



# EXPERIMENTAL MODELS

## RD12/0034

## INDEX

### **IOBA-Eye Institute, University of Valladolid, Valladolid:**

- 1- Neuroretina organotypic culture
- 2- Proliferative vitreoretinopathy (Intravitreal platelet-rich plasma)
- 3- Proliferative vitreoretinopathy (Intravitreal platelets)
- 4- Autologous translocation of retinal pigment epithelium-choroid graft
- 5- Endophthalmitis (Intravitreal *S. aureus*)
- 6- \*Fresh retinal pigment epithelial (RPE) cells
- 7- \*Fresh retinal stem cells (RSCs) from ciliary margin
- 8- \*Chronic-Inflammatory Ocular Surface (SV-40 immortalized human corneal epithelial (HCE) cell line)
- 9- Limbal stem cell deficiency (Pig)
- 10- Limbal stem cell deficiency (Rabbit)

### **Laboratory of Neurophysiology, Faculty of Medicina, University of Barcelona, Barcelona (Hospital Clínico San Carlos, Madrid):**

- 11- Dry eye (Removing lacrimal gland)
- 12- \*Trabecular meshwork cell lines

### **Experimental Ophthalmology, University of Murcia, Murcia:**

- 13- Transient retinal ischemia by selective ligation of the ophthalmic vessels
- 14- Transient retinal ischemia by increasing the intraocular pressure
- 15- Selective motoneuron degeneration by injection of substances in oculomotor muscles
- 16- Selective axotomy-induced RGC death by microcrush lesion of optic nerve
- 17- Selective axotomy-induced RGC death by crush lesion of optic nerve
- 18- Selective axotomy-induced RGC death by intraocular transection of the optic nerve
- 19- Regenerative responses of injured neurons in the central nervous system through peripheral nerve grafts
- 20- Degenerative retinal conditions by inherited retinal dystrophy (RCS and P23H-1)
- 21- Laser-induced ocular hypertension
- 22- Light-induced retinal degeneration

**Ophthalmology Department, Hospital Vall Hebron, Barcelona:**

- 23- Laser-induced choroidal neovascularization (C57BL)
- 24- Retinal toxicity after inner limiting membrane (ILM) dyeing

**University of Navarra, Pamplona:**

- 25- Laser-induced choroidal neovascularization
- 26- Factor H (CFH) and Apolipoprotein E (apoE) deficiency (C57BL6/J)

**IIS Aragón (Aragon Research Institute), LIM (*Laboratorio de Investigación Molecular*), Zaragoza:**

- 27- Retinitis pigmentosa model (P23H-1)

**Universidad de Alcala, Madrid (Hospital General de Guadalajara, Guadalajara):**

- 28- Retinal degeneration model (Rd10)
- 29- Achromatopsia model
- 30- Retinal degeneration by excitatory aminoacids intraocular injection

**University of Alicante, Alicante:**

- 31- Experimental Glaucoma (DBA/2J mouse)
- 32- Retinitis pigmentosa (P23H-3)
- 33- Retinitis pigmentosa (Rd10)
- 34- \*Retinal cells signalling pathways and efficacy/toxicity of compounds (661W, RGC5, R28 and MU-PH1 cell lines)

**Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid:**

- 35- \*Achondroplasia (RCJ3.1C5.18 cell line)
- 36- Alzheimer's disease (B6C3-Tg(APP<sup>swe</sup>,PSEN1<sup>dE9</sup>)85Dbo/J)
- 37- Experimental Glaucoma
- 38- \*Glaucoma (Rabbit non-pigmented ciliary epithelium cell line)
- 39- \*Ocular Infection (Immortalized Human Corneal Limbal Epithelial Cells (HCLEC))
- 40- \*Ocular infection (Immortalized Human Conjunctival Epithelial Cell Lines (HCjE))

- 41- Retinal ganglion cells (RGC) degeneration (DBA/2J)
- 42- \*Retinal degeneration/Glaucoma (Ganglion cell line)
- 43- Experimental Corneal wound healing
- 44- \*Corneal wound healing (Rabbit corneal cell line)

**Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, University**

**Complutense of Madrid, Madrid:**

- 45- Experimental glaucoma
- 46- Chorioretinal ischemia induced by hypercholesterolemia
- 47- Laser photocoagulation of the retina and choroid
- 48- Organotypic retinal cultures
- 49- Experimental glaucoma

**Ophthalmic Research Unit “Santiago Grisolia”, Faculty of Medicine,**

**University of Valencia; and University and Polytechnic Hospital La Fe; Valencia:**

- 50- Chronic Glaucoma induction by a series of intracameral injections of hyaluronic acid (Wistar rat)
- 51- Proliferation, apoptosis and angiogenesis in ophthalmic diseases (C57BL/6 mouse)
- 52- Neuroprotection and apolipoprotein E (apoE<sup>-/-</sup> mouse)
- 53- \*Inflammation and immune response in retinal pigment epithelial cell cultures [immortalized human retinal pigment epithelial cell line (ARPE19)]: Immune aggression in vitro model
- 54- Development of the visual system
- 55- Development of the visual system
- 56- Preclinical safety of intravitreal docosahexaenoic acid in a rabbit model

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| <b>Experimental Model</b><br><b>1</b> | <b>Neuroretina organotypic culture</b>  |
| <b>Target Disease</b>                 | Retinal degeneration  |
| <b>Species</b>                        | Human, Pig ( <i>Sus scrofa domestica</i> )  |
| <b>Short Description</b>              | <p>Organotypic retina culture, from human and other mammals, has been demonstrably useful in improving our knowledge of retinal physiology and pathobiology. Furthermore, in organotypic cultures the morphology and functionality of the organ is temporarily retained, and experimental conditions are under control.</p> <p>In brief, eyes are dissected to remove the iris and the lens. The vitreous is then removed from the posterior eyecup by cotton swabs. The neuroretina is detached as a whole by paintbrushing and cutting the optic nerve. Finally, the neuroretina is unrolled in a Petri dish and cut into 5x5 mm explants. Samples are explanted on Transwell culture dishes with the photoreceptor layer facing the membrane, and cultured in Neurobasal A medium supplemented with B-27.</p>  |
| <b>Scientific Publications</b>        | <ul style="list-style-type: none"> <li>- Fernandez-Bueno I, Pastor JC, Gayoso MJ, Alcalde I, Garcia MT. <b>Müller and macrophage-like cell interactions in an organotypic culture model of porcine neuroretina</b>. Mol Vis 2008; 14:2148-56.</li> <li>- Fernandez-Bueno I, Fernandez-Sanchez L, Gayoso MJ, Garcia-Gutierrez MT, Pastor JC, Cuenca N. <b>Time course modifications in organotypic culture of human neuroretina</b>. Exp Eye Res 2012; 104:26-38.</li> <li>- Fernandez-Bueno I, Garcia-Gutierrez MT, Srivastava GK, Gayoso MJ, Gonzalo-Orden JM, Pastor JC. <b>Adalimumab (TNF-blocker) reduces the expression of GFAP immunoreactivity increased by exogenous TNF<math>\alpha</math> in an organotypic culture of porcine neuroretina</b>. Molecular Vision 2013. Epub ahead of print.</li> </ul> |
| <b>Institution</b>                    | IOBA-Eye Institute, University of Valladolid, Valladolid  |

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| <b>Experimental Model</b><br><b>2</b> | <b>Proliferative vitreoretinopathy (Intravitreal platelet-rich plasma)</b>  |
| <b>Target Disease</b>                 | Proliferative vitreoretinopathy (PVR)   |
| <b>Species</b>                        | Rabbit ( <i>Oryctolagus cuniculus</i> )   |
| <b>Short Description</b>              | Intravitreal injection of 0.15ml of PRP, transconjunctival cryotherapy and vitrectomy are performed. PRP is prepared from fresh citrated rabbit blood and injected into the vitreous cavity through the equator, using a 25g needle after pupillary dilatation.   |
| <b>Scientific Publications</b>        | <ul style="list-style-type: none"> <li>- Piñon RM, Pastor JC, Saornil MA, Goldaracena MB, Layana AG, Gayoso MJ, Guisasola J. <b>Intravitreal and subretinal proliferation induced by platelet-rich plasma injection in rabbits</b>. Curr Eye Res 1992; 11:1047-55</li> <li>- Goldaracena MB, Pastor JC, Saornil MA, Garcia-Layana A, De la Fuente LF. <b>[An effective model of PVR]</b>. Arch. Soc. Esp. Oftal. 1994; 67:127-34</li> <li>- Goldaracena MB, Garcia-Layana A, Pastor JC, Saornil MA, de la Fuente F, Gayoso MJ. <b>The role of retinotomy in an experimental rabbit model of proliferative vitreoretinopathy</b>. Curr Eye Res 1997; 16:422-7</li> </ul> |
| <b>Institution</b>                    | IOBA-Eye Institute, University of Valladolid, Valladolid  |

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| <b>Experimental Model</b><br><b>3</b> | <b>Proliferative vitreoretinopathy (Intravitreal platelets)</b>   |
| <b>Target Disease</b>                 | Proliferative vitreoretinopathy (PVR)   |
| <b>Species</b>                        | Pig ( <i>Sus scrofa domestica</i> )   |
| <b>Short Description</b>              | Animals receive four 3-mm-long retinectomies in the posterior retina, a partial mechanical vitectomy (about 1ml of central vitreous), and six cryoapplications at the retinal periphery. In addition, platelet concentrated plasma (10 <sup>6</sup> platelets/mm <sup>3</sup> ) is injected intravitreally. |
| <b>Scientific Publications</b>        | - Garcia-Layana A, Pastor JC, Saornil MA, Gonzalez G. <b>Porcine model of proliferative vitreoretinopathy with platelets.</b> Curr Eye Res 1997; 16:556-63  |
| <b>Institution</b>                    | IOBA-Eye Institute, University of Valladolid, Valladolid  |

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| <b>Experimental Model<br/>4</b> | <b>Autologous translocation of retinal pigment epithelium-choroid graft</b>   |
| <b>Target Disease</b>           | Age-related macular degeneration (AMD)  |
| <b>Species</b>                  | Pig ( <i>Sus scrofa domestica</i> )   |
| <b>Short Description</b>        | Autologous translocation of the choroid and RPE is carried out in porcine eyes closely following a technique described by van Meurs & Van Den Biesen (2003). Briefly, a standard 20G pars plana lensectomy and a pars plana vitrectomy are performed. The central retina is detached by the subretinal injection of Ringer's lactate solution through a retinotomy performed with a 39G angled rigid microinjection cannula. Recipient RPE and Bruch's membrane are left intact. Afterwards, demarcation of a rectangular area of 2x2 mm, using an endolaser probe, at the donor nasal midperiphery is performed. Using a bimanual technique with vitreous forceps and scissors, a full-thickness graft of neuroretina, RPE and choroid is carefully separated from the sclera. The graft, then consisting of the RPE and choroid, is translocated to the recipient bed in the central and a bubble of perfluorooctane is injected. Finally, after fluid/air exchange, the eye is filled up with 1000 Cst silicone oil. |
| <b>Scientific Publications</b>  | - Fernandez-Bueno I, Rodriguez de la Rúa E, Hileeto D, Parrado ML, Regueiro-Purriños M, Sala-Puigdollers A, Srivastava GK, Gonzalo-Orden JM, Pastor JC. <b>Histology and immunochemistry evaluation of autologous translocation of RPE-choroid graft in porcine eyes.</b> Acta Ophthalmol Scan 2012. Epub ahead of print.   |
| <b>Institution</b>              | IOBA-Eye Institute, University of Valladolid, Valladolid  |

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| <b>Experimental Model</b><br><b>5</b> | <b>Endophthalmitis (Intravitreal S. aureus)</b>   |
| <b>Target Disease</b>                 | Endophthalmitis   |
| <b>Species</b>                        | Rabbit ( <i>Oryctolagus cuniculus</i> )   |
| <b>Short Description</b>              | Rabbits were injected with approximately 200 CFU of a typed strain of S. aureus intravitreally.   |
| <b>Scientific Publications</b>        | <ul style="list-style-type: none"> <li>- Del Nozal MJ, Bernal JL, Pampliega A, Marinero P, López MI, Coco R. <b>High-performance liquid chromatographic determination of vancomycin in rabbit serum, vitreous and aqueous humour after intravitreal injection of the drug.</b> J Chromatogr A 1996; 727:231-8</li> <li>- Coco RM, López MI, Pastor JC, Nozal MJ. <b>Pharmacokinetics of intravitreal vancomycin in normal and infected rabbit eyes.</b> J Ocul Pharmacol Ther 1998; 14:555-63.</li> <li>- Coco RM, Lopez MI, Pastor JC. <b>Pharmacokinetics of 0.5 mg of a single and multiple dose of intravitreal vancomycin in infected rabbit eyes.</b> J Ocul Pharmacol Ther 2000;16(4):373-81.</li> </ul> |
| <b>Institution</b>                    | IOBA-Eye Institute, University of Valladolid, Valladolid  |

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| <b>Experimental Model</b><br><b>6</b> | <b>Fresh retinal pigment epithelial (RPE) cells</b>   |
| <b>Target Disease</b>                 | Retinal degeneration  |
| <b>Species</b>                        | Human, Pig ( <i>Sus scrofa domestica</i> )  |
| <b>Short Description</b>              | <p>Retinal diseases such as dry AMD, retinitis pigmentosa and many others are still non-curable or currently used therapeutic approaches are insufficiently effective. Their pathogenesis, likely multifactorial, involving a complex interaction of metabolic, functional, genetic and environmental factors, remain poorly understood. Although major abnormalities are seen in four functionally interrelated tissues, i.e., photoreceptors, retinal pigment epithelium (RPE), Bruch's membrane and choriocapillaries, the impairment of RPE cell functions is an early and crucial event in the cellular and molecular pathways leading to clinically relevant retinal changes. Detecting changes in RPE cells and repairing the pathways involved by using cellular and molecular based strategies are crucial for developing an effective therapy.</p> <p>For this reason, our laboratory is involved in investigation based on human RPE cells. We develop collaboration with the University Hospital of Valladolid for obtaining human eye globes for isolating, cultivating pure fresh human RPE cells using our established protocols (Immunol Methods. 2013 Jan 11).</p> <p>Furthermore, porcine eye resembles with human eye in many properties such as similar size, anatomy and histology. Furthermore, retinal development in pig eye shows substantial similarity to human retinal development. These characteristics make pig eyes and their RPE cells an ideal model for performing pre-clinical tests. For this reason, our laboratory is involved in investigation based on pig RPE cells. We develop a collaboration with slaughter-house, Valladolid for obtaining pig eye globes for isolating, cultivating pure fresh pig RPE cells using our established protocols (Exp Eye Res. 2011;93:956-62.).</p> <p>In summary, we offer fresh pure human and porcine RPE cells for investigation purpose.</p> |
| <b>Scientific Publications</b>        | <p>- Srivastava GK, Reinoso R, Singh AK, Fernandez-Bueno I, Martino M, Garcia-Gutierrez MT, Pastor JC, Corell A. <b>Flow cytometry assessment of the purity of human retinal pigment epithelial primary cell cultures.</b> J Immunol Methods. 2013 Jan 11.</p> <p>- Srivastava, G., Martin, L., Singh, A., Rodriguez-Cabello, J. and Pastor, J. <b>Evaluation of human retinal pigment epithelial cells growth on elastin-like recombinamers substrates.</b> Acta Ophthalmologica, 2011;89: 0.</p> <p>- Srivastava GK, Reinoso R, Singh AK, Fernandez-Bueno I, Hileeto D, Martino M, Garcia-Gutierrez MT, Merino JM, Alonso NF, Corell A, Pastor JC. <b>Trypan Blue staining method for quenching the autofluorescence of RPE cells for improving protein expression analysis.</b> Exp Eye Res. 2011;93:956-62.</p>   |
| <b>Institution</b>                    | IOBA-Eye Institute, University of Valladolid, Valladolid  |

