IJO_746_22

Commentary: A short-term chick embryo *in vivo* xenograft model to study retinoblastoma cancer stem cells

This commentary builds upon the recent study of Nair *et al.*, 2022 entitled "A short-term chick embryo *in vivo* xenograft model to study retinoblastoma cancer stem cells" published in the Indian Journal of ophthalmology. The study describes an *in vivo* chick embryo-based xenograft model for the assessment of cancer stem cells (CSCs) in retinoblastoma. In this study, the authors have married the well-known and universally accepted chick embryo chorioallantoic membrane (CE-CAM) assay introduced by Auerbach *et al.*, 1974[1] with their previous knowledge and experience on properties of CSCs in retinoblastoma[2] to develop an *in vivo* xenograft model.

The authors have earlier demonstrated using flow cytometry-based study that the $FSC^{lo}/SSC^{lo}/CD133^{lo}$ subpopulations of Y79 retinoblastoma cells are the CSCs.[2] The authors also list the advantages of CE-CAM over the other transgenic and non-transgenic rodent models[3,4] in terms of short growth period, ease of manipulation and visualization, and also native immunodeficiency state, which makes it an ideal *in vivo* model for assessment. The authors have lucidly and elegantly carried out all the necessary experiments using gross morphological visualization, confocal/*in vivo* imaging techniques, and conventional histological techniques for demonstrating the usefulness of the CE-CAM assay in the assessment of metastasis in retinoblastoma. The use of imaging techniques for the assessment of tumor nodules and DiI-based spontaneous metastatic spread in the embryo need special mention. The assessment of the primary tumor in terms of the nodule and the metastasis by imaging correlates well with the histopathological findings validating the *in vivo* model.

The authors themselves have specified the limitations in the current study and scope for future studies in terms of re-evaluation of the incubation period of the slow-growing tumor cells, use of less-invasive cell lines such as WERI-Rb1, and use of a more stable cell tracker such as Green fluorescent protein (GFP) in place of less stable DiI and enhanced imaging methods for the assessment of whole egg with the shell.

Although the *in vivo* CE-CAM model has its own advantages compared to the current xenograft models of retinoblastoma, it may not be considered equivalent or less desirable to an orthotopic model,[5] which assesses the tumor in the native site and mimics the actual disease process in terms of primary tumor growth, metastatic activity, and response to therapeutics in countries with high economy.

Given the low resources and minimal access to transgenic and immunodeficient rodent models in several developing countries including India, this method of integrating CE-CAM assay with the magnetic assisted cell sorting/flow cytometry-based sorting of CSCs seem to be highly beneficial in the clinical setting for the assessment of patient-derived xenografts for screening existing as well as novel therapeutics.

Krishnakumar Subramanian

L&T Ocular Pathology, Vision Research Foundation, Chennai, Tamil Nadu, India

Correspondence to: Dr. Krishnakumar Subramanian, L&T Ocular Pathology Department, No 41, College Road, Nungambakkam, Chennai - 600 006, Tamil Nadu, India.
E-mail: drkk@snmail.org

References

1. Auerbach R, Kubai L, Knighton D, Folkman J. A simple procedure for the long-term cultivation of chicken embryos. Dev Biol 1974;41:391-4.
2. Nair RM, Balla MM, Khan I, Kalathur RK, Kondaiah P, Vemuganti GK. *In vitro* characterization of CD133lo cancer stem cells in Retinoblastoma Y79 cell line. BMC Cancer 2017;17:779.
3. Nair RM, Kaliki S, Vemuganti GK. Animal models in retinoblastoma research. Saudi J Ophthalmol 2013;27:141–6.
4. Nair RM, Vemuganti GK. Transgenic models in retinoblastoma research. Ocul Oncol Pathol 2015;1:207–13.
5. Cassoux N, Thuleau A, Assayag F, Aerts I, Decaudin D. Establishment of an orthotopic xenograft mice model of retinoblastoma suitable for preclinical testing. Ocul Oncol Pathol 2015;1:200-6.

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_746_22

Cite this article as: Subramanian K. Commentary: A short-term chick embryo *in vivo* xenograft model to study retinoblastoma cancer stem cells. Indian J Ophthalmol 2022;70:1712.