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التوثيق الالكتروني والميكروفيلم

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EVALUATION OF METALLOPROTEINASE INHIBITORS IN THE TREATMENT OF INTRAOCULAR ANGIOGENESIS AND PROLIFERATION

Thesis

Submitted in partial fulfillment of the requirements of the MD degree in

Ophthalmology

By

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CONTENTS

To the soul of my mother

To the souls of my daughters

To my great wife

To my family

ABBREVIATIONS

- AMD or ARMD — Age related macular degeneration
- CAM — Chorioallantoic membrane
- CDI — Cartilage derived inhibitor
- CNV — Choroidal neovascularization
- CNVM — Choroidal neovascular membrane
- CNVPT — Choroidal neovascularization prevention trial
- D — Diopter
- ECM — Extracellular matrix
- EM — Electron microscopy
- ERG — Electroretinogram
- ERM — Epiretinal membrane
- FA — Fluorescein angiography
- FGF — Fibroblast growth factor
- Fig. — Figure
- H & E — Hematoxylin and eosin
- ICG — Indocyanine green
- IGF — Insulin growth factor
- IL — Interleukin
- IOP — Intraocular pressure
- IPM — Interphotoreceptor matrix
- IRBP — Interphotoreceptor retinoid binding protein
- KDa — Kilo dalton
- LDL — Low density lipoprotein
- LM — Light microscopy
- LTA — Laser target angiography
- mm — Millimeter
- MMPIs — Matrix metalloproteinase inhibitors
- MMPs — Matrix metalloproteinases
- MPSG — Macular Photocoagulation Study Group

- m-RNA — Messenger ribonucleic acid
- MT-MMP — Membrane type matrix metalloproteinase
- mw — Milliwatt
- OCT — Optical coherence tomography
- PA — Plasminogen activator
- PDEF — Platelet derived growth factor
- PDR — Proliferative diabetic retinopathy
- PDT — Photodynamic therapy
- PED — Pigment epithelium detachment
- PEDF — Pigment epithelium derived factor
- PF-4 — Platelet factor 4
- POHS — Presumed ocular histoplasmosis
- PVR — Proliferative vitreoretinopathy
- RBCs — Red blood cells
- RD — Retinal detachment
- RPE — Retinal pigment epithelium
- SFD — Sorsby's fundus dystrophy
- SLO — Scanning laser ophthalmoscope
- SRF — Subretinal fluid
- SRNM — Subretinal neovascular membrane
- TAAC — Triamcinolone acetonide acetate
- TGF — Transforming growth factor
- TIMPs — Tissue inhibitors of matrix metalloproteinases
- TNF — Tumor necrosis factor
- TSP — Thrompospondin
- μ — Micron
- μl — Micro liter
- VEGF — Vascular endothelial growth factor

INTRODUCTION

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ANATOMY OF THE HUMAN RETINAL PIGMENT EPITHELIUM (RPE) AND CHOROID

Anatomy of RPE cells: (Fig.,1)

General topography: The human retinal pigment epithelium cells form a single layer formed of hexagonal shaped cuboidal cells of neuroectodermal origin.[1] The RPE cells begin at the edge of the optic nerve head and extend peripherally to the ora serrata. Anterior to the ora serrata, the RPE continues as the pigment epithelium of the pars plana. The RPE has Bruch's membrane as its basal border, with the blood supply derived from the subjacent choriocapillaries. At its apex, the RPE cells are in intimate contact with the outer segments of the photoreceptor cells. The RPE cells are tightly packed against one another with little extracellular space between neighboring cells.[2]

In cross sections, the RPE cell varies in shape, depending on its age and location within the eye. In young adults, the RPE cells tend to be tall (14 μm) and somewhat narrow (10 μm) at the posterior pole, whereas at the ora serrata the cells are flatter and wider (60 μm) and have a cuboidal configuration. In the intervening equatorial zone, the RPE cells have their greatest variation in size and shape, compared with the posterior pole and ora serrata region. The total number of RPE cells per human eye can vary from 4.2 to 6.1 million. RPE cells have brown color, owing to their melanin granules. Within the macular zone, histological observations confirm the fact that the RPE cells are taller and contain more melanin than RPE cells elsewhere. This accounts, in part, for the clinical observation that the macula has a darker appearance than the retinal tissue elsewhere. Also contributing to this color difference is the yellow pigment xanthophyll glycol, located in the Henle's layer of the macula, which also acts as a filter during fluorescein angiography.[3]

Retinal pigment epithelium cell boundaries:

(a) *Apical surface*:

The apical surface of RPE faces the subretinal space, in which the outer segments of the photoreceptor cells (rods and cones) are located. The apical surface of RPE is