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| <b>Experimental Model</b><br><b>7</b> | <b>Fresh retinal stem cells (RSCs) from ciliary margin</b>   |
| <b>Target Disease</b>                 | Retinal degeneration   |
| <b>Species</b>                        | Human, Pig ( <i>Sus scrofa domestica</i> )   |
| <b>Short Description</b>              | <p>Retinal diseases such as dry AMD, retinitis pigmentosa and many others are still non-curable or currently used therapeutic approaches are insufficiently effective. The pathogenesis remains poorly understood. Major abnormalities are seen in four functionally interrelated tissues, i.e., photoreceptors, retinal pigment epithelium (RPE), Bruch's membrane and choriocapillaries. Stem cell therapy showed favorable out comes.</p> <p>Retinal stem cells (RSCs) are present during embryonic development; they persist in quiescent forms in the adult mammalian eye in ciliary marginal zone. They have the ability to differentiate into different retinal cell type. Thus, they are promising for developing stem cell based treatments for retinal diseases. For this reason, our laboratory is involved in investigation based on human RSCs. We develop collaboration with Universitary Hospital of Valladolid for obtaining human eye globes for isolating, cultivating pure fresh human RSCs using our established protocols.</p> <p>Furthermore, porcine eye resembles with human eye in many properties such as similar size, anatomy and histology. Furthermore, retinal development in pig eye shows substantial similarity to human retinal development. These characteristics make pig eyes and their RSCs an ideal model for performing pre-clinical tests. For this reason, our laboratory is involved in investigation based on pig RSCs. We develop collaboration with slaughter-house, Valladolid for obtaining pig eye globes for isolating, cultivating pure fresh pig RSCs using our established protocols.</p> <p>In summary, we offer fresh pure human and porcine RSCs for investigation purpose.</p> |
| <b>Scientific Publications</b>        | - Srivastava GK, Rodríguez-Crespo D, Casado-Coterillo C, Singh AK, Garcia-Gutierrez MT., Coronas J, Pastor JC.: <b>Evaluation of retinal stem cells adhesion, growth, viability and protein expression on chitosan surface.</b> ISER meeting, Berlin, July, 2012.  |
| <b>Institution</b>                    | IOBA-Eye Institute, University of Valladolid, Valladolid   |

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| <b>Experimental Model</b><br><b>8</b>               | <b>Chronic-Inflammatory Ocular Surface (SV-40 immortalized human corneal epithelial (HCE) cell line)</b>   |
| <b>Target Disease</b>                               | Chronic-inflammatory ocular surface diseases   |
| <b>Species</b>                                      | Human  |
| <b>Short Description</b><br><b>(max. 250 words)</b> | <p>Although there are available therapies for acute-moderate ocular surface diseases, there is a lack of effective therapy for the treatment of more chronic-severe inflammatory diseases. These chronic-severe diseases are characterized for the possibility of corneal damage, that may lead to a sight-threatening outcome.</p> <p>It is clear that secreted molecules from inflammatory cells are responsible for many of the features observed in ocular inflammatory diseases. However, there is growing evidence showing that epithelial cells are active participants in inflammation, as they express and produce a large number of molecules implicated in the initiation and perpetuation of the inflammation process. For that reason, epithelial cells, and in our case corneal epithelial cells, are considered as a potential target for therapeutic interventions.</p> <p>This experimental model represents an in vitro model of ocular inflammation for the study of the implication of the corneal epithelium in the development of chronic-severe inflammatory diseases that may lead to visual loss.</p> <p>In this model, the SV-40 immortalized human corneal epithelial (HCE) cell line (Araki-Sasaki et al., IOVS 1995) has been exposed to different cytokines, including Th1 (INF-<math>\gamma</math>), Th2 (IL-4, IL-13) and Th17 (IL-17), and to TNF-<math>\alpha</math> and TGF-<math>\beta</math>. HCE response in terms of cytokine/chemokine secretion and/or several receptor types' expression has been characterized.</p> |
| <b>Scientific Publications</b>                      | <p>- Enríquez de Salamanca A, Calder V, Gao J, Galatowicz B, Garcia-Vazquez C, Fernández I, Stern ME, Diebold Y, Calonge M. <b>Cytokine responses by conjunctival epithelial cells: an in vitro model of ocular inflammation.</b> Cytokine. 2008; 44:160-167</p> <p>- Benito MJ, Calder V, Corrales RM, García Vázquez C, Narayanan S, Herreras JM, Stern ME, Calonge M, Enríquez de Salamanca A. <b>Effect of TGF-<math>\beta</math> on ocular surface epithelial cells.</b> Exp Eye Res. 2013; 107:88-100.</p> <p>- Arranz-Valseiro I, Schulze U, Contreras-Ruiz L, García-Posadas L, López-García A, Paulsen F, Diebold Y. <b>Involvement of corneal epithelial cells in the Th17 response in an in vitro bacterial inflammation model.</b> Mol Vis. 2013; 19:85.</p>   |
| <b>Institution</b>                                  | IOBA-Eye Institute, University of Valladolid, Valladolid   |

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| <b>Experimental Model</b><br><b>9</b>               | <b>Limbal Stem Cell Deficiency</b>  |
| <b>Target Disease</b>                               | Limbal Stem Cell Deficiency   |
| <b>Species</b>                                      | Pig ( <i>Sus scrofa domestica</i> )   |
| <b>Short Description</b><br><b>(max. 250 words)</b> | <p>An animal model of total LSCD was developed in pigs. 4-week-old male pigs were tranquilized with an intramuscular injection of Midazolam (0.35 mg/kg), Ketamine (5 mg/kg) and Atropine (0.02 mg/kg). Anesthesia induction was performed with an intravenous injection of Propofol (3-4mg/kg). Ocular surface was rinsed with sterile saline and 2.5% iodine solution. N-heptanol-based denudation of the corneal surface was done. Then, 360° cryogenic lesions were applied to the entire limbal area. A device was constructed to this end and the procedure was standardized. Intraorbital triamcinolone was immediately injected after surgery and systemic antibiotics were given for the 1st post-op week. After creation of the injury the eyelid was closed.</p> <p>Animals were weekly evaluated and scored by the same two independent researchers for: edema, opacification, neovascularisation, and re-epithelization. Photographs were taken at each evaluation point. Corneal impression cytologies were taken weekly to detect goblet cells. Histopathology analyses at the end of follow-up evaluated the degree of damage created in the limbal niche and the presence of inflammation and goblet cells (as a sign of conjunctival in-growth) in the central cornea. Additional evaluations were performed by laser scanning confocal microscopy (HRT-III Rostock Cornea Module) at the end of follow-up (12 weeks).</p> <p>Severe corneal scarring, neovascularization, opacification, and epithelial defects (fluorescein staining in green) were observed after 4 weeks and were maintained throughout the follow-up, resembling human LSCD. The presence of goblet cells in the central cornea was observed in corneal impression cytologies, resembling the conjunctival in-growth of human LSCD. Confocal microscopy demonstrated vascularization, inflammatory cells and goblet cells in the central cornea and complete (360°) limbal destruction, corroborated by pathology examination.</p> |
| <b>Scientific Publications</b>                      | - Galindo S, Plata-Cordero M, Vuelta E, Iglesias J, Regueiro M, Gonzalo-Orden M, Hileeto D, Nieto-Miguel T, Herreras JM, Calonge M. <b>Ocular Surface Failure Due to Limbal Stem Cell Deficiency (LSCD): Development of Two Efficient Animal Models.</b> Invest Ophthalmol Vis Sci 2012; 53: E-Abstract 3516  |
| <b>Institution</b>                                  | IOBA-Eye Institute, University of Valladolid, Valladolid  |

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| <b>Experimental Model</b><br><b>10</b>              | <b>Limbal stem cell deficiency (Rabbit)</b>  |
| <b>Target Disease</b>                               | Limbal stem cell deficiency  |
| <b>Species</b>                                      | Rabbit ( <i>Oryctolagus cuniculus</i> ): New Zealand White   |
| <b>Short Description</b><br><b>(max. 250 words)</b> | A partial Limbal Stem Cell Deficiency (LSCD) model was created in rabbits. Rabbits (weighing 4-4.5 kg) were anesthetized with intramuscular injection of 50 mg/Kg ketamine (Imalgene 1000®, Merial, Lyon, France) and 7 mg/Kg xilasyn (Rompun®, Bayer AG, Leverkusen, Germany), complemented with topical ophthalmic anesthetic combined (Colircusi®, Alcon, Barcelona, Spain). Denudation of corneal surface was made by cotton swab soaked with n-hepanol for 1 minute, and then, cornea was stained with fluorescein sodium to ensure of the removal of corneal epithelium. Surgical 180° limbal peritomy (temporal limbus, from 7 to 1 o'clock) was performed by crescent knife. Topical anti-inflammatory and antibiotics (Maxitrol® and Tobrex®, Alcon), intramuscular analgesics (0.02 mg/Kg buprenorphine, Buprex®), and subcutaneous antibiotics (5 mg/Kg enrofloxacin, Alsir®, Esteve, Barcelona, Spain) were administered daily for 5 days. Corneal neovascularization, corneal opacity and epithelial defects were clinically scored weekly by two different researchers. Histopathology analyses at the end of follow-up evaluated the degree of damage created in the limbal niche and the presence of inflammation and goblet cells (as a sign of conjuntival in-growth) in the central cornea. Rabbit corneas developed epithelial defects, scarring, neovascularization, and opacification after 3 weeks, resembling human LSCD. Pathology analyses showed complete destruction of the injured area (180°) and mild inflammation of the non-injured area. |
| <b>Scientific Publications</b>                      | - Galindo S, Plata-Cordero M, Vuelta E, Iglesias J, Regueiro M, Gonzalo-Orden M, Hileeto D, Nieto-Miguel T, Herreras JM, Calonge M. <b>Ocular Surface Failure Due to Limbal Stem Cell Deficiency (LSCD): Development of Two Efficient Animal Models.</b> Invest Ophthalmol Vis Sci 2012; 53: E-Abstract 3516   |
| <b>Institution</b>                                  | IOBA-Eye Institute, University of Valladolid, Valladolid   |

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| <b>Experimental Model</b><br><b>11</b> | <b>Dry eye (Removing lacrimal gland)</b>  |
| <b>Target Disease</b>                  | Dry eye   |
| <b>Species</b>                         | Guinea Pig ( <i>Cavia porcellus</i> ), Rat ( <i>Rattus norvegicus</i> )   |
| <b>Short Description</b>               | Experimental animal model of Dry eye by surgically removing main lacrimal gland from one eye. The model produces a significant reduction of tearing volume and characteristics of dry eye disease as measured up to four weeks in the ipsilateral eye. Some contralateral effects can be also present.  |
| <b>Scientific Publications</b>         | <ul style="list-style-type: none"> <li>- <b>Effects of Long-Term Eye Dryness on Voltage-Gated Na<sup>+</sup> Currents of Guinea-Pig Cold-Sensitive Ocular Trigeminal Ganglion Neurons.</b> <i>ARVO Meeting Abstracts March 26, 2012 53:1792</i></li> <li>- <b>Cyclosporine A Decreases Hyperexcitability of Corneal Cold Receptor Terminals by Altering Action Potential Generation in Experimental Dry Eye.</b> <i>ARVO Meeting Abstracts March 26, 2012 53:1795</i></li> <li>- <i>Article submitted to publication</i></li> </ul> |
| <b>Institution</b>                     | Laboratory of Neurophysiology, Faculty of Medicina, University of Barcelona, Barcelona (Hospital Clínico San Carlos, Madrid)  |

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| <b>Experimental Model</b><br><b>12</b> | <b>Trabecular meshwork cell lines</b>  |
| <b>Target Disease</b>                  | Glaucoma, aqueous humor outflow  |
| <b>Species</b>                         | Human  |
| <b>Short Description</b>               | Lines of trabecular meshwork cells to study cellular aspects of the cells that form the trabecular meshwork tissue and regulate the passage of aqueous humour through the conventional route.<br>Cell lines include TM5 (normotensive trabecular meshwork cells) and HTM-3 (human trabecular meshwork cells derived from a normotensive patient).  |
| <b>Scientific Publications</b>         | - Li A, Leung CT, Peterson-Yantorno K, Stamer WD, Civan MM. <b>Cytoskeletal dependence of adenosine triphosphate release by human trabecular meshwork cells</b> . Invest Ophthalmol Vis Sci. 2011 Oct 10;52(11)<br>- Pang IH, Shade DL, Clark AF, Steely HT, DeSantis L. <b>Preliminary characterization of a transformed cell strain derived from human trabecular meshwork</b> . Curr Eye Res. 1994 Jan;13(1):51-63. |
| <b>Institution</b>                     | Laboratory of Neurophysiology, Faculty of Medicina, University of Barcelona, Barcelona (Hospital Clínico San Carlos, Madrid)   |

