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Identification of tumorigenic retinal stem-like cells in human solid retinoblastomas

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Retinoblastoma (RB) is the most common malignant tumor of the retina in human children. Although it has been hypothesized for a long time that RB derives from multipotent retinal stem cells (RSCs) or retinoblasts, the direct evidence that the presence of tumorigenic RSCs in RB tumors is still lacking. Some studies indicate that malignant tumors contain tumor stem cells similar to their normal tissue stem cell counterparts. With *in vitro* culture and differentiation method we demonstrate that tumorigenic retinal stem-like cells (RSLCs) indeed exist in RB lesions and that RB tumor-derived cultures encompass undifferentiated cells capable of extensive proliferation as clonal nonadherent neurospheres and can differentiate into different retinal cells *in vitro*. Interestingly, cultured cells expressed retinal development related genes including nestin, CD133, pax6, chx10 and Rx, and overexpressed Bmi-1, a gene required for self-renewal and proliferation of stem cells. Importantly, when these cultured cells were intraocularly transplanted into SCID mice, they gave rise to new tumors with histomorphological features and immunophenotypes similar to their parental primary RBs. The results show that RBs contain tumorigenic RSLCs that contribute to tumorigenesis. This study provides a new insight to investigate the histogenesis of RBs and establishes a model for other RB research.

***Keywords*:** retinoblastoma, tumor stem cell, retinal stem cell, tumorigenesis

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