Distribution of Glucocorticoid and Mineralocorticoid Receptors and 11β-Hydroxysteroid Dehydrogenases in Human and Rat Ocular Tissues

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Purpose. The administration of glucocorticoids as topical or systemic medications may lead to the development of ocular hypertension through the induction of morphologic and biochemical changes in the trabecular meshwork leading to a reduction in the facility of aqueous outflow. Glucocorticoids exert their physiological effects by binding to and activating glucocorticoid and mineralocorticoid receptors. The activity of glucocorticoids is critically regulated at a prereceptor level by the two isozymes of 11β-hydroxysteroid dehydrogenase. The purpose of this study was to determine the distribution of glucocorticoid target receptors and the isozymes of 11β-hydroxysteroid dehydrogenase (11 β-HSD) that regulate the activity of glucocorticoids at a prereceptor level in human and rat ocular tissues.

Methods. Horizontal sections of normal adult human and rat eyes were cut and hybridized with 35S-labeled cRNA probes specific for the glucocorticoid receptor, mineralocorticoid receptor, and 11β-HSD types 1 and 2 using in situ hybridization. Immunohistochemical analysis of glucocorticoid and mineralocorticoid receptors using monoclonal antibodies was carried out on rat eye tissue sections. Whole rat eyes were homogenized and the activity of 11β-HSD types 1 and 2 in the eye assessed as the percentage conversion of tritiated corticosterone to tritiated 11-dehydrocortico-

sterone when corticosterone was added to the homogenate.

Results. In the rat ocular tissues mRNAs encoding glucocorticoid receptor, mineralocorticoid receptor, and 11β-HSD types 1 and 2 were detected in nonpigmented ciliary epithelium, trabecular meshwork, corneal epithelium and endothelium, and anterior lens epithelium. Immunohistochemistry confirmed the presence of glucocorticoid and mineralocorticoid receptors at these sites. Activity of both isozymes of 11β-HSD was demonstrated in homogenized rat eyes (percentage conversion of tritiated corticosterone to 11-dehydrocorticosterone; mean ± SD, 11β-HSD 1 = 15% ± 5.3%, 11β-HSD 2 = 7.9% ± 2.8%). In both human and rat eyes, expression of mRNAs encoding glucocorticoid receptor and 11β-HSD type 1 was high in the trabecular meshwork and lens epithelium, whereas expression of mRNAs encoding the mineralocorticoid receptor and 11β-HSD type 2 was high in nonpigmented ciliary epithelium and corneal epithelium and endothelium.

Conclusions. Glucocorticoid target receptors and the enzymes regulating glucocorticoid activity at these receptors are present in mammalian ocular tissues, which regulate aqueous humor formation and outflow. Alteration in the number or affinity of receptors or in the activity of regulatory enzymes may alter the susceptibility of certain individuals to the effects of glucocorticoids on intraocular pressure. (Invest Ophthalmol Vis Sci. 2000;41:1629–1638)

Topical or systemic administration of glucocorticoids (GCs) produces a rise in intraocular pressure in a proportion of the normal population1 by decreasing the facility of aqueous outflow.2 If this pressure rise is sustained it may result in optic disc cupping and visual field loss similar to that seen in primary open-angle glaucoma (POAG). Glucocorticoids may cause a reduction in aqueous outflow through the many cellular and morphologic changes that they induce in trabecular meshwork (TM) cells. These changes include alterations in extracellular matrix production,3–6 cell size,7–9 nuclear size7 and DNA content,7 cytoskeletal organization,8,9 phagocytic activity,10 and protease activity.11 In addition, dexamethasone has been shown to alter Na–K–Cl cotransport,12 an effect that, by altering TM cell volume, may affect the facility of aqueous outflow in intact TM. Glucocorticoid responsiveness occurs with a far higher prevalence among POAG patients than among normal subjects, with over 90% of POAG patients being considered GC responders,13 compared with 30% to 35% of...
the normal population. Steroid responders have been reported to be at increased risk of developing POAG compared with nonresponders,14 and there are numerous reports of raised intraocular pressure in patients with Cushing’s syndrome,15 a collection of clinical signs and symptoms caused by chronically elevated levels of endogenous GCs.