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| <b>Experimental Model<br/>13</b> | <b>Transient retinal ischemia by selective ligation of the ophthalmic vessels</b>  |
| <b>Target Disease</b>            | Ischemia-induced retinal ganglion cells (RGC) degeneration   |
| <b>Species</b>                   | Rat ( <i>Rattus norvegicus</i> )   |
| <b>Short Description</b>         | <p>To investigate the pattern of RGC loss that follows transient ischemia of the retina induced by selective ligation of the ophthalmic vessels (SLOV). Ischemia-induced RGC death is a progressive event that takes place in at least two phases: an early rapid and a later more protracted period of cell loss. The amount and duration of these periods of cell loss are determined by the duration of the period of ischemia.</p> <p>In brief, the left ON head is exposed in the orbit, the superior aspect of its dural sheath is opened longitudinally, and a 10-0 nylon suture is introduced between the dural sheath and the ON and tied around the sheath, to interrupt blood flow through the ophthalmic vessels, which run in an inferior and nasal aspect within the sheath. Care is taken not to damage the ON. Interruption of retinal blood flow during ischemia is assessed by direct ophthalmoscopy of the eye fundus through the surgical microscope. The animals that do not show a complete interruption of retinal blood flow during the ischemic period are excluded. At the end of the ischemic period, the ligation is released, and retinal reperfusion is assessed through the surgical microscope. The animals that do not show a complete recovery of retinal blood flow within the first few minutes after the ligation is released are also excluded. Eye fundus inspection is facilitated, because most eyes appeared mydriatic after the induction of transient ischemia. When necessary, a drop of 1% tropicamide is applied topically to induce mydriasis.</p> |

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| <p><b>Scientific Publications</b></p> | <p>- Jehle T, Dimitriu C, Auer S, Knoth R, Vidal-Sanz M, Gozes I, Lagrèze WA. <b>The neuropeptide NAP provides neuroprotection against retinal ganglion cell damage after retinal ischemia and optic nerve crush.</b> Graefes Arch Clin Exp Ophthalmol. 2008 Sep;246(9):1255-63. Erratum in: Graefes Arch Clin Exp Ophthalmol. 2008; 246(9):1355.</p> <p>- Lönnngren U, Näpänkangas U, Lafuente M, Mayor S, Lindqvist N, Vidal-Sanz M, Hallböök F. <b>The growth factor response in ischemic rat retina and superior colliculus after brimonidine pre-treatment.</b> Brain Res Bull. 2006; 11;71(1-3):208-18.</p> <p>- Vidal-Sanz M, Lafuente M, Sobrado-Calvo P, Selles-Navarro I, Rodriguez E, Mayor-Torroglosa S, Villegas-Perez MP. <b>Death and neuroprotection of retinal ganglion cells after different types of injury.</b> Neurotox Res. 2000;2(2-3): 215-27.</p> <p>- Mayor-Torroglosa S, De la Villa P, Rodríguez ME, López-Herrera MP, Avilés-Trigueros M, García-Avilés A, de Imperial JM, Villegas-Pérez MP, Vidal-Sanz M. <b>Ischemia results 3 months later in altered ERG, degeneration of inner layers, and deafferented tectum: neuroprotection with brimonidine.</b> Invest Ophthalmol Vis Sci. 2005; 46(10):3825-35.</p> <p>- Avilés-Trigueros M, Mayor-Torroglosa S, García-Avilés A, Lafuente MP, Rodríguez ME, Miralles de Imperial J, Villegas-Pérez MP, Vidal-Sanz M. <b>Transient ischemia of the retina results in massive degeneration of the retinotectal projection: long-term neuroprotection with brimonidine.</b> Exp Neurol. 2003; 184(2):767-77.</p> <p>- Lafuente López-Herrera MP, Mayor-Torroglosa S, Miralles de Imperial J, Villegas-Pérez MP, Vidal-Sanz M. <b>Transient ischemia of the retina results in altered retrograde axoplasmic transport: neuroprotection with brimonidine.</b> Exp Neurol. 2002; 178(2):243-58.</p> <p>- Lafuente MP, Villegas-Pérez MP, Mayor S, Aguilera ME, Miralles de Imperial J, Vidal-Sanz M. <b>Neuroprotective effects of brimonidine against transient ischemia-induced retinal ganglion cell death: a dose response in vivo study.</b> Exp Eye Res. 2002; 74(2):181-9.</p> <p>- Lafuente MP, Villegas-Pérez MP, Sellés-Navarro I, Mayor-Torroglosa S, Miralles de Imperial J, Vidal-Sanz M. <b>Retinal ganglion cell death after acute retinal ischemia is an ongoing process whose severity and duration depends on the duration of the insult.</b> Neuroscience. 2002;109(1):157-68.</p> <p>- Vidal-Sanz M, Lafuente MP, Mayor-Torroglosa S, Aguilera ME, Miralles de Imperial J, Villegas-Pérez MP. <b>Brimonidine's neuroprotective effects against transient ischaemia-induced retinal ganglion cell death.</b> Eur J Ophthalmol. 2001; 11 Suppl 2:S36-40.</p> <p>- Lafuente MP, Villegas-Pérez MP, Sobrado-Calvo P, García-Avilés A, Miralles de Imperial J, Vidal-Sanz M. <b>Neuroprotective effects of alpha(2)-selective adrenergic agonists against ischemia-induced retinal ganglion cell death.</b> Invest Ophthalmol Vis Sci. 2001; 42(9):2074-84.</p> <p>- Vidal-Sanz M, Lafuente MP, Mayor S, de Imperial JM, Villegas-Pérez MP. <b>Retinal ganglion cell death induced by retinal ischemia. neuroprotective effects of two alpha-2 agonists.</b> Surv Ophthalmol. 2001; 45 Suppl 3:S261-7; discussion S273-6.</p> |
| <p><b>Institution</b></p>             | <p>Experimental Ophthalmology, University of Murcia, Murcia</p>   |

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| <b>Experimental Model</b><br><b>14</b> | <b>Transient retinal ischemia by increasing the intraocular pressure</b>  |
| <b>Target Disease</b>                  | Retinal ganglion cells (RGC) degeneration   |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )   |
| <b>Short Description</b>               | <p>To investigate the pattern of RGC loss that follows transient ischemia of the retina induced by elevation of intraocular pressure (IOP). Ischemia-induced RGC death is a progressive event that takes place in at least two phases: an early rapid and a later more protracted period of cell loss. The amount and duration of these periods of cell loss are determined by the duration of the period of ischemia.</p> <p>To increase the IOP, two 6-0 silk sutures are placed on the bulbar conjunctiva of the eye just below and above the corneoscleral limbus and are used to pull tangentially in opposite directions until the blood flow to the retina is interrupted completely. Sutures were tied to a metal frame designed for these experiments to maintain the IOP above systolic arterial levels throughout the transient ischemic period. Interruption of the blood flow to the retina is assessed constantly by examining the fundus of the eye through the operating microscope, and the sutures are retightened when needed to maintain interruption of the intraretinal blood flow. To permit microscopic observation of the eye fundus and, thus, of retinal blood flow, the pupil is dilated with a drop of 1% tropicamide, and the corneal surface is covered with a drop of 2% hydroxipropilmethylcellulose and a coverslip. During the periods of retinal ischemia, interruption of the blood flow to the iris also was observed. At the end of the transient ischemic period, the conjunctival sutures were released slowly, and this is followed by the complete restoration of the blood flow to the retina and the iris.</p> |
| <b>Scientific Publications</b>         | - Sellés-Navarro I, Villegas-Pérez MP, Salvador-Silva M, Ruiz-Gómez JM, Vidal-Sanz M. <b>Retinal ganglion cell death after different transient periods of pressure-induced ischemia and survival intervals. A quantitative in vivo study.</b> Invest Ophthalmol Vis Sci. 1996 Sep;37(10):2002-14. PMID: 8814140   |
| <b>Institution</b>                     | Experimental Ophthalmology, University of Murcia, Murcia  |

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| <b>Experimental Model<br/>15</b> | <b>Selective motoneuron degeneration by injection of substances in oculomotor muscles</b>  |
| <b>Target Disease</b>            | Abducens motoneurons degeneration  |
| <b>Species</b>                   | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )  |
| <b>Short Description</b>         | <p>To investigate in vivo the survival of abducens motoneurons (AMNs) at different periods of time after a single intramuscular injection of the neurotoxin botulinum toxin A (BTxA) or doxorubicin (DXR) in the abducens muscle.</p> <p>The AMNs were labeled with fluorogold (FG) applied intramuscularly in the lateral rectus muscle. The numbers of labeled neurons were determined in adult control animals, in young animals that had received BTxA and in adult rats that had received DXR, at various survival times.</p> <p>The intramuscular injection of BTxA in young animals does not induce significant motoneuron death, while DXR injection causes variable amounts of motoneuron death that is related both to the survival period and to the amount of DXR injected</p> |
| <b>Scientific Publications</b>   | - Gómez-Ramírez AM, Villegas-Pérez MP, Miralles de Imperial J, Salvador-Silva M, Vidal-Sanz M. <b>Effects of intramuscular injection of botulinum toxin and doxorubicin on the survival of abducens motoneurons</b> . Invest Ophthalmol Vis Sci. 1999 Feb;40(2):414-24. PMID: 9950601  |
| <b>Institution</b>               | Experimental Ophthalmology, University of Murcia, Murcia   |

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| <b>Experimental Model<br/>16</b> | <b>Selective axotomy-induced RGC death by microcrush lesion of optic nerve</b>   |
| <b>Target Disease</b>            | Retinal ganglion cells (RGC) degeneration  |
| <b>Species</b>                   | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )  |
| <b>Short Description</b>         | <p>Injury of the optic nerve has served as an important model for the study of cell death and axon regeneration in the CNS.</p> <p>Microcrush lesion of the optic nerve, which completely transects all RGC axons and minimizes the amount of secondary damage, creates a well-defined injury site. The microcrush lesion of the optic nerve is an excellent model to study strategies designed to promote axon regeneration in the inhibitory white matter environment.</p> <p>In brief, the left optic nerve is exposed through a superior temporal approach, and the dural sheath is slit longitudinally, taking care to avoid the ophthalmic artery. Microcrush lesions are made with 10-0 sutures used to completely constrict the optic nerve by holding a tight knot for 60 s and then releasing the suture. The fundis oculi is examined to verify the integrity of the retinal blood circulation. Animals whose retinas show ischemic damage are discarded.</p> |
| <b>Scientific Publications</b>   | <p>- Ellezam B, Dubreuil C, Winton M, Loy L, Dergham P, Sellés-Navarro I, McKerracher L. <b>Inactivation of intracellular Rho to stimulate axon growth and regeneration</b>. Prog Brain Res. 2002; 137:371-80.</p> <p>- Ellezam B, Selles-Navarro I, Manitt C, Kennedy TE, McKerracher L. <b>Expression of netrin-1 and its receptors DCC and UNC-5H2 after axotomy and during regeneration of adult rat retinal ganglion cells</b>. Exp Neurol. 2001; 168(1):105-15.</p> <p>- Sellés-Navarro I, Ellezam B, Fajardo R, Latour M, McKerracher L. <b>Retinal ganglion cell and nonneuronal cell responses to a microcrush lesion of adult rat optic nerve</b>. Exp Neurol. 2001; 167(2):282-9.</p> <p>- Lehmann M, Fournier A, Selles-Navarro I, Dergham P, Sebok A, Leclerc N, Tigyi G, McKerracher L. <b>Inactivation of Rho signaling pathway promotes CNS axon regeneration</b>. J Neurosci. 1999; 1;19(17):7537-47.</p>   |
| <b>Institution</b>               | Experimental Ophthalmology, University of Murcia, Murcia   |

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| <b>Experimental Model</b><br><b>17</b> | <b>Selective axotomy-induced RGC death by crush lesion of optic nerve</b>  |
| <b>Target Disease</b>                  | Retinal ganglion cells (RGC) degeneration  |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )  |
| <b>Short Description</b>               | <p>Intraorbital nerve crush (IONC) is a type of injury in which RGC axons are interrupted by pressure without a physical gap among the edges of the injury. However, there is a high variability among the results reported using this kind of lesion which are mainly due to the diversity of tools utilized, to the distance from the eye where the ON is injured and to the pressure exerted, which, if not enough, results in a partial lesion with a variable number of axons spared. In our IONC model, pressing the ON at 3 mm from the eye with watchmaker's forceps during 10 s, resulted in complete interruption of the retinofugal projection, as demonstrated by their failure to transport CTB orthogradely and FG retrogradely, even several months after the lesion.</p> <p>In brief, to perform Intraorbital nerve crush (IONC) injury an incision is made in the superior orbital rim, the superoexternal orbital contents are dissected, and the superior and external rectus muscles are removed, then the optic nerve (ON) is crushed during 10 s at 3 mm from the optic disc using watchmaker's forceps. Before and after the procedure, the eye fundus is observed through the operating microscope to assess the integrity of the retinal blood flow.</p>  |
| <b>Scientific Publications</b>         | <p>- Parrilla-Reverter G, Agudo M, Nadal-Nicolás F, Alarcón-Martínez L, Jiménez-López M, Salinas-Navarro M, Sobrado-Calvo P, Bernal-Garro JM, Villegas-Pérez MP, Vidal-Sanz M. <b>Time-course of the retinal nerve fibre layer degeneration after complete intra-orbital optic nerve transection or crush: a comparative study.</b> Vision Res. 2009; 49(23):2808-25.</p> <p>- Parrilla-Reverter G, Agudo M, Sobrado-Calvo P, Salinas-Navarro M, Villegas-Pérez MP, Vidal-Sanz M. <b>Effects of different neurotrophic factors on the survival of retinal ganglion cells after a complete intraorbital nerve crush injury: a quantitative in vivo study.</b> Exp Eye Res. 2009; 15;89(1):32-41.</p> <p>- Nadal-Nicolás FM, Jiménez-López M, Sobrado-Calvo P, Nieto-López L, Cánovas-Martínez I, Salinas-Navarro M, Vidal-Sanz M, Agudo M. <b>Brdn3a as a marker of retinal ganglion cells: qualitative and quantitative time course studies in naive and optic nerve-injured retinas.</b> Invest Ophthalmol Vis Sci. 2009; 50(8):3860-8.</p> <p>- Agudo M, Pérez-Marín MC, Sobrado-Calvo P, Lönnngren U, Salinas-Navarro M, Cánovas I, Nadal-Nicolás FM, Miralles-Imperial J, Hallböök F, Vidal-Sanz M. <b>Immediate upregulation of proteins belonging to different branches of the apoptotic cascade in the retina after optic nerve transection and optic nerve crush.</b> Invest Ophthalmol Vis Sci. 2009; 50(1):424-31.</p> <p>- Agudo M, Pérez-Marín MC, Lönnngren U, Sobrado P, Conesa A, Cánovas I, Salinas-Navarro M, Miralles-Imperial J, Hallböök F, Vidal-Sanz M. <b>Time course profiling of the retinal transcriptome after optic nerve transection and optic nerve crush.</b> Mol Vis. 2008; 3;14:1050-63.</p> <p>- Jehle T, Dimitriu C, Auer S, Knoth R, Vidal-Sanz M, Gozes I, Lagrèze WA. <b>The neuropeptide NAP provides neuroprotection against retinal ganglion cell damage after retinal ischemia and optic nerve crush.</b> Graefes Arch Clin Exp Ophthalmol. 2008; 246(9):1255-63. Erratum in: Graefes Arch Clin Exp Ophthalmol. 2008; 246(9):1355.</p> |
| <b>Institution</b>                     | Experimental Ophthalmology, University of Murcia, Murcia   |

