to postnatal days 4–8 integrate more efficiently compared with photoreceptors at more mature stages. We show conclusively that ESCs can provide a source of photoreceptors for retinal cell transplantation.