Electron microscopic studies comparing postmortem eyes of POAG and GC-induced glaucoma cases have reported similar but not identical morphologic changes in the TM16 (increased accumulation of extracellular material). POAG specimens typically show so-called sheath-derived plaques in the cribriform layer of the TM and beneath the inner wall endothelium of Schlemm’s canal.17 Specimens from cases of corticosteroid glaucoma typically show accumulation of a fingerprint-like-arranged basement membrane material in the cribriform and outer corneoscleral regions and also a fine fibrillar material beneath the inner wall endothelium of Schlemm’s canal.16

Glucocorticoids exert their effects by binding to intracellular receptors of two types, glucocorticoid (GR) and mineralocorticoid (MR) receptors. The ligand-receptor complex then migrates to the nucleus and binds to specific DNA sequences called glucocorticoid response elements (GRE), altering the transcription of target genes.18 This, in turn, leads to altered synthesis of proteins. Glucocorticoid receptors have previously been demonstrated in human TM,19 whereas MRs have been shown to be present in rabbit,20 bovine,21 and human22,23 ocular tissues. In addition Starka et al. have previously demonstrated effects of cortisol and aldosterone on ionic composition of the lens and aqueous humor.24 Recently, an additional level of control of GC action has been identified. The isozymes of 11β-hydroxysteroid dehydrogenase (11β-HSD) act as important regulators of GC activity at a prereceptor level.25–27 These isozymes catalyze the interconversion of cortisol, the major glucocorticoid in the human, to its inactive metabolite cortisone (corticosterone to 11-dehydrocorticosterone in the rat). In vivo, the type 1 isozyme participates as a reductase, converting inert cortisone to active cortisol, thereby increasing the access of cortisol to GR.25 The type 2 isozyme acts primarily as a high affinity dehydrogenase in vivo, converting active cortisol to inactive cortisone and thereby conferring aldosterone specificity on intrinsically noneffective MRs in aldosterone target tissues such as the distal nephron of the kidney.26,27 Deficiency of 11β-HSD type 2 results in the syndrome of apparent mineralocorticoid excess (SAME)28,29 in which cortisol illicitly activates MRs, causing sodium retention, systemic hypertension, and hypokalemia. These processes may also occur in other salt-transporting epithelia. We investigated, using in situ hybridization and immunohistochemistry, the distribution of GR and MR and 11β-HSD types 1 and 2 in human and rat ocular tissues. We also investigated the activity of 11β-HSD types 1 and 2 in homogenized rat ocular tissues using enzyme activity assays.

METHODS

Riboprobes

Rat cDNA clones for GRs,30 MRs,31 and 11β-HSD type 132 and type 233 were linearized using the appropriate restriction enzyme. Antisense and sense complementary RNA probes were synthesized from the resulting templates using the appropriate RNA polymerases and [α-35S]UTP (>1000 Ci/mM; Amersham Life Science, Little Chalfont, Buckinghamshire, UK). Human cDNA clones for GR,34 MR,35 11β-HSD type 135 and type 236 were linearized using the appropriate restriction enzymes. Antisense and sense complementary RNA probes were synthesized from the resultant templates using the appropriate RNA polymerases. Probes were purified on Nick columns (Pharmacia Biotech, Uppsala, Sweden) and checked for size and purity on denaturing polyacrylamide gels.

In Situ Hybridization

All procedures used in these studies followed the tenets of the Declaration of Helsinki and the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Informed consent was obtained before obtaining human tissue samples. Full ethical approval was granted for all portions of this study by the Lothian Health Research Ethics subcommittee and by the Western General Hospital NHS Trust Research and Development Ethics Committee. Rat eyes were obtained from healthy adult male Lister-Hooded rats and paraffin-embedded. Human eyes (obtained from Glaucoma Research Foundation, San Francisco, CA, and the Queen Victoria Hospital, East Grinstead West Sussex, UK) were cut in lateral and medial parasagittal.
planes, and sections were paraffin-embedded. Horizontal sections (5-μm thick) were cut using a microtome (Leitz GmbH, Wetzlar, Germany) and sections placed on 3-aminopropyltriethoxysilane (APES 2%; Sigma, St. Louis, MO)–coated slides. Sections were deparaffinized by immersion in histoclear (2 × 10 mins; Fisher Scientific, Loughborough, Leicestershire, UK).

Histoclear was removed by washing in ethanol (100% × 2 minutes; Merck, Poole, UK). Sections were rehydrated by immersion in graded alcohols (100%, 100%, 95%, 85%, 70%, 50%, 50% ethanol). Ethanol was removed by washing in sodium chloride (0.9%). This was followed by immersion in Triton-X (0.3%; Koch Light, Suffolk, UK) in 1× phosphate-buffered saline (1× PBS for 15 minutes) after which sections were washed twice in 1× PBS (5 minutes). Tissue sections were then digested in trizma–HCl (100 mM, pH 8; Sigma), EDTA (50 mM; Sigma) containing proteinase K (30 minutes, 37°C; Sigma), then washed in glycine (0.1%; Merck) in 1× PBS. Sections were then postfixed in paraformaldehyde (4%; Fisher Scientific), washed in 1× PBS (2 × 5 minutes) followed by acetylation in acetic anhydride (0.25%; Sigma) in triethanolamine (0.1 M, pH 8; Sigma), washed in 1× PBS (1 × 3 minutes), dehydrated in graded alcohols, and air-dried. Sections were incubated with prehybridization buffer made up of diethylpyrocarbonate water, sodium chloride (5 M), trizma base (1 M), 50 mM sodium phosphate–3 M, trizma base (1 M), 50 mM sodium chloride (37°C; Sigma), then washed in glycine (0.1% Merck) in 1× PBS. Sections were then digested in trizma–HCl (100 mM, pH 8; Sigma), EDTA (50 mM; Sigma) containing proteinase K (30 minutes, 37°C; Sigma), then washed in glycine (0.1% Merck) in 1× PBS. Sections were then postfixed in paraformaldehyde (4%; Fisher Scientific), washed in 1× PBS (2 × 5 minutes) followed by acetylation in acetic anhydride (0.25%; Sigma) in triethanolamine (0.1 M, pH 8; Sigma), washed in 1× PBS (1 × 3 minutes), dehydrated in graded alcohols, and air-dried. Sections were then washed in prehybridization buffer made up of diethylpyrocarbonate water, sodium chloride (5 M), trizma base (1 M), 50 mM Denhardt’s (Sigma), salmon testes DNA (Sigma), EDTA (250 mM; Sigma), and yeast tRNA (GIBCO–BRL Products, Paisley, UK) in deionized formamide (50°C × 2 hours; Sigma). Hybridization was carried out by incubation with 35S-labeled riboprobe (1 × 106 cpm) in hybridization buffer containing diethylpyrocarbonate water, sodium chloride (5 M), trizma base (1 M), 50 mM Denhardt’s, salmon testes DNA, EDTA (250 mM; Sigma), and yeast tRNA in deionized formamide (50°C × 16 hours). After hybridization, sections were washed in SSC (15 minutes) and incubated with RNase A (100 μg/ml, 37°C for 1 hour; Sigma). Sections were then washed to increasing stringencies to a maximum of 0.1× SSC (60°C for 1 hour). After dehyration through graded alcohols, sections were placed against hypervilfilm βmax (2 weeks at 4°C; Amersham) and autoradiographs developed. After this, sections were dipped in photographic emulsion (NTB-2; Kodak, Rochester, NY) and exposed (4°C for 3 weeks) before being developed and counterstained with hematoxylin and eosin (Sigma).

Areas of specific mRNA expression on tissue sections were identified by the appearance of silver grains. Grain counting (SEE-Scan Image Analysis Systems UK) was performed on antisense and corresponding sense sections. Background counts (counts from sense sections) were subtracted from antisense counts and results expressed as multiples of background. Positive control sections were used as follows: rat hippocampus (GR, MR and 11β-HSD type 1), rat kidney (11β-HSD type 2), human cerebellum (GR), human liver (11β-HSD type 1), and human kidney (MR and 11β-HSD type 2).

**Immunohistochemistry**

Whole rat eyes were removed and placed in a 10% solution of formaldehyde in phosphate buffer (pH 7) for 48 hours. Eyes were then processed through graded alcohols (70%, 80%, 100% × 3; 90 minutes each) and xylene (2 × 90 minutes; Merck Ltd.) and embedded in paraffin wax. Tissue sections (5-μm thick) were cut by microtome (Leitz) and placed onto APES-coated tissue slides. Slide sections were deparaffinized using xylene, which was removed by immersing sections in absolute ethanol. Sections were rehydrated by immersion in ethanol (70%) followed by water. Slides were then immersed in hydrogen peroxide (3%; AAH Pharmaceuticals, Huddersfield, UK) to block endogenous peroxidase and washed in water.

Endogenous biotin was blocked using a biotin blocking kit (Vector Laboratories, Burlingame, CA). Monoclonal antibodies, Mab-7 (1/1000) against GR (provided courtesy of Kjel Fuxe, Karolinska Institute, Sweden) and MR-4 (1/1000) against MR (provided courtesy of Zygmunt S. Krozowski, Baker Medical Institute, Prahan, Victoria, Australia), were applied to tissue sections and unbound antibody removed by washing with PBS (0.05 M). Sections were next treated with biotin-labeled secondary goat antibody, with unbound antibody again being removed by washing in PBS (0.05 M; 30 minutes at 22°C). A streptavidin/biotinylated peroxidase complex (DAKO Ltd., Cambridge, UK) was added as a tertiary agent and bound to biotin on the secondary antibody. Unbound avidin was removed by washing in PBS (0.05 M). Hydrogen peroxide (3%) was added to the sections along with the potential dye diaminobenzidine (DAB; Sigma). Tissue sections were counterstained using Mayer’s hematoxylin. Sections were then dehydrated by immersion in graded ethanol (70%, 80%, 100%) and finally immersed in xylene and coverslipped using DPX mountant.

**Figure 2.** Human in situ hybridization studies for MR and 11β-HSD type 2. Silver grains denote areas of mRNA expression. (A) Mineralocorticoid receptor antisense corneal epithelium. (B) Mineralocorticoid receptor sense corneal epithelium (C) Mineralocorticoid receptor antisense ciliary epithelium. (D) Mineralocorticoid receptor antisense lens epithelium. (E) 11β-HSD type 2 antisense corneal epithelium. (F) 11β-HSD type 2 sense corneal epithelium. (G) 11β-HSD type 2 antisense ciliary epithelium. (H) 11β-HSD type 2 antisense TM. LE, lens epithelium; CE, corneal epithelium; SC, Schlemm’s canal; NPE, nonpigmented ciliary epithelium; PE, pigmented ciliary epithelium. Magnification, (A, C through H) ×40; (B) ×100, oil.

**Figure 3.** Rat immunohistochemistry for GR and MR. (A) Glucocorticoid receptor ciliary process. (B) Glucocorticoid receptor, ciliary process, negative control. (C) Glucocorticoid receptor drainage angle. (D) Glucocorticoid receptor drainage angle, negative control. (E) Mineralocorticoid receptor lens epithelium. (F) Mineralocorticoid receptor lens epithelium, negative control. (G) Glucocorticoid receptor lens epithelium. (H) Glucocorticoid receptor lens epithelium, negative control. LE, lens epithelium; SC, Schlemm’s canal; NPE, non-pigmented ciliary epithelium; CP, ciliary process. Arrowsheads point to specific GR and MR staining. Magnification, ×40. (Figure 3 appears on page 1634.)
FIGURE 3.
Enzyme Activity Assay

The activity of 11β-HSD types 1 and 2 was investigated by measuring the ability of homogenized rat eyes to convert tritiated corticosterone to tritiated 11-dehydrocorticosterone in the presence of the essential cofactors NADP and NAD\(^+\) for 11β-HSD types 1 and 2, respectively. Pooled tissues from 10 rat eyes were homogenized in Krebs’ buffer (250 μl; without bovine serum albumin [BSA]) in 3 × 10 second bursts in an Ystral Homogenizer (Scientific Instrument Center, Liverpool, UK) and assayed for protein colorimetrically (Biorad Laboratories, Hemel Hempstead, Herts, UK) using the Lowry method.\(^{39,40}\) Incubations were performed in triplicate at 37°C in 250 μl containing 1.12 \(×\) 10\(^{-8}\) M [1,2,6,7-\(^3\)H\(_4\)]-corticosterone (Amersham Life Science; 84 Ci/mM), ethanol 1% vol/vol, BSA 0.2 g/dl, and tissue homogenate at 500 μg protein/ml and in the presence or absence of NAD\(^+\) or NADP\(^+\) (2 mM; Sigma). The protein concentration was chosen to be in the linear part of the relationship before the assessment of enzyme activity. Separation was achieved using a C\(_{18}\) Microbondapak Column (30 cm; Millipore Waters, Watford, UK), using a mobile phase of methanol:water (65:35) at a flow rate of 3.9 ml/min. Radio-detection was carried out by online liquid scintillation counting (Optiflow, 3.5 ml/min; Berthold, Berlin, Germany) and results presented as percentage of 11-dehydrocorticosterone to total of 11-dehydrocorticosterone and corticosterone. Incubations were also carried out in the absence of protein and cofactor to allow the subtraction of conversion under these conditions.

RESULTS

Human Eyes

The results of studies on human eyes are shown in Table 1 and Figures 1 and 2. In human eyes the expression of GR mRNA (Fig. 1) was present in nonpigmented ciliary epithelium, TM, lens epithelium, corneal epithelium, and corneal endothelium. Expression was highest in lens epithelium, TM, and nonpigmented ciliary epithelium. Glucocorticoid receptor mRNA was also noted to a lesser extent in corneal epithelium and endothelium. Expression of MR mRNA (Fig. 2) was highest in nonpigmented ciliary epithelium, corneal endothelium, and corneal epithelium. Expression was also found, although to a lesser extent, in lens epithelium and TM. 11β-HSD type 1 mRNA was expressed mainly in TM, lens epithelium, and in nonpigmented ciliary epithelium (Fig. 1). Expression was also detected in corneal epithelium and endothelium. 11β-HSD type 2 mRNA (Fig. 2) was expressed most highly in nonpigmented ciliary epithelium and in corneal epithelium. Expression was also present in corneal endothelium, TM, and lens epithelium. Control sections showed positive expression of MR and 11β-HSD type 2 (kidney), GR (cerebellum), and 11β-HSD type 1 (liver). In human eyes, mRNA expression for GR, MR, and 11β-HSDs was not detected in iris stroma, corneal stroma, or sclera.

Rat Eyes

Immunohistochemistry. Immunohistochemical studies on rat eye sections confirmed the presence of the protein product of GR- and MR-specific mRNAs in lens epithelium, nonpigmented ciliary epithelium, and TM (Fig. 3). Mineralocorticoid receptor was expressed to a lesser extent than GR in keeping with the findings of in situ hybridization.

Enzyme Activity Assay. Activity of 11β-HSD types 1 and 2 was confirmed in homogenized rat eyes. Activity was expressed as percentage conversion of tritiated corticosterone to tritiated 11-dehydrocorticosterone (Fig. 4).

In Situ Hybridization. The results of studies on rat eyes are shown in Table 2 and Figure 5. In rat eyes, the expression of mRNAs encoding GR, MR, and 11β-HSD types 1 and 2 was present in the lens, nonpigmented ciliary epithelium, and TM. Glucocorticoid receptor mRNA was expressed highly in cells of the TM, anterior lens epithelium, corneal epithelium, and nonpigmented ciliary epithelium. Mineralocorticoid receptor mRNA was expressed less highly than GR, and expression was highest in nonpigmented ciliary epithelium, corneal epithelium, and corneal endothelium. Expression of 11β-HSD type 1 mRNA was also lower than GR and was most noticeable in anterior lens epithelium, corneal endothelium, and tissues of the TM. 11β-HSD type 2 mRNA was expressed to a lesser extent.
extent than the type 1 isozyme, and expression was greatest in corneal endothelium, nonpigmented ciliary epithelium, and TM (Table 2). Expression of mRNAs for GR, MR, and 11β-HSDs was not detected in iris stroma, corneal stroma, ciliary muscle, or sclera.

DISCUSSION

This study investigated the distribution of glucocorticoid target receptors (GR and MR) and enzymes, which regulate glucocorticoid hormone activity at these receptors (11β-HSD types 1 and 2) in human and rat ocular tissues. In this study we demonstrated expression of GR, MR, and 11β-HSD types 1 and 2 in lens, TM, ciliary epithelium, and corneal epithelium and endothelium. The pattern of mRNA expression was similar in human and rat ocular tissues. We also noted that MR and 11β-HSD type 2 mRNA expression colocalized in nonpigmented ciliary epithelium and cornea, whereas GR mRNA expression colocalized with that of 11β-HSD type 1 in lens and TM. We have therefore demonstrated glucocorticoid target receptors (GR and MR) and regulatory enzymes (11β-HSD types 1 and 2) at sites in ocular tissues responsible for both the secretion and outflow of aqueous humor. This suggests that these tissues may be potential sites of action for steroid hormones with glucocorticoid and mineralocorticoid activity. Previous work by Weinreb and coauthors demonstrated the presence of functional GRs in cultured human TM cells. We have now demonstrated the presence of GR in lens epithelium and in nonpigmented ciliary epithelium in addition to TM of human and rat eyes. These findings are of interest given the well-documented effects of glucocorticoids on intraocular pressure and their ability to induce cataract. The access of GCs to GR in the brain and liver is regulated by the action of 11β-HSD type 1. We have now shown 11β-HSD type 1 mRNA to be present in cornea, nonpigmented ciliary epithelium, ciliary muscle, lens, and TM of human and rat eyes. This colocalization of GR and 11β-HSD type 1 suggests that the ocular tissue is another site in the body that has the capacity to regulate the activity of GCs at a prereceptor level and corresponds with previous observations suggesting a functional relationship between GR and 11β-HSD type 1 in brain and kidney. Hormones possessing mineralocorticoid activity act through MR to influence ion and fluid transport mechanisms in many cell types. Ion and fluid transport mechanisms play an important role in several key processes in the eye, including secretion of aqueous humor and maintenance of corneal transparency. Previous immunohistochemical studies have demonstrated the presence of MR in ocular tissues, including ciliary epithelium, cornea, and lens. Further studies by Schwartz and Wysocki and Starka et al. have identified aldosterone binding sites in mammalian ocular tissues, including nonpigmented ciliary epithelium and lens. Starka et al. also demonstrated the ability of aldosterone to alter the ionic composition of the lens and aqueous humor. In addition our studies have demonstrated the presence of MR in the TM and cornea of rat and human eyes. Mineralocorticoid receptor has been shown to bind both cortisol and aldosterone. In the distal nephron, in vivo, the presence of 11β-HSD type 2 ensures aldosterone-selective access to nonspecific MR. 11β-HSD type 2 has not been reported previously in the eye. We have demonstrated this isozyme in cornea, nonpigmented ciliary epithelium, lens, and TM of human and rat eyes. The colocalization of MR and 11β-HSD type 2 may indicate selective access for aldosterone to MR in ocular tissues.

There is a considerable body of evidence to suggest a role for glucocorticoids in the pathogenesis of disorders of intraocular pressure (e.g., POAG). Glucocorticoid-induced cellular and morphologic changes in TM may affect resistance to aqueous humor outflow and lead to ocular hypertension and similar, although not identical, ultrastructural changes have been found in the TM of patients with both corticosteroid-induced glaucoma and POAG. The effects of GCs on ocular tissues in disease states such as POAG may be the result of higher circulating levels of GCs in the blood and aqueous humor, with a previous report showing an ocular hypotensive response in rabbits to RU486, a steroid receptor antagonist.

However, alterations in the number or affinity of target receptors (GR and MR) or indeed the activity of the 11β-HSDs will also alter the effects of GCs at a cellular level (e.g., steroid-resistant asthma, hypertension, and apparent mineralocorticoid excess) and, thus, alter the impact of GCs on intraocular pressure. Mutations in the 11β-HSD type 2 gene cause impairment in renal MR function, and changes in hepatic 11β-HSD type 1 function have been correlated with obesity. It remains to be investigated whether or not alterations in these crucial enzymes occur in disorders of intraocular pressure.

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References


Figure 5. Rat in situ hybridization studies for GR, MR, and 11β-HSD types 1 and 2. Silver grains denote areas of mRNA expression. (A) 11β-HSD type 2 antisense ciliary epithelium. (B) 11β-HSD type 2 sense ciliary epithelium. (C) Glucocorticoid receptor antisense drainage angle. (D) Glucocorticoid receptor antisense ciliary epithelium. (E) Mineralocorticoid receptor antisense corneal epithelium. (F) Mineralocorticoid receptor antisense ciliary epithelium. (G) 11β-HSD type 1 antisense ciliary epithelium. (H) 11β-HSD type 1 antisense corneal epithelium. CE, corneal epithelium; SC, Schlemm’s canal; NPE, non-pigmented ciliary epithelium; PE, pigmented ciliary epithelium. Magnification, ×40.