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| <b>Experimental Model<br/>18</b> | <b>Selective axotomy-induced RGC death by intraocular transection of the optic nerve</b>   |
| <b>Target Disease</b>            | Retinal ganglion cells (RGC) degeneration  |
| <b>Species</b>                   | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )  |
| <b>Short Description</b>         | <p>Death of retinal ganglion cells (RGCs) is the cause of blindness in several diseases, including glaucoma. In recent years, much effort has gone into attempting to elucidate the causes and mechanisms of RGC loss so that strategies can be developed to counteract the process. Intraorbital optic nerve transection (IONT) results in the loss of the injured neurons, the RGCs and within the following two weeks post-lesion, approximately 80% of the RGC population is lost, only approximately 15% of the RGCs remain in the retina. A variety of substances have been shown to attenuate RGC death after ONT, with brain derived neurotrophic factor (BDNF) receiving particular attention. This model has allowed quantitative studies on the capacity of axotomized RGCs for axonal regeneration. Moreover, IONT is a valuable model not only for investigation into pathways that contribute to RGC death but also as a model for neuronal apoptosis in the CNS.</p> <p>In experimental animals, the left optic nerve (ON) is cut close to its origin in the optic disc to axotomize the entire population of RGCs. To access the ON at the back of the eye, an incision is made in the skin overlying the superior orbital rim, the supero-external orbital contents were dissected, and the superior and external rectus muscles are sectioned. The dura mater of the ON is opened longitudinally, and the ON is transected completely as close as possible to the eye. Care is taken not to damage the retinal blood supply, which enters the eye separately in the inferonasal aspect of the ON sheath.</p> |

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| <p><b>Scientific Publications</b></p> | <p>- Galindo-Romero C, Avilés-Trigueros M, Jiménez-López M, Valiente-Soriano FJ, Salinas-Navarro M, Nadal-Nicolás F, Villegas-Pérez MP, Vidal-Sanz M, Agudo-Barriuso M. <b>Axotomy-induced retinal ganglion cell death in adult mice: quantitative and topographic time course analyses.</b> Exp Eye Res. 2011; 92(5):377-87.</p> <p>- Sánchez-Migallón MC, Nadal-Nicolás FM, Jiménez-López M, Sobrado-Calvo P, Vidal-Sanz M, Agudo-Barriuso M. <b>Brain derived neurotrophic factor maintains Brn3a expression in axotomized rat retinal ganglion cells.</b> Exp Eye Res. 2011; 92(4):260-7.</p> <p>- Alarcón-Martínez L, de la Villa P, Avilés-Trigueros M, Blanco R, Villegas-Pérez MP, Vidal-Sanz M. <b>Short and long term axotomy-induced ERG changes in albino and pigmented rats.</b> Mol Vis. 2009; 17;15:2373-83.</p> <p>- Chidlow G, Casson R, Sobrado-Calvo P, Vidal-Sanz M, Osborne NN. <b>Measurement of retinal injury in the rat after optic nerve transection: an RT-PCR study.</b> Mol Vis. 2005; 2;11:387-96.</p> <p>- Casson RJ, Chidlow G, Wood JP, Vidal-Sanz M, Osborne NN. <b>The effect of retinal ganglion cell injury on light-induced photoreceptor degeneration.</b> Invest Ophthalmol Vis Sci. 2004; 45(2):685-93.</p> <p>Peinado-Ramón P, Salvador M, Villegas-Pérez MP, Vidal-Sanz M. <b>Effects of axotomy and intraocular administration of NT-4, NT-3, and brain-derived neurotrophic factor on the survival of adult rat retinal ganglion cells. A quantitative in vivo study.</b> Invest Ophthalmol Vis Sci. 1996; 37(4):489-500.</p> <p>- Villegas-Pérez MP, Vidal-Sanz M, Rasminsky M, Bray GM, Aguayo AJ. Rapid and protracted phases of retinal ganglion cell loss follow axotomy in the optic nerve of adult rats. J Neurobiol. 1993; 24(1):23-36.</p> <p>- McKerracher L, Vidal-Sanz M, Essagian C, Aguayo AJ. <b>Selective impairment of slow axonal transport after optic nerve injury in adult rats.</b> J Neurosci. 1990; 10(8):2834-41.</p> <p>- Aguayo AJ, Bray GM, Carter DA, Villegas-Perez MP, Vidal-Sanz M, Rasminsky M. <b>Regrowth and connectivity of injured central nervous system axons in adult rodents.</b> Acta Neurobiol Exp (Wars). 1990; 50(4-5):381-9.</p> <p>- Vidal-Sanz M, Villegas-Pérez MP, Bray GM, Aguayo AJ. <b>Persistent retrograde labeling of adult rat retinal ganglion cells with the carbocyanine dye dil.</b> Exp Neurol. 1988; 102(1):92-101.</p> <p>- Villegas-Pérez MP, Vidal-Sanz M, Bray GM, Aguayo AJ. <b>Influences of peripheral nerve grafts on the survival and regrowth of axotomized retinal ganglion cells in adult rats.</b> J Neurosci. 1988; 8(1):265-80.</p> |
| <p><b>Institution</b></p>             | <p>Experimental Ophthalmology, University of Murcia, Murcia</p>   |

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| <b>Experimental Model<br/>19</b>              | <b>Regenerative responses of injured neurons in the central nervous system through peripheral nerve grafts</b>  |
| <b>Target Disease</b>                         | Retinal ganglion cell (RGC) axons regeneration  |
| <b>Species</b>                                | Rat ( <i>Rattus norvegicus</i> )  |
| <b>Short Description<br/>(max. 250 words)</b> | <p>The pattern of axonal regeneration, specificity of reinnervation, and terminal arborization in the brainstem by axotomized retinal ganglion cell axons is studied in rats with peripheral nerve grafts linking the retina with ipsilateral regions of the brainstem, including dorsal and lateral aspects of the diencephalon and lateral aspect of the superior colliculus. Functional studies on the restoration of the pupillary light reflex by regenerating retinal ganglion cell axons have been carried out with this experimental model.</p> <p>In brief, autologous segments of the left common peroneal nerve are used to link the retina with the brainstem. The optic nerve of the left eye is exposed intraorbitally, and after longitudinal incision of the meningeal sheath, the nerve is completely transected close to the sclera without affecting the retinal blood supply. One end of a 3-cm-long autologous common peroneal nerve segment is apposed to the ocular stump with three 10/0 monofilament sutures. At the same time, the distal end of the PN segment is inserted into the ipsilateral side of the brainstem.</p> |

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| <p><b>Scientific Publications</b></p> | <p>- Vidal-Sanz M, Avilés-Trigueros M, Whiteley SJ, Sauvé Y, Lund RD. <b>Reinnervation of the pretectum in adult rats by regenerated retinal ganglion cell axons: anatomical and functional studies.</b> Prog Brain Res. 2002;137:443-52.</p> <p>- Avilés-Trigueros M, Sauvé Y, Lund RD, Vidal-Sanz M. <b>Selective innervation of retinorecipient brainstem nuclei by retinal ganglion cell axons regenerating through peripheral nerve grafts in adult rats.</b> J Neurosci. 2000; 1;20(1):361-74.</p> <p>- Whiteley SJ, Sauvé Y, Avilés-Trigueros M, Vidal-Sanz M, Lund RD. <b>Extent and duration of recovered pupillary light reflex following retinal ganglion cell axon regeneration through peripheral nerve grafts directed to the pretectum in adult rats.</b> Exp Neurol. 1998; 154(2): 560-72.</p> <p>- Vidal-Sanz M, Bray GM, Aguayo AJ. <b>Regenerated synapses persist in the superior colliculus after the regrowth of retinal ganglion cell axons.</b> J Neurocytol. 1991; 20(11):940-52. Erratum in: J Neurocytol 1992; 21(3):234.</p> <p>- Aguayo AJ, Rasminsky M, Bray GM, Carbonetto S, McKerracher L, Villegas-Pérez MP, Vidal-Sanz M, Carter DA. <b>Degenerative and regenerative responses of injured neurons in the central nervous system of adult mammals.</b> Philos Trans R Soc Lond B Biol Sci. 1991; 29;331(1261): 337-43.</p> <p>- Bray GM, Villegas-Pérez MP, Vidal-Sanz M, Carter DA, Aguayo AJ. <b>Neuronal and nonneuronal influences on retinal ganglion cell survival, axonal regrowth, and connectivity after axotomy.</b> Ann N Y Acad Sci. 1991; 633:214-28.</p> <p>- Aguayo AJ, Bray GM, Rasminsky M, Zwimpfer T, Carter D, Vidal-Sanz M. <b>Synaptic connections made by axons regenerating in the central nervous system of adult mammals.</b> J Exp Biol. 1990; 153:199-224.</p> <p>- <b>Slow transport rates of cytoskeletal proteins change during regeneration of axotomized retinal neurons in adult rats.</b> McKerracher L, Vidal-Sanz M, Aguayo AJ. J Neurosci. 1990; 10(2): 641-8.</p> <p>- Vidal Sanz M. <b>[Regeneration of the visual system in the rat. Essay rewarded by the Premio de la Academia Curso 1989].</b> An R Acad Nac Med (Madr). 1990;107(1):17-49.</p> <p>- Aguayo AJ, Bray GM, Carter DA, Villegas-Perez MP, Vidal-Sanz M, Rasminsky M. <b>Regrowth and connectivity of injured central nervous system axons in adult rodents.</b> Acta Neurobiol Exp (Wars). 1990; 50(4-5):381-9.</p> <p>- Keirstead SA, Rasminsky M, Fukuda Y, Carter DA, Aguayo AJ, Vidal-Sanz M. <b>Electrophysiologic responses in hamster superior colliculus evoked by regenerating retinal axons.</b> Science. 1989; 13;246(4927):255-7.</p> <p>- Villegas-Pérez MP, Vidal-Sanz M, Bray GM, Aguayo AJ. <b>Influences of peripheral nerve grafts on the survival and regrowth of axotomized retinal ganglion cells in adult rats.</b> J Neurosci. 1988; 8(1):265-80.</p> <p>- Vidal-Sanz M, Bray GM, Villegas-Pérez MP, Thanos S, Aguayo AJ. <b>Axonal regeneration and synapse formation in the superior colliculus by retinal ganglion cells in the adult rat.</b> J Neurosci. 1987; 7(9):2894-909.</p> <p>- Bray GM, Villegas-Pérez MP, Vidal-Sanz M, Aguayo AJ. <b>The use of peripheral nerve grafts to enhance neuronal survival, promote growth and permit terminal reconnections in the central nervous system of adult rats.</b> J Exp Biol. 1987;132:5-19.</p> <p>- Bray GM, Vidal-Sanz M, Aguayo AJ. <b>Regeneration of axons from the central nervous system of adult rats.</b> Prog Brain Res. 1987; 71:373-9.</p> <p>- Aguayo AJ, Vidal-Sanz M, Villegas-Pérez MP, Bray GM. <b>Growth and connectivity of axotomized retinal neurons in adult rats with optic nerves substituted by PNS grafts linking the eye and the midbrain.</b> Ann N Y Acad Sci. 1987;495:1-9.</p> <p>- Keirstead SA, Vidal-Sanz M, Rasminsky M, Aguayo AJ, Levesque M, So KF. <b>Responses to light of retinal neurons regenerating axons into peripheral nerve grafts in the rat.</b> Brain Res. 1985; 16;359(1-2):402-6.</p> <p>- Munz M, Rasminsky M, Aguayo AJ, Vidal-Sanz M, Devor MG. <b>Functional activity of rat brainstem neurons regenerating axons along peripheral nerve grafts.</b> Brain Res. 1985; 5;340 (1):115-25.</p> |
| <p><b>Institution</b></p>             | <p>Experimental Ophthalmology, University of Murcia, Murcia</p>   |

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| <b>Experimental Model</b><br><b>20</b> | <b>Degenerative retinal conditions by inherited retinal dystrophy (RCS and P23H-1)</b>  |
| <b>Target Disease</b>                  | Retinal degeneration  |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ): Royal College of Surgeons (RCS) and P23H-1  |
| <b>Short Description</b>               | The dystrophic Royal College of Surgeons (RCS) and the P23H-1 rats are two well known animal models of photoreceptor inherited degenerative diseases. Both models suffer an almost complete photoreceptor degeneration due to a defect in the MERTK (RCS) or in the rhodopsin (P23H) gene.<br>RCS-p <sup>+</sup> - (dystrophic) and RCS-p <sup>+</sup> rdy <sup>+</sup> - (nondystrophic) pigmented rats and P23H-1 albino rats are available. These animals may be used to study the events taking place during retinal degeneration or to test strategies to prevent this degeneration, such as light exposure prevention, neurotrophic factor administration or intraocular cell transplantation.  |
| <b>Scientific Publications</b>         | <ul style="list-style-type: none"> <li>- García-Ayuso D, Salinas-Navarro M, Agudo M, Cuenca N, Pinilla I, Vidal-Sanz M, Villegas-Pérez MP. <b>Retinal ganglion cell numbers and delayed retinal ganglion cell death in the P23H rat retina.</b> Exp Eye Res. 2010; 91(6):800-10.</li> <li>- Marco-Gomariz MA, Hurtado-Montalbán N, Vidal-Sanz M, Lund RD, Villegas-Pérez MP. <b>Phototoxic-induced photoreceptor degeneration causes retinal ganglion cell degeneration in pigmented rats.</b> J Comp Neurol. 2006; 10;498(2):163-79.</li> <li>- Wang S, Villegas-Pérez MP, Holmes T, Lawrence JM, Vidal-Sanz M, Hurtado-Montalbán N, Lund RD. <b>Evolving neurovascular relationships in the RCS rat with age.</b> Curr Eye Res. 2003; 27(3):183-96.</li> <li>- Wang S, Villegas-Pérez MP, Vidal-Sanz M, Lund RD. <b>Progressive optic axon dystrophy and vacuslar changes in rd mice.</b> Invest Ophthalmol Vis Sci. 2000; 41(2):537-45.</li> <li>- Villegas-Pérez MP, Lawrence JM, Vidal-Sanz M, Lavail MM, Lund RD. <b>Ganglion cell loss in RCS rat retina: a result of compression of axons by contracting intraretinal vessels linked to the pigment epithelium.</b> J Comp Neurol. 1998; 2;392(1):58-77.</li> <li>- Villegas-Pérez MP, Vidal-Sanz M, Lund RD. <b>Mechanism of retinal ganglion cell loss in inherited retinal dystrophy.</b> Neuroreport. 1996; 12;7(12):1995-9.</li> </ul> |
| <b>Institution</b>                     | Experimental Ophthalmology, University of Murcia, Murcia  |

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| <b>Experimental Model</b><br><b>21</b> | <b>Laser-induced ocular hypertension</b>   |
| <b>Target Disease</b>                  | Retinal ganglion cells (RGC) degeneration  |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )  |
| <b>Short Description</b>               | <p>In adult rats and mice, perilimbar and episcleral vein photocoagulation induces ocular hypertension, which in turn results in devastating damage of the RGC population. In wide triangular sectors, preferentially located in the dorsal retina, RGCs lose their retrograde axonal transport, first by a functional impairment and after by mechanical causes. This axonal damage affects up to 80% of the RGC population, and eventually causes their death, with somal and intra-retinal axonal degeneration that resembles that observed after optic nerve crush. Importantly, while ocular hypertension affects the RGC population, it spares non-RGC neurons located in the ganglion cell layer of the retina. In addition, functional and morphological studies show permanent alterations of the inner and outer retinal layers, indicating that further to a crush-like injury of axon bundles in the optic nerve head there may be additional insults to the retina, perhaps of ischemic nature.</p> <p>To induce ocular hypertension, the left eyes of anesthetized animal are treated during a single session with a series of diode laser (532 nm, Quantel Medical, Clermont-Ferrand, France) burns. The laser beam is delivered directly, without any lenses, aimed at the limbal and episcleral veins. The spot size, duration, and power are set up according to the experimental animal species used and pigmented condition (albino or pigmented).</p> |

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| <p><b>Scientific Publications</b></p> | <p>- Agudo-Barriuso M, Villegas-Pérez M, de Imperial JM, Vidal-Sanz M. <b>Anatomical and functional damage in experimental glaucoma.</b> Curr Opin Pharmacol. 2013; 13(1):5-11.</p> <p>- Gallego BI, Salazar JJ, de Hoz R, Rojas B, Ramírez AI, Salinas-Navarro M, Ortín-Martínez A, Valiente-Soriano FJ, Avilés-Trigueros M, Villegas-Perez MP, Vidal-Sanz M, Triviño A, Ramírez JM. <b>IOP induces upregulation of GFAP and MHC-II and microglia reactivity in mice retina contralateral to experimental glaucoma.</b> J Neuroinflammation. 2012; 14;9:92.</p> <p>- Vidal-Sanz M, Salinas-Navarro M, Nadal-Nicolás FM, Alarcón-Martínez L, Valiente-Soriano FJ, de Imperial JM, Avilés-Trigueros M, Agudo-Barriuso M, Villegas-Pérez MP. <b>Understanding glaucomatous damage: anatomical and functional data from ocular hypertensive rodent retinas.</b> Prog Retin Eye Res. 2012; 31(1):1-27.</p> <p>- Nguyen JV, Soto I, Kim KY, Bushong EA, Oglesby E, Valiente-Soriano FJ, Yang Z, Davis CH, Bedont JL, Son JL, Wei JO, Buchman VL, Zack DJ, Vidal-Sanz M, Ellisman MH, Marsh-Armstrong N. <b>Myelination transition zone astrocytes are constitutively phagocytic and have synuclein dependent reactivity in glaucoma.</b> Proc Natl Acad Sci U S A. 2011; 18;108(3):1176-81.</p> <p>- Cuenca N, Pinilla I, Fernández-Sánchez L, Salinas-Navarro M, Alarcón-Martínez L, Avilés-Trigueros M, de la Villa P, Miralles de Imperial J, Villegas-Pérez MP, Vidal-Sanz M. <b>Changes in the inner and outer retinal layers after acute increase of the intraocular pressure in adult albino Swiss mice.</b> Exp Eye Res. 2010; 91(2):273-85.</p> <p>- Ramírez AI, Salazar JJ, de Hoz R, Rojas B, Gallego BI, Salinas-Navarro M, Alarcón-Martínez L, Ortín-Martínez A, Avilés-Trigueros M, Vidal-Sanz M, Triviño A, Ramírez JM. <b>Quantification of the effect of different levels of IOP in the astroglia of the rat retina ipsilateral and contralateral to experimental glaucoma.</b> Invest Ophthalmol Vis Sci. 2010; 51(11):5690-6.</p> <p>- Salinas-Navarro M, Alarcón-Martínez L, Valiente-Soriano FJ, Ortín-Martínez A, Jiménez-López M, Avilés-Trigueros M, Villegas-Pérez MP, de la Villa P, Vidal-Sanz M. <b>Functional and morphological effects of laser-induced ocular hypertension in retinas of adult albino Swiss mice.</b> Mol Vis. 2009. 5;15:2578-98.</p> <p>- Salinas-Navarro M, Alarcón-Martínez L, Valiente-Soriano FJ, Jiménez-López M, Mayor-Torroglosa S, Avilés-Trigueros M, Villegas-Pérez MP, Vidal-Sanz M. <b>Ocular hypertension impairs optic nerve axonal transport leading to progressive retinal ganglion cell degeneration.</b> Exp Eye Res. 2010; 90(1): 168-83.</p> |
| <p><b>Institution</b></p>             | <p>Experimental Ophthalmology, University of Murcia, Murcia</p>  |

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| <b>Experimental Model</b><br><b>22</b> | <b>Light-induced retinal degeneration</b>   |
| <b>Target Disease</b>                  | Photoreceptor and Retinal Degeneration  |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )   |
| <b>Short Description</b>               | <p>Light-induced retinal damage (phototoxicity) selectively brings about photoreceptor cell death. Thus, this model is useful for studying the potential mechanisms underlying photoreceptor death and the subsequent retinal degeneration processes, since it mimics the photoreceptor degeneration that forms the main characteristic of human diseases such as retinitis pigmentosa or age-related macular degeneration. Moreover, it is useful to investigate the anatomic and functional changes triggered by light exposure in the experimental animal retina.</p> <p>In brief, before light exposure, left pupil mydriasis is induced by topical application of a drop of 1% atropine. The right eye is not dilated to be used for comparison. Because the severity of retinal phototoxicity in rodents depends on the time of the day when exposure starts (circadian rhythm) and on the previous light exposure (rearing conditions and dark adaptation period), the exposure always began between 10 and 12 AM and after 12 h of dark adaptation. Animals are individually exposed to 24 h of continuous fluorescent cold white light. Fluorescent bulbs are situated in the ceiling right above the animal cages, which are transparent. Light intensity within the cages is 3,000±100lx. Mydriasis is inspected 12 h after the initiation of light exposure, and when necessary, a second drop of atropine is instilled in the left eye at this time.</p> |
| <b>Scientific Publications</b>         | <p>- Montalbán-Soler L, Alarcón-Martínez L, Jiménez-López M, Salinas-Navarro M, Galindo-Romero C, Bezerra de Sá F, García-Ayuso D, Avilés-Trigueros M, Vidal-Sanz M, Agudo-Barriuso M, Villegas-Pérez MP. <b>Retinal compensatory changes after light damage in albino mice</b>. Mol Vis. 2012; 18:675-93.</p> <p>- García-Ayuso D, Salinas-Navarro M, Agudo-Barriuso M, Alarcón-Martínez L, Vidal-Sanz M, Villegas-Pérez MP. <b>Retinal ganglion cell axonal compression by retinal vessels in light-induced retinal degeneration</b>. Mol Vis. 2011; 17:1716-33.</p> <p>- Marco-Gomariz MA, Hurtado-Montalbán N, Vidal-Sanz M, Lund RD, Villegas-Pérez MP. <b>Phototoxic-induced photoreceptor degeneration causes retinal ganglion cell degeneration in pigmented rats</b>. J Comp Neurol. 2006; 10;498 (2):163-79.</p>  |
| <b>Institution</b>                     | Experimental Ophthalmology, University of Murcia, Murcia  |

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| <b>Experimental Model</b><br><b>23</b> | <b>Laser-induced choroidal neovascularization (C57BL)</b>   |
| <b>Target Disease</b>                  | Age-related macular degeneration (AMD)  |
| <b>Species</b>                         | Mouse ( <i>Mus musculus</i> ): C57BL  |
| <b>Short Description</b>               | Choroidal Neovascularization was induced by laser breakage (Diode laser) in mouse C57BL Bruch's membrane. Laser was used at several intensities (100-250mv/100ms), but the best results were obtained with 250mv/ms in five focus points. Neovessels were visualized by confocal microscopy, using endothelial cells labeling (Von Willebrand and DIL heart perfusion). |
| <b>Scientific Publications</b>         | No scientific publications yet.   |
| <b>Institution</b>                     | Ophthalmology Department, Hospital Vall Hebron, Barcelona   |

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| <b>Experimental Model</b><br><b>24</b> | <b>Retinal toxicity after inner limiting membrane (ILM) dyeing</b>   |
| <b>Target Disease</b>                  | Traction maculopathies   |
| <b>Species</b>                         | Pig ( <i>Sus scrofa domestica</i> )  |
| <b>Short Description</b>               | Vital dyes facilitate vitreoretinal surgery by visualizing nearly transparent structures such the inner limiting membrane (ILM). It is beyond question that vital dyes being injected into human eye need to be safe and potential toxic effects have to be ruled out in advance. To perform a long term toxicity study, after general anesthesia 3 animals were submitted to dark adaptation for 30 min for electroretinography test. Before surgery animals were ophthalmologic examined by indirect ophthalmoscopy and slit lamp to evaluate any abnormality. It was performed vitrectomy and injection of the new ILM dye in vitreous cavity of the right eye. Left eye was used as control. Retinal toxicity was assessed by ERG, histology and retinal ganglion cell quantification 7 days after dye administration. |
| <b>Scientific Publications</b>         | No scientific publications yet.  |
| <b>Institution</b>                     | Ophthalmology Department, Hospital Vall Hebron, Barcelona  |

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| <b>Experimental Model</b><br><b>25</b> | <b>Laser-induced choroidal neovascularization</b>   |
| <b>Target Disease</b>                  | Wet Age-related macular degeneration (AMD), High myopia   |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )   |
| <b>Short Description</b>               | <p>Laser-induced murine coroidal neovascularization (LI-CNV) model. Eyes are dilated with tropicamide 1% and 4-12 laser photocoagulation sites are placed around the optic disc to induce CNV. A diode laser (810 nm) is used and bubble formation confirmed the rupture of Bruch's membrane.</p> <p>The development of de CNV process is controlled by periodical fluorescein angiographies and the atrophic area is measured by CD31 flat mount immunofluorescence.</p> <p>This animal model can be used to evaluate the activity of anti or pro-angiogenic substances administrated by intravitreal, subretinal or endovenous injections or oral administration.</p> |
| <b>Scientific Publications</b>         | <p>- Recalde S, Zarranz-Ventura J, Fernández-Robredo P, García-Gómez PJ, Salinas-Alamán A, Borrás-Cuesta F, Dotor J, García-Layana A. <b>Transforming growth factor-<math>\beta</math> inhibition decreases diode laser-induced choroidal neovascularization development in rats: P17 and P144 peptides.</b> Invest Ophthalmol Vis Sci. 2011; 9;52(10):7090-7.</p> <p>- García-Layana A, Vásquez G, Salinas-Alamán A, Moreno-Montañés J, Recalde S, Fernández-Robredo P. <b>Development of laser-induced choroidal neovascularization in rats after retinal damage by sodium iodate injection.</b> Ophthalmic Res. 2009; 42(4):205-12.</p>                              |
| <b>Institution</b>                     | University of Navarra, Pamplona   |

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| <b>Experimental Model</b><br><b>26</b> | <b>Factor H (CFH) and Apolipoprotein E (apoE) deficiency (C57BL6/J)</b>   |
| <b>Target Disease</b>                  | Retinal degeneration  |
| <b>Species</b>                         | Mouse ( <i>Mus musculus</i> ): C57BL6/J   |
| <b>Short Description</b>               | <p>Animals deficient or partially deficient for complement factor H (CFH) and Apolipoprotein E (apoE) genes are models of retinal degeneration. All the animals are C57BL6/J background.</p> <p>These animals presented retinal alteration such as large amount of vacuoles, Bruch's membrane (BM) is swollen and deposits are found between BM and RPE.</p> <p>We are studying apoE<sup>-/-</sup> CFH<sup>-/-</sup>, apoE<sup>+/-</sup> /CFH<sup>+/-</sup> and apoE<sup>-/-</sup>/CFH<sup>+/-</sup> genotypes.</p> <p>These animal models could be used to study de influence of CFH and the complement system in retinal degeneration. Another application could be the combination of these mice with coroidal neovascularization process (i.e.) to investigate the implication of these genes in the development of wet AMD from the dry form of the pathology.</p> |
| <b>Scientific Publications</b>         | - Garcia-Garcia L, Fernandez-Robredo P, Recalde S, Moreno-Orduña M, Fernandez-Garcia V, Caire J, Marchena-Fernandez MA, de la Villa P, Garcia-Layana A. <b>Effects Of The Absence Of both Complement Factor H And Apolipoprotein E On Retinal Morphology In Mice</b> . ARVO May 2012.   |
| <b>Institution</b>                     | University of Navarra, Pamplona   |

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| <b>Experimental Model</b><br><b>27</b>              | <b>Retinitis pigmentosa model (P23H-1)</b>   |
| <b>Target Disease</b>                               | Retinitis pigmentosa   |
| <b>Species</b>                                      | Rat ( <i>Rattus norvegicus</i> ): P23H line 1  |
| <b>Short Description</b><br><b>(max. 250 words)</b> | Autosomal Dominant Model of RP degeneration, discover by Mat Lavail, at the University of California, San Francisco, USA. The rat shows a progressive loss of rod photoreceptors with 40% diminish ONL at the first month.   |
| <b>Scientific Publications</b>                      | <ul style="list-style-type: none"> <li>- La Vail MM. <b>Survival of some photoreceptor cells in albino rats following long term exposure to continuous light.</b> Invest Ophthalmol 1976; 15:64-70.</li> <li>- Cuenca N, Pinilla I, Sauvé Y, Wang S, Lu B, Lund RD. <b>Regressive and reactive changes in the connectivity patterns of rod and cone pathways of P23H transgenic rat retina.</b> Neuroscience 2004; 127: 301-317.</li> <li>- Pinilla I, Sauvé Y, Lund RD. <b>Enhanced cone dysfunction in rat homozygous for the P23H rhodopsin mutation.</b> Neuroscience Letters 2005; 382: 16-21.</li> </ul> |
| <b>Institution</b>                                  | IIS Aragón (Aragon Research Institute), LIM (Laboratorio de Investigación Molecular), Zaragoza   |

