Retinoic Acid- and Retinol Binding Proteins in Melanomas and Retinoblastomas

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Key Words

Retinoic acid-binding protein
Retinol-binding protein
Melanoma
Retinoblastoma
Retinoids

Abstract

Cellular retinoic acid-binding proteins (CRABP) and cellular retinol-binding protein (CRBP) can be found in cells and nuclei. They function in the same way as receptors. CRABP and CRBP were studied in 9 cases of choroidal melanoma and in 3 of retinoblastoma. CRABP was found in 2 cases of melanoma and in 3 cases of retinoblastoma. CRBP was found in 1 melanoma.

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Introduction Materials and Methods

Intracellular retinoic acid (CRABP)- and retinol-binding proteins (CRBP) have been demonstrated in normal and pathological tissues. These binding proteins display the characteristics of receptors with high binding affinity and specificity, but limited capacity. Retinoic acid affects cellular differentiation, especially of epithelial cells, and vitamin A plays a well-defined role in the physiology of vision [1]. Vitamin A acid has also been shown to have antineoplastic activity, the absence of which could result in the development of tumors. Retinoids are retinoic acid derivatives and have been successfully used in the treatment of skin disorders, precancerous states, and malignant tumors [2, 3]. In this study we investigated CRABP and CRBP in melanomas and retinoblastomas.

The enucleated eye was opened immediately after surgical removal, the retina was dissected away, and a portion of the tumor was stored in liquid nitrogen. The eyeball containing the remaining portion of the tumor was fixed in formalin for subsequent histological examination. CRABP and CRBP determinations were performed by sucrose gradient centrifugation. Briefly, the tumor was homogenized and centrifuged at 130,000 g for 30 min. The resulting cytosol was incubated for 5 h at 4 °C with 3H-retinoic acid, layered on a 5–20% sucrose gradient, and centrifuged at 224,000 g for 15 h at 4 °C.

Radioactivity sedimenting in the 2 S region of the sucrose gradients was interpreted as 3H-retinoic acid binding protein complex [3]. Nine melanomas of the choroid membrane and three retinoblastomas were analyzed for the presence of CRABP and CRBP.

Results

The results are shown in tables I and II. Table I shows the concentrations of CRABP Retinoic Acid- and Retinol Binding Proteins in Melanomas and Retinoblastomas

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Table I. Concentrations of CRABP and CRBP in malignant melanomas (pmol/mg)

and CRBP in nine malignant melanomas of the choroid. In 2 cases the CRABP was positive, 1 of them also displayed CRBP. Table II shows that all retinoblastomas contained retinoic acid binding sites. CRABP was 54 pmol (mg protein)⁻¹ in the first case, and detectable in the other cases, but a laboratory error precluded quantitation.

Discussion

It is assumed that the CRABP complex is translocated into the cell nucleus and interacts specifically with the DNA resulting in gene expression followed by RNA and protein synthesis. Retinoic acid plays a significant role in growth regulation and cellular differentiation [1]. Probably the expression of CRABP and CRBP is a sign of differentiation [4]. CRABP can also bind the retinoic acid derived compounds known as retinoids. Several groups of investigators have found that retinoids inhibit the growth of melanomas and retinoblastomas in cell culture [5, 6]. We therefore believe that in the two melanomas and in the three retinoblastomas, where we found the binding protein for retinoic acid, retinoids could play a therapeutic role in the case of relapse.

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