

Establishment of patient-derived xenografts of retinoblastoma and choroidal melanoma on the avian chorioallantoic membrane

Nimita Kant, Perumal Jayaraj¹, Seema Sen², Harshita Rupani³, Pranavi Kumar¹, Shefali Dahiya¹, Palak Chugh¹, Muskaan Gupta¹, Manisha Sengar³

Purpose: To develop a viable *in vivo* chorioallantoic membrane (CAM) model to study the growth and invasion of patient-derived retinoblastoma (RB) and choroidal melanoma (CM) xenografts (PDXs). The study utilizes primary tumor samples instead of cancer cell lines, which provides a more authentic representation of tumors due to conserved morphology and heterogeneity. **Methods:** Fertilized chicken eggs were procured, windowed, and their CAM layers were dropped. On embryonic development day (EDD) 10, freshly cut patient-derived CM and RB tumors were implanted on the CAM layer and the setup was incubated for 7 days. The tumor-embedded CAM layer was harvested on EDD 17, and the extracted tumor samples were subjected to hematoxylin and eosin staining and immunohistochemical analysis to evaluate the extent of tumor invasion. **Results:** Significant changes in the vascularity around the RB and CM PDXs were observed, indicating an angiogenic environment. The cross-sectional histological view of the tumor implant site revealed the invasion of both the tumors into the CAM mesoderm. Invasion of CM into CAM mesoderm was visualized in the form of pigmented nodules, and that of RB was indicated by synaptophysin and Ki-67 positivity in Immunohistochemistry (IHC). **Conclusion:** The CAM xenograft model was successfully able to support the growth of CM and RB PDXs and their invasion in CAM, thus presenting as a feasible alternative to mammalian models for studying tumorigenicity and invasiveness of ocular tumors. Moreover, this model can further be utilized to develop personalized medicine by inoculating patient-specific tumors for preclinical drug screening.

Key words: CAM, chicken, chorioallantoic membrane, choroidal melanoma, eye cancer, ocular cancer, patient-derived xenograft, retinoblastoma, uveal melanoma

Uveal melanoma (UM), arising from the melanocytes of the uveal tract, is the most common cause of primary malignant intraocular neoplasm in the western world.^[1] It originates from iris (4%), ciliary body (6%), or choroid (85–90%), the latter being the most prevalent form.^[2] UM is characteristically distinct from cutaneous melanoma which originates from the melanocytes confined within the basal layer of the epidermis.^[3] Prognosis and metastasis of all UMs are majorly affected by mutations in *GNAQ* and *GNA11* genes.^[4] Nearly 50% of the afflicted individuals succumb to metastasis within 10 years of diagnosis.^[5]

Choroidal melanoma (CM) accounts for more than 70% cases of UM, rendering it the second most predominant form of malignant tumors. Despite the advancement in therapeutics, the median survival of patients with CM is less than a year.^[6] Its common metastatic sites are the liver (90%), lungs (24%), and

bones (16%) owing to its heterogeneous spread.^[1] Depending on the extent of tumor growth, its treatment could vary from brachytherapy, endoresection, exoresection to the complete removal of the eyeball.^[6,7] High metastatic potential and low survival incidence of CM make it more pertinent to oncology research.

Among children, retinoblastoma (RB) is the most widespread intraocular tumor, arising in both heritable and nonheritable forms, accounting for approximately 8000 cases annually.^[8,9] It is caused by a mutation in both RB1 alleles in a retinal cell; early lesions of RB are found in the inner nuclear layer of the retina.^[10,11] Like UM, it is also metastatic in nature and if left untreated, it is highly likely to spread outside the eye and invade the central nervous system via the optic nerve. Through metastases in the bloodstream, it can also spread in regional lymph nodes, bones, lungs, and liver, making it very important to study its characteristics.^[12,13]

Access this article online

Website:
www.ijo.in
DOI:
10.4103/ijo.IJO_1494_22

Quick Response Code:



P. Jayaraj

Department of Zoology, Shivaji College, University of Delhi, New Delhi, ¹Department of Zoology, Sri Venkateswara College, University of Delhi, Delhi, ²Department of Ocular Pathology, Dr. Rajendra Prasad Centre for Ophthalmic Science, All India Institute of Medical Science, New Delhi, ³Department of Zoology, Deshbandhu College, University of Delhi, New Delhi, India

Correspondence to: Dr. Perumal Jayaraj, Department of Zoology, Sri Venkateswara College (University of Delhi), Benito Juarez Road, Dhaula Kuan, Delhi, India. E-mail: jay.aiims@gmail.com

Received: 23-Jun-2022

Revision: 22-Nov-2022

Accepted: 12-Dec-2022

Published: 03-Mar-2023

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Cite this article as: Kant N, Jayaraj P, Sen S, Rupani H, Kumar P, Dahiya S, et al. Establishment of patient-derived xenografts of retinoblastoma and choroidal melanoma on the avian chorioallantoic membrane. Indian J Ophthalmol 2023;71:977-82.