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| <b>Experimental Model</b><br><b>28</b>              | <b>Retinal degeneration model (Rd10)</b>  |
| <b>Target Disease</b>                               | Photoreceptors Degeneration   |
| <b>Species</b>                                      | Mouse ( <i>Mus musculus</i> ): Rd10   |
| <b>Short Description</b><br><b>(max. 250 words)</b> | Rd10 mouse model of retinal degeneration. This animal consists on a mouse model of heredodegenerative disease. The animal express a mutation in the gene of the beta subunit of 6 phosphodiesterase, which determines a progressive loss of rod photoreceptor starting at 25 postnatal day (p25). By p40 more that 95 % of retinal photoreceptors have degenerated. |
| <b>Scientific Publications</b>                      | - Barhoum, R. Martínez-Navarrete, G; Corrochano, S.; Germain, F.; de la Rosa, E.J.; de la Villa, P. & Cuenca, N. <b>Time course of functional and structural modifications during retinal degeneration in the rd10 mouse.</b> Neuroscience, 155 :698-713 (2008)   |
| <b>Institution</b>                                  | Universidad de Alcala, Madrid (Hospital General de Guadalajara, Guadalajara)  |

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| <b>Experimental Model</b><br><b>29</b>              | <b>Achromatopsia model</b>  |
| <b>Target Disease</b>                               | Dysfunction of cone photoreceptors (achromatopsia)  |
| <b>Species</b>                                      | Mouse ( <i>Mus musculus</i> )   |
| <b>Short Description</b><br><b>(max. 250 words)</b> | Gnat Mouse model of retinal disease.<br>This animal consists on a mouse model of achromatopsia. The animal express a mutation in the gene the cone transducin, which determines an absolute lack of cone response.  |
| <b>Patent</b>                                       | - Patent: Zurita Redondo, E.; Montoliu José, L.; Fernandez López, A.; de la Villa Polo P.; Gonzalez-Neira, A.; Benitez Ortiz J. <b>Nuevo Modelo Animal de Acromatopsia</b> . P201231296. Spain. <i>Consejo Superior de Investigaciones Científicas, Universidad de Alcalá and Centro Nacional de Investigaciones Oncológicas, CIBER-Enfermedades Raras.</i> |
| <b>Institution</b>                                  | Universidad de Alcala, Madrid (Hospital General de Guadalajara, Guadalajara)  |

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| <b>Experimental Model<br/>30</b>       | <b>Retinal degeneration by excitatory aminoacids intraocular injection</b>   |
| <b>Target Disease</b>                  | Induced Retinal Degeneration   |
| <b>Species</b>                         | Mouse ( <i>Mus musculus</i> )  |
| <b>Short Description</b>               | <p>Mouse model of retinal disease caused by excitotoxicity.</p> <p>This animal consists on a mouse model of retinal degeneration that includes cells of the inner retina. The disease is induced by eye injection of a mixture of excitatory aminoacid agonists. A significant loss of inner retinal cells is accounted according to the drug concentration. The degree of functional response of the retina and inner retinal degeneration is addressed by electrophysiological and structural methods.</p> |
| <b>Scientific Publications/ Patent</b> | In progress  |
| <b>Institution</b>                     | Universidad de Alcala, Madrid (Hospital General de Guadalajara, Guadalajara)   |

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| <b>Experimental Model</b><br><b>31</b> | <b>Experimental Glaucoma (DBA/2J mouse)</b>   |
| <b>Target Disease</b>                  | Glaucoma  |
| <b>Species</b>                         | Mouse ( <i>Mus musculus</i> ): DBA/2J   |
| <b>Short Description</b>               | The DBA/2J mouse glaucoma model spontaneously develops essential iris atrophy, pigment dispersion, and glaucomatous age-related changes, including an increase of intraocular pressure causing the death of retinal ganglion cells and optic nerve atrophy.   |
| <b>Scientific Publications</b>         | <ul style="list-style-type: none"> <li>- Libby RT, Anderson MG, Pang I-H, et al. <b>Inherited glaucoma in DBA/2J mice: pertinent disease features for studying the neurodegeneration.</b> Visual neuroscience. 2005;22(5):637–48</li> <li>- Steele MR, Inman DM, Calkins DJ, Horner PJ, Vetter ML. <b>Microarray analysis of retinal gene expression in the DBA/2J model of glaucoma.</b> Invest Ophthalmol Vis Sci. 2006; 47(3):977–85.</li> </ul> |
| <b>Institution</b>                     | University of Alicante, Alicante  |

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| <b>Experimental Model</b><br><b>32</b> | <b>Retinitis pigmentosa (P23H-3)</b>   |
| <b>Target Disease</b>                  | Retinitis pigmentosa   |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ): P23H line 3  |
| <b>Short Description</b>               | Model for study retinal degeneration. Autosomal Dominant Model of RP degeneration, discover by Mat Lavail, at the University of California, San Francisco, USA. The rat shows a progressive loss of rod photoreceptors with 40% diminish ONL at the first month.   |
| <b>Scientific Publications</b>         | <ul style="list-style-type: none"> <li>- La Vail MM. <b>Survival of some photoreceptor cells in albino rats following long term exposure to continuous light.</b> Invest Ophthalmol 1976; 15:64-70.</li> <li>- Fernández-Sánchez L, Lax P, Pinilla I, Martín-Nieto J, Cuenca N. <b>Tauroursodeoxycholic acid (TUDCA) prevent retinal degeneration in transgenic P23H rats.</b> Invest Ophthalmol Vis Sci. 2011; 52:4998-5008</li> <li>- Fernández-Sánchez L, Lax P, Esquivá G, Martín-Nieto J, Pinilla I, Cuenca N. <b>Safranal, a saffron constituent, attenuates retinal degeneration in P23H rats.</b> PLoS One. 2012; 7(8):e43074</li> </ul> |
| <b>Institution</b>                     | University of Alicante, Alicante   |

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| <b>Experimental Model</b><br><b>33</b> | <b>Retinitis pigmentosa (Rd10)</b>  |
| <b>Target Disease</b>                  | Retinitis pigmentosa  |
| <b>Species</b>                         | Mouse ( <i>Mus musculus</i> ): Rd10   |
| <b>Short Description</b>               | In this model, a point mutation in exon 13 of the B-PDE gene leads to the rapid, large-scale loss of rod photoreceptors within first weeks of postnatal life.<br>Morphological and physiological studies have shown that the rd10 mouse model may be a good model to assess rescue approaches.  |
| <b>Scientific Publications</b>         | - Barhoum R; Martínez-Navarrete G.C; Corrochano S; Germain F; Fernandez-Sanchez. L; De La Rosa E.J; De La Villa P; Cuenca N. <b>Functional and structural modifications and time course of retinal degeneration in the rd10 mouse.</b> Neuroscience. 2008; 155:698-713.<br>- Pang JJ, Dai X, Boye SE, Barone I, Boye SL, Mao S, Everhart D, Dinculescu A, Liu L, Umino Y, Lei B, Chang B, Barlow R, Strettoi E, Hauswirth WW. <b>Long-term retinal function and structure rescue using capsid mutant AAV8 vector in the rd10 mouse, a model of recessive retinitis pigmentosa.</b> Mol Ther. 201; 19(2):234-42. |
| <b>Institution</b>                     | University of Alicante, Alicante  |

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| <b>Experimental Model</b><br><b>34</b> | <b>Retinal cells signalling pathways and efficacy/toxicity of compounds (661W, RGC5, R28 and MU-PH1 cell lines)</b>   |
| <b>Target Disease</b>                  | Retinal cells signalling pathways and efficacy/toxicity of compounds  |
| <b>Species</b>                         | Mouse ( <i>Mus musculus</i> ): cell lines 661W and MU-PH1<br>Rat ( <i>Rattus norvegicus</i> ): cell lines RGC5 and R28  |
| <b>Short Description</b>               | Several cell lines to study signalling pathways and the efficacy/toxicity of neuroprotective compounds.<br>Cell line 661W cell line provide a tool to study photoreceptor. From Dr. Muayyad R. Al-Ubaidi.<br>Cell line RGC5 cell line provide a tool to study ganglion cells. From Dr. Agarwal.<br>Cell line R28 cell line provide a tool to study several retinal cell types. From Dr. Seigel.<br>Cell line MU-PH1 cell line provide a tool to study Stem cells/photoreceptors. From University of Alicante.   |
| <b>Scientific Publications</b>         | - Al-Ubaidi MR, Matsumoto H, Kurono S, Singh A. <b>Proteomics profiling of the cone photoreceptor cell line, 661W recent advances in retinal degeneration.</b> Advances in Experimental Medicine and Biology. 2008; 613:301-11<br>- Krishnamoorthy, R.R. Agarwal, P. Prasanna G, Vopat, K. Lambert, W. Sheedlo, H.J. Pang I.-H.. Shade, D. Wordinger, R.J.. Yorio, T Clark, A.F Agarwal. N. <b>Characterization of a transformed rat retinal ganglion cell line.</b> Molecular Brain Research. 2001; 86;1:1-12<br>- Seigel GM, Mutchler AL, Adamus G, Imperato-Kalmar EL. <b>Recoverin expression in the R28 retinal precursor cell line.</b> In Vitro Cell Dev Biol Anim. 1997; 33(7):499-502<br>- Gómez-Vicente V, Flores A, Lax P, Murciano C, Yáñez A, Gil MI, Cuenca N, Gozalbo D, Maneu V. <b>Characterization of a new murine retinal cell line (MU-PH1) with glial, progenitor and photoreceptor characteristics.</b> Exp Eye Res. 2013 |
| <b>Institution</b>                     | University of Alicante, Alicante  |

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| <b>Experimental Model</b><br><b>35</b> | <b>Achondroplasia (RCJ3.1C5.18 cell line)</b>   |
| <b>Target Disease</b>                  | Achondroplasia  |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ): RCJ3.1C5.18 cell line   |
| <b>Short Description</b>               | RCJ3.1C5.18 cells, a chondrogenic precursor cell line derived from multipotential mesenchymal rat stem cells were transfected with full-length human mutant FGF receptor type 3, ACH FGF receptor type 3 (FGF receptor type 3G380R). Expression of FGF receptor type 3 was regulated by a tetracycline suppression system, the receptor is expressed in the absence of tetracycline in the culture medium. We have tested the ability of pyridoxal-5'-phosphate-6-azophenyl-2', 4'-disulfonate (PPADS) to decrease the overactivation and signalling of FGF receptor type 3 in achondroplastic chondrocytes. PPADS reduced the tyrosine phosphorylation of FGF receptor type 3 triggered by fibroblast growth factor 9 (FGF9) (50% reduction), as well as the activation of extracellular signal-regulated kinases 1 and 2 (ERK1/2) pathway. As a consequence of this inhibitory effect on ERK1/2 activity the loss of extracellular matrix was also reversed by PPADS. The action of PPADS seems to be due to a mechanism independent of P2 receptor antagonism. |
| <b>Scientific Publications</b>         | - Guzmán-Aránguez A, Crooke A, Yayon A, Pintor J. <b>Effect of PPADS on achondroplastic chondrocytes: Inhibition of FGF receptor type 3 over-activity</b> . European Journal of Pharmacology. 2008; 584:72–77   |
| <b>Institution</b>                     | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid   |

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| <b>Experimental Model</b><br><b>36</b> | <b>Alzheimer's disease (B6C3-Tg(APPswe,PSEN1dE9)85Dbo/J)</b>  |
| <b>Target Disease</b>                  | Alzheimer's   |
| <b>Species</b>                         | Mouse ( <i>Mus musculus</i> ): B6C3-Tg(APPswe,PSEN1dE9)85Dbo/J  |
| <b>Short Description</b>               | Double transgenic mice express a chimeric mouse/human amyloid precursor protein (Mo/HuAPP695swe) and a mutant human presenilin 1 (PS1-dE9) both directed to CNS neurons. Both mutations are associated with early-onset Alzheimer's disease. The "humanized" Mo/HuAPP695swe transgene allows the mice to secrete a human A-beta peptide. Both the transgenic peptide and holoprotein can be detected by antibodies specific for human sequence within this region (Signet Laboratories' monoclonal 6E10 antibody). The included Swedish mutations (K595N/M596L) elevate the amount of A-beta produced from the transgene by favoring processing through the beta-secretase pathway. This "humanized" Mo/HuAPP695swe protein is immunodetected in whole brain protein homogenates. The transgenic mutant human presenilin protein (PS1-dE9), which in high levels displaces detectable endogenous mouse protein, is also immunodetected in whole brain protein homogenates. The donating investigator reports that transgenic mice develop beta-amyloid deposits in brain by six to seven months of age. |
| <b>Scientific Publications</b>         | - Bakalash S; Pham M; Koronyo Y; Salumbides BC; Kramerov A; Seidenberg H; Berel D; Black KL; Koronyo-Hamaoui M. <b>Egr1 expression is induced following glatiramer acetate immunotherapy in rodent models of glaucoma and Alzheimer's disease.</b> Invest Ophthalmol Vis Sci. 2011; 52(12): 9033-46.<br><br>- Reiserer RS; Harrison FE; Syverud DC; McDonald MP. <b>Impaired spatial learning in the APP + PSEN1DeltaE9 bigenic mouse model of Alzheimer's disease.</b> Genes Brain Behav. 2007; 6(1):54-65.  |
| <b>Institution</b>                     | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid   |

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| <b>Experimental Model</b><br><b>37</b> | <b>Experimental Glaucoma</b>   |
| <b>Target Disease</b>                  | Glaucoma (IOP)   |
| <b>Species</b>                         | Rabbit ( <i>Oryctolagus cuniculus</i> ): New Zealand White   |
| <b>Short Description</b>               | New Zealand white rabbits IOP modifications measured by Tonopen XL after applying substances like Adenosine tetraphosphate or antagonists of adrenoceptors and cholinceptors, Ap4.         |
| <b>Scientific Publications</b>         | - Pintor J, Peláez T, Peral A. <b>Adenosine Tetraphosphate, Ap4, a Physiological Regulator of Intraocular Pressure in Normotensive Rabbit Eyes.</b> J Pharmacol Exp Ther. 2004 308:468-473 |
| <b>Institution</b>                     | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid  |

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| <b>Experimental Model</b><br><b>38</b> | <b>Glaucoma (Rabbit non-pigmented ciliary epithelium cell line)</b>   |
| <b>Target Disease</b>                  | Glaucoma (PIO)  |
| <b>Species</b>                         | Rabbit ( <i>Oryctolagus cuniculus</i> )   |
| <b>Short Description</b>               | We have demonstrated that 5-methoxycarbonylamino-N-acetyltryptamine (5-MCA-NAT), reduces intraocular pressure (IOP) in rabbits. In addition, we have reported a link between hypotensive effect of 5-MCA-NAT and sympathetic nervous system. Moreover, it is known that aqueous humour production is controlled by the activation of adrenoceptors (ADRs) present in the ocular ciliary epithelium. Thus, the aim of this study is to investigate if the hypotensive effect of 5-MCA-NAT is due to a regulation of ciliary ADR genes expression. To confirm this we followed the effect of 5-MCA-NAT on rabbit IOP for 144 consecutive hours. A sustained IOP reduction for up to 72 h (P<0.01) was seen. In addition, changes in ADRB2 and ADRA2A mRNA were measured in cultured rabbit nonpigmented ciliary epithelial cells. After 5-MCA-NAT treatment, a significant downregulation of ADRB2 and upregulation of ADRA2A was observed. These results provide the regulation of ADRs mRNA by 5-MCA-NAT. |
| <b>Scientific Publications</b>         | - Crooke A, Huete-Toral F, Martínez-Águila A, Alarma-Estrany P, Pintor J. <b>Regulation of ocular adrenoceptor genes expression by 5-MCA-NAT: implications for glaucoma treatment.</b> Pharmacogenetics and Genomics. 2011; 21(9):587-9   |
| <b>Institution</b>                     | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid   |

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| <b>Experimental Model</b><br><b>39</b> | <b>Ocular Infection (Immortalized Human Corneal Limbal Epithelial Cells (HCLEC))</b>  |
| <b>Target Disease</b>                  | Ocular Infection  |
| <b>Species</b>                         | Human   |
| <b>Short Description</b>               | We utilized a stable tetracycline-inducible RNA interfering system targeting the core 1 $\beta$ 1,3-galactosyltransferase (C1galt1 or T-synthase), a critical galactosyltransferase required for the synthesis of core 1 O-glycans, to explore the role of mucin-type carbohydrates in apical endocytic trafficking in human corneal keratinocytes. Using cell surface biotinylation and subcellular fractionation, we found increased accumulation of plasma membrane protein in endosomes after C1galt1 depletion. Confocal laser scanning microscopy and fluorometry revealed increased translocation of negatively charged fluorescent nanospheres after C1galt1 knockdown sustained by an active transport process and largely independent of apical intercellular junctions. Internalization of nanospheres could be blocked by dynasore, nocodazole, chlorpromazine, and hyperosmotic sucrose, suggesting a mechanism for clathrin-coated pit budding and vesicular trafficking. This possibility was supported by experiments showing nanosphere colocalization with clathrin heavy chain in the cytoplasm. |
| <b>Scientific Publications</b>         | - Guzman-Arangué A, Woodward AM, Pintor J, Argüeso P. <b>Targeted Disruption of Core 1 <math>\beta</math>1,3-galactosyltransferase (C1galt1) Induces Apical Endocytic Trafficking in Human Corneal Keratinocytes.</b> PLoS ONE. 2012; 7 (5): e36628. doi:10.1371/journal.pone.0036628   |
| <b>Institution</b>                     | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid   |

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| <b>Experimental Model<br/>40</b>              | <b>Ocular infection (Immortalized Human Conjunctival Epithelial Cell Lines (HCjE))</b>   |
| <b>Target Disease</b>                         | Ocular infection   |
| <b>Species</b>                                | Human  |
| <b>Short Description<br/>(max. 250 words)</b> | The immortalized conjunctival (HCjE) cell lines exhibit the mucin gene expression repertoire of their native epithelia. These cell lines will be useful in determining regulation of ocular surface mucin gene expression and, potentially, goblet cell differentiation. |
| <b>Scientific Publications</b>                | - Gipson IK, Spurr-Michaud S, Argüeso P, Tisdale A, Ng TF, Russo CL. <b>Mucin Gene Expression in Immortalized Human Corneal-Limbal and Conjunctival Epithelial Cell Lines</b> . Invest Ophthalmol Vis Sci. 2003; 44(6)   |
| <b>Institution</b>                            | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid  |

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| <b>Experimental Model</b><br><b>41</b> | <b>Retinal ganglion cells (RGC) degeneration (DBA/2J)</b>  |
| <b>Target Disease</b>                  | Degeneration of retinal ganglion cells   |
| <b>Species</b>                         | Mouse ( <i>Mus musculus</i> ): DBA/2J  |
| <b>Short Description</b>               | <p>DBA/2J is a widely used inbred strain that is valuable in a large number of research areas, including cardiovascular biology, neurobiology, and sensorineural research.</p> <p>Aging DBA/2J mice develop progressive eye abnormalities that closely mimic human hereditary glaucoma. Defects include iris pigment dispersion, iris atrophy, anterior synechia (adhesion of the iris to the cornea), and elevated intraocular pressure (IOP). The onset of disease symptoms begins between three and four months of age with 56% of females and 15% of males showing signs of iris pigment epithelium loss and transillumination of the peripheral iris. By six to seven months of age, all mice demonstrate significant widespread transillumination and thickening of the iris border. Elevation of IOP is evident in some females by six months of age. By nine months of age, both sexes exhibit elevated IOP, with pressures higher in females (mean: 20.3 +/-79; 1.8 mmHg) compared to males (mean: 16.2 +/-79; 1.4 mmHg). Retinal histopathology reveals retinal ganglion cell, as well as GABAergic and cholinergic amacrine cell, loss. (Moon JI <i>et al.</i> 2005). Two alleles contribute to the eye phenotype, <i>GpnmbR150X</i> and <i>Tyrp1sa</i>; both are present in DBA/2J mice.</p> |
| <b>Scientific Publications</b>         | <p>- Anderson MG, Smith RS, Hawes NL, Zabaleta A, Chang B, Wiggs JL, John SWM. <b>Mutations in genes encoding melanosomal proteins cause pigmentary glaucoma in DBA/2J mice.</b> Nature Genetics. 2001; 30, 81-85</p> <p>- John SWM, Smith RS, Savinova OV, Hawes NL, Chang B, Turnbull D, Roderick MDTH, Heckenlively JR. <b>Essential Iris Atrophy, Pigment Dispersion, and Glaucoma in DBA/2J Mice.</b> Invest Ophthalmol Vis Sci. 1998; 39(6)</p>  |
| <b>Institution</b>                     | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid  |

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| <b>Experimental Model</b><br><b>42</b> | <b>Retinal degeneration/Glaucoma (Ganglion cell line)</b>   |
| <b>Target Disease</b>                  | Retinal degeneration and Glaucoma   |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ): Transformed Rat Retinal Ganglion Cell Line  |
| <b>Short Description</b>               | Retinal cells were isolated from postnatal day 1 (PN1) rats and transformed with the c2 E1A virus. In order to isolate retinal ganglion cells (RGC), single cell clones were chosen at random from the transformed cells. Expression of Thy-1 (a marker for RGC), glial fibrillary acidic protein (GFAP, a positive marker for Muller cells), HPC-1/ syntaxin (a marker for amacrine cells), 8A1 (a marker for horizontal and ganglion cells) and neurotrophins was studied using reverse transcriptase-polymerase chain reaction (RT-PCR), immunoblotting and immunocytochemistry. One of the retinal cell clones, designated RGC-5, was positive for Thy-1, Brn-3C, Neuritin, NMDA receptor, GABA-B receptor, and synaptophysin expression and negative for GFAP, HPC-1, and 8A1, suggesting that it represented a putative RGC clone. The results of RT-PCR analysis were confirmed by immunocytochemistry for Thy-1 and GFAP. These cells may be valuable in understanding of retinal ganglion cell biology and physiology including in vitro manipulations in experimental models of glaucoma. |
| <b>Scientific Publications</b>         | - Krishnamoorthy RR, Agarwal P, Prasanna G, Vopat K, Lambert W, Sheedlo HJ, Pang IH, Shade D, Wordinger RJ, Yorio T, Clark AF, Agarwal N. <b>Characterization of a transformed rat retinal ganglion cell line.</b> Molecular Brain Research. 2001; 86:1–12  |
| <b>Institution</b>                     | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid   |

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| <b>Experimental Model</b><br>43 | <b>Experimental corneal wound healing</b>  |
| <b>Target Disease</b>           | Corneal wound healing  |
| <b>Species</b>                  | Rabbit ( <i>Oryctolagus cuniculus</i> ): New Zealand White   |
| <b>Short Description</b>        | Corneal wounds were made in both eyes by anaesthetising the animals. After topical anaesthesia with oxibuprocaine and tetracaine corneal wounds were made to the epithelia of both eyes by applying a 3-mm disc of Whatman no. 1 paper soaked in n-heptanol. Discs were placed in the centre of the cornea and left there for 30 s (Cintron et al., 1979). Eyes were washed repeatedly with isotonic saline solution. The wounds were stained with 2% fluorescein and eyes were examined with a slit lamp. Images were taken, managed and analysed with appropriated software. |
| <b>Scientific Publications</b>  | - Pintor J, Bautista A, Carracedo G, Peral A. <b>UTP and diadenosine tetraphosphate accelerate wound healing in the rabbit cornea.</b> Ophthalmic and Physiological Optics. 2004; 24: 186–193<br>- Mediero A, Guzmán-Aranguez A, Crooke A, Peral A, Pintor J. <b>Corneal re-epithelialization stimulated by diadenosine polyphosphates recruits RhoA/ROCK and ERK1/2 pathways.</b> Invest Ophthalmol Vis Sci. 2008; 49(11): 4982-92  |
| <b>Institution</b>              | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid  |

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| <b>Experimental Model<br/>44</b> | <b>Corneal wound healing (Rabbit corneal cell line)</b>   |
| <b>Target Disease</b>            | Corneal wound healing   |
| <b>Species</b>                   | Rabbit ( <i>Oryctolagus cuniculus</i> ): Corneal cell line, SIRC (Statens Seruminstitut Rabbit Cornea)  |
| <b>Short Description</b>         | Rabbit <i>P2Y<sub>2</sub>-R</i> cDNA was cloned using a combination of degenerate reverse transcription polymerase chain reaction (RT-PCR) and rapid amplification of cDNA ends (RACE). To test the efficacy of synthesized siRNAs targeting <i>P2Y<sub>2</sub>-R</i> , immunocytochemistry, immunohistochemistry, and quantitative RT-PCR (qRT-PCR) assays were performed. Migration assays were performed both in vitro and in vivo by wounding the epithelium with a pipette tip and n-heptanol, respectively. These wounds were performed 72 h after siRNA transfection either in the presence or the absence of the P2Y <sub>2</sub> agonist, 100 μM Ap <sub>4</sub> A (diadenosine tetraphosphate). |
| <b>Scientific Publications</b>   | - Crooke A, Mediero A, Guzmán-Aránguez A, Pintor J. <b>Silencing of P2Y<sub>2</sub> receptor delays Ap<sub>4</sub>A-corneal re-epithelialization process</b> . Mol Vis. 2009; 15: 1169–1178.  |
| <b>Institution</b>               | Biochemistry and Molecular Biology IV Department, Faculty of Optics and Optometry, University Complutense of Madrid, Madrid   |

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| <b>Experimental Model</b><br>45 | <b>Experimental glaucoma</b>   |
| <b>Target Disease</b>           | Glaucoma   |
| <b>Species</b>                  | Rabbit ( <i>Oryctolagus cuniculus</i> ): New Zealand White   |
| <b>Short Description</b>        | Experimental glaucoma is produced by unilateral injection of 0.86 mg of $\alpha$ -chymotrypsin diluted in 0.13 of saline into the posterior chamber. This enzyme exerts effects on aqueous humor outflow routes and induces glaucoma in 82% of the animals. The animals show an IOP increase and glaucomatous cupping of optic disc. Elevated IOP is observed as soon as 72 h post injection and remain significantly higher than control 40 days after injection.   |
| <b>Scientific Publications</b>  | <p>- Fernández R, Triviño A, Ramírez JM, García M, Ramírez AI, Salazar JJ, Fernández A, Gutkowska J. <b>Immunoreactive atrial natriuretic factor in aqueous humor: Its concentration is increased with high intraocular pressure in rabbit eyes</b>. Vision Res. 1990; 30: 1305-1310.</p> <p>- Fernandez R, Ramírez JM, Triviño A, Sánchez B, Paraiso P, García M, Ramírez AI, Salazar JJ, Fernández-Cruz A, Gutkowska J. <b>Experimental glaucoma significantly decreases atrial natriuretic factor (ANF) receptors in the ciliary proceses of the rabbit eye</b>. Exp Eye Res. 1991; 53: 591-596</p> |
| <b>Institution</b>              | Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, University Complutense of Madrid, Madrid  |

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| <b>Experimental Model</b><br><b>46</b> | <b>Chorioretinal ischemia induced by hypercholesterolemia</b>   |
| <b>Target Disease</b>                  | Age-related macular degeneration (MAD) , ischemia, atherosclerosis  |
| <b>Species</b>                         | Rabbit ( <i>Oryctolagus cuniculus</i> ): New Zealand White  |
| <b>Short Description</b>               | <p>Laboratory rabbits have been widely used for the study of atherosclerosis for several reasons: they exhibit hypercholesterolemia within a few days of administration of a cholesterol-enriched diet and high sensitivity to the inducement of atheromatic lesions similar to human.</p> <p>The hypercholesterolemia is induced feeding the rabbits with a standard diet enriched with 0.5% cholesterol for 8 months.</p> <p>Weight and serum samples are recorded immediately before the experiment and monitored monthly thereafter. Serum values of total cholesterol, triglycerides, phospholipids, high-density lipoproteins (HDL), low-density lipoproteins (LDL) and very-low-density lipoproteins (VLDL) are analyzed. Blood samples are taken from the marginal vein of the ear and analyzed with commercially available enzymatic kits following the manufacturer's instructions.</p>   |
| <b>Scientific Publications</b>         | <ul style="list-style-type: none"> <li>- Triviño A, Ramírez AI, Salazar JJ, De Hoz R, Rojas B, Padilla E, Tejerina T, Ramírez JM. <b>A cholesterol-enriched diet induces ultrastructural changes in retinal and macroglial rabbit cells.</b> Exp Eye Res. 2006; 83: 357-366</li> <li>- Salazar JJ, Ramírez AI, De Hoz R, Ruiz E, Tejerina T, Triviño A, Ramírez JM. <b>Alterations in the choroid in hypercholesterolemic rabbits: reversibility after normalization of cholesterol levels.</b> Exp Eye Res. 2007; 84: 412-422.</li> <li>- Ramírez AI, Salazar JJ, De Hoz R, Rojas B, Ruiz E, Tejerina T, Ramírez JM, Triviño A. <b>Macroglial and retinal changes in hypercholesterolemic rabbits after normalization of cholesterol levels.</b> Exp Eye Res. 2006; 83: 1423-38.</li> <li>- Rojas B, Ramirez AI, Salazar JJ, de Hoz R, Redondo A, Raposo R, Mendez, MT, Tejerina MT, Triviño A, Ramirez JM. <b>Low-dosage statins reduce choroidal damage in hypercholesterolemic rabbits.</b> Acta Ophthalmol. 2011; 89: 660-669.</li> <li>- Salazar JJ, Ramírez AI, de Hoz R, <b>Rojas B</b>, Ruiz E, Tejerina T, Triviño A, Redondo AM, Ramírez JM. <b>A cholesterol-enriched diet induces ultrastructural changes in the retina and optic nerve of rabbits.</b> In: Glial Cells in Health and Disease (Proceedings of the The VIII European Meeting). Bologna; Medimond, eds. 2007; pages: 35-39.</li> <li>- Ramírez JM, Salazar JJ, de Hoz R, Rojas B, Gallego BI, Ramírez AI, Triviño A. <b>Choroidal vessel wall: hypercholesterolaemia-induced dysfunction and potential role of statins.</b> In: Current Basic and Pathological Approaches to the Function of Muscle Cells and Tissues - From Molecules to Humans. Haruo Sugi (Ed.) 2012; chapter 12, pages: 255-298.</li> <li>- Triviño A, de Hoz R, Rojas B, Gallego BI, Ramírez AI, Salazar JJ, Ramírez JM. <b>Effects of Hypercholesterolemia in the retina.</b> In: Ocular Diseases. Adedayo Adio (Ed.) 2012; chapter 1, pages: 1-42.</li> </ul> |
| <b>Institution</b>                     | Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, University Complutense of Madrid, Madrid   |

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| <b>Experimental Model</b><br>47 | <b>Laser photocoagulation of the retina and choroid</b>  |
| <b>Target Disease</b>           | Sight-impairing retinal disorders, such as age-related macular degeneration (AMD), and advanced stages of this disease, including choroidal neovascular elements.  |
| <b>Species</b>                  | Rabbit ( <i>Oryctolagus cuniculus</i> ): New Zealand White   |
| <b>Short Description</b>        | Transpupillary photocoagulation is performed by diode laser emitting at a wavelength of 810nm. Laser parameters used are 200 μm spot size; 150 mW power and 0.2 sec exposure time. The laser can be applied as a single-pulse mode or as a micropulsed mode (frequency 100 Hz).  |
| <b>Scientific Publications</b>  | - Triviño A, Ramírez JM, Andrés MV, Salazar JJ, Ramírez AI, García-Sánchez J. <b>Comparison between chorioretinal effects of the single-pulse versus micropulsed diode laser in pigmented rabbits.</b> Laser and Light 1997; 8: 31-38.<br>- Gómez-Ulla F, Marín F, Ramírez JM, Triviño A. <b>La mácula senil.</b> Barcelona; Edika-Med S.A. 1993. 250 pages. |
| <b>Institution</b>              | Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, University Complutense of Madrid, Madrid  |

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| <b>Experimental Model</b>      | <b>Organotypic retinal cultures</b>  |
| <b>48</b>                      |  |
| <b>Target Disease</b>          | Retinal diseases   |
| <b>Species</b>                 | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )  |
| <b>Short Description</b>       | <p>Organotypic cell cultures provide a convenient tool for studying the development of the CNS. They permit the manipulation of fluid and cell environments and are therefore an ideal complement to studies in vivo. Moreover, organotypic cultures have the advantage of retaining their cytoarchitecture, a condition that cannot be fulfilled by dissociated or reaggregate cell cultures. In addition, they are an useful tool to perform preclinical drug testing.</p> <p>Neonatal murine animals are quickly decapitated and the eyes are immediately enucleated under sterile conditions. Eyeballs are maintained in sterile medium enriched with glucose and after enzymatic digestion, the retina and the attached pigment epithelium are dissected. Following dissection, four radial cuts are made to flatten the tissue. The retina with the pigment epithelium are placed with the ganglion cell layer facing up into the upper compartment of a culture chamber containing sterile enriched medium in the lower compartment. The explants are maintained in an incubator with an atmosphere of 5% CO<sub>2</sub>, balanced air and 100% humidity at 37°C. The medium is changed the first day in culture and every second day thereafter. After days in vitro the cultures could be fixed for analysis under light microscopy or electron microscopy.</p> |
| <b>Scientific Publications</b> | Ongoing  |
| <b>Institution</b>             | Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, University Complutense of Madrid, Madrid  |

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| <b>Experimental Model</b><br><b>49</b> | <b>Experimental glaucoma</b>   |
| <b>Target Disease</b>                  | Glaucoma   |
| <b>Species</b>                         | Rat ( <i>Rattus norvegicus</i> ), Mouse ( <i>Mus musculus</i> )  |
| <b>Short Description</b>               | <p>The induction of unilateral ocular hypertension is achieved in anesthetized rats or mice by treating the animals in a single session with a series of diode laser burns. The laser beam is directly delivered without any lenses, aimed at the limbal and episcleral veins. The spot size, duration, and power are 50-100 <math>\mu\text{m}</math>, 0.5 s and 0.3 W, respectively. Each eye received between 55-76 burns.</p> <p>In rats, the IOP increases between 34 and 125% over the baseline within the first 72 h after lasering and peak at 12 h. At 1 and 2 weeks the IOP is approximately 35 and 39% over baseline. By three weeks the IOP starts to decline, acquiring close to normal levels at 12 weeks.</p> <p>In mice, a substantial increase of the IOP is evident 24h after lasering, this continuing for 4 days and then gradually returning to the basal value after the fifth day, so that by one week after lasering, the IOP values in the treated animals are comparable for both eyes.</p> |
| <b>Scientific Publications</b>         | <p>- Ramírez AI, Salazar JJ, de Hoz R, Rojas B, Gallego BI, Salinas-Navarro M, Alarcón-Martínez L, Ortín-Martínez A, Avilés-Trigueros M, Vidal-Sanz M, Triviño A, Ramírez JM. <b>Quantification of the effect of different levels of IOP in the astroglia of the rat retina ipsilateral and contralateral to experimental glaucoma.</b> Invest Ophthalmol Vis Sci. 2010; 5:5690-5696.</p> <p>- Gallego BI, Salazar JJ, de Hoz R, Rojas B, Ramírez AI, Salinas-Navarro M, Ortín-Martínez A, Valiente-Soriano FJ, Avilés-Trigueros M, Villegas-Pérez MP, Vidal-Sanz M, Triviño A, Ramirez JM. <b>IOP induces upregulation of GFAP and MHC-II and microglia reactivity in mice retina contralateral to experimental glaucoma.</b> J Neuroinflammation. 2012; 9(1):92.</p>   |
| <b>Institution</b>                     | Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, University Complutense of Madrid, Madrid  |

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| <b>Experimental Model</b><br>50 | <b>Chronic Glaucoma induction by a series of intracameral injections of hyaluronic acid (Wistar rat)</b>   |
| <b>Target Disease</b>           | Glaucoma   |
| <b>Species</b>                  | Rat ( <i>Ratus Norvergicus</i> ): wistar   |
| <b>Short Description</b>        | <p>Wistar rats (aged 6 months) were weekly injected during 10 consecutive weeks in the anterior chamber with either high density hyaluronic acid (left eyes) or balanced salt solution (right eyes). Other rats were used as the controls. Intraocular pressure and electrorretinograms were performed.</p> <p>After euthanized, rat aqueous humor (AH) was collected in criotubes, while the retina and optic nerve were processed to morphologic, morphometric and immunohistochemic assays.</p> <p>Protons available in metabolites can be managed by high resolution nuclear magnetic resonance (1H-NMR) spectroscopy, to simultaneously quantify metabolites within biological fluids, according to their chemical shift.</p> <p>Metabolomic profile of the AH was assessed in this chronic glaucoma rat model to better understand biochemical mechanisms related to the AH homeostasis in normal and pathologic conditions.</p> <p>Microscopic data mimics glaucomatous retinal-optic nerve changes, validating our rat chronic glaucoma model.</p> <p>Furthermore, a database of 1H-NMR from various AH metabolites were obtained. Compounds identified as alanine, valine, lysine, leucine, tyrosine, fenilalanine, N-acetil glutamate, acetoacetate, glutamine, taurine, oxo-glutarate, glucose, VLDL cholesterol, and lactate correlated well with data from conventional techniques, but significantly different relative intensity values were found in the AH spectrums from the glaucoma eyes, as compared to both the sham-operated and control rats. With this rat chronic glaucoma model, a different metabolomic profile was detected in the aqueous humor.</p> |
| <b>Scientific Publications</b>  | - Mayordomo A, Lopez-Murcia M, Morales JM, Diaz-Llopis M, Pinazo-Durán MD, <b>Metabolomics of the aqueous humor in glaucomatous rats.</b> Ophthalmic Res 2013.   |
| <b>Institution</b>              | Ophthalmic Research Unit "Santiago Grisolia", Faculty of Medicine, University of Valencia, Valencia  |

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| <b>Experimental Model</b><br>51 | <b>Proliferation, apoptosis and angiogenesis in ophthalmic diseases (C57BL/6 mouse)</b>  |
| <b>Target Disease</b>           | Retinopathies  |
| <b>Species</b>                  | Mice ( <i>Mus Musculus</i> ): C57BL/6  |
| <b>Short Description</b>        | <p>Adult C57BL/6 mice were genetically manipulated to obtain transgenic mice with two extra copies of p53 gene (super p53; sp53-tg/tg) by Prof. Manuel Serrano (National Center for Oncology Research; CNIO, Madrid). This model has been extensively used for ophthalmic studies by our research group. The p53 gene encodes for proteins that regulates cell cycle. Our main goal is to analyse the role of p53 gene in the molecular events involving retinal angiogenesis and/or apoptosis.</p> <p>Increased p53 gene dosage suggest a set of actions in mice retina mainly by regulating the sensitivity to endogenous oxidative stress and by controlling the expression of molecules involved in cell proliferation, survival and death.</p>  |
| <b>Scientific publications</b>  | <ul style="list-style-type: none"> <li>- Gallego-Pinazo R, Zanón-Moreno V, Sanz S, Andrés V, Serrano M, García-Cao I, Pinazo-Durán MD. <b>Biochemical characterization of the optic nerve in mice overexpressing the P53 gen.</b> Oxidative stress assays. Arch Soc Esp Oftalmol. 2008;83:105-11.</li> <li>- Gallego-Pinazo R, Pinazo-Durán MD, Serrano M. <b>The cell cycle and gene p53. An approach to molecular ophthalmology.</b> Arch Soc Esp Oftalmol. 2010; 85:229-231.</li> <li>- Pinazo-Duran MD. <b>Genetics and something else.</b> Arch Soc Esp Oftalmol. 2012;87:35-37</li> <li>- Marco-Ramirez C, Gallego-Pinazo R, Zanon-Moreno V, Garcia-Medina JJ, Galbis-Estrada C, Ramirez-Sebastian AI. <b>P53 gene protects the retina by regulating endogenous oxidative stress.</b> Ophthalmic Res. 2013</li> <li>- Salazar JJ, Gallego-Pinazo R, De Hoz R, Rojas B, Serrano M, Pinazo-Duran MD, Ramirez-Sebastian JM. <b>Retinal astroglia display morphologic changes in the super p53 mice model.</b> Plos One 2013.</li> </ul> |
| <b>Institution</b>              | Ophthalmic Research Unit "Santiago Grisolia", Faculty of Medicine, University of Valencia, Valencia  |

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| <b>Experimental Model</b><br>52 | <b>Neuroprotection and apolipoprotein E (apoE<sup>-/-</sup> mouse)</b>  |
| <b>Target Disease</b>           | Retinopathies and Neuropathies  |
| <b>Species</b>                  | Mice ( <i>Mus Musculus</i> ): apoE <sup>-/-</sup>   |
| <b>Short Description</b>        | <p>To study the retinal astroglia by their intermediate filament protein in the apoE knock out (apoE<sup>-/-</sup>) mice.</p> <p>The apoE <sup>-/-</sup> mice and wild type counterparts eyes were processed to immunohistochemical and biochemical methods. Retinal wholemounts were immunostained with antibodies against GFAP. Retinal homogenates were processed to GFAP expression. Statistical processing was done by the SPSS 15.0 program. In comparison with naïve, astrocytes in apoE<sup>-/-</sup> mice showed several changes as follows: there was a significantly reduced astrocyte profiles density in the whole retinas. Moreover, the GFAP expression was significantly decreased; as shown by the immunohistochemical and immunoblotting assays.</p> <p>We are trying to address morphologic and molecular facts that help managing vitreo retinal disorders closely related to visual impairment.</p> <p>We speculate that apoE could enhance the protective effects of astrocytes on eye neurons and neurodegeneration disorders.</p> |
| <b>Scientific publications</b>  | <p>- Lopez-Sanchez E, Frances-Muñoz E, Diez-Juan A, Andres V, Menezo JL, Pinazo-Duran MD. <b>Optic nerve alterations in apolipoprotein E deficient mice.</b></p> <p>Eur J Ophthalmol. 2003; 13(6):560-5.</p>  |
| <b>Institution</b>              | Ophthalmic Research Unit "Santiago Grisolia", Faculty of Medicine, University of Valencia, Valencia   |

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| <b>Experimental Model<br/>53</b> | <b>Inflammation and immune response in retinal pigment epithelial cell cultures [immortalized human retinal pigment epithelial cell line (ARPE19)]: Immune aggression in vitro model</b>   |
| <b>Target Disease</b>            | Retinopathies  |
| <b>Species</b>                   | Human: cell line (ARPE19)  |
| <b>Short Description</b>         | Discrimination of potential pathogens with the toll-like receptors (TLRs) is main objective of the innate immune system. This recognition leads to expression of genes such as inflammatory cytokines and co-stimulatory molecules. We deal with analyzing the pro-inflammatory capacity of cultured human retinal pigment epithelium (RPE) in response to TLRs challenge.<br>A human RPE cell line (ARPE19) was established by trypsinization of a primary RPE culture resulting in a uniform cell population (displaying strong growth potential). We assessed pro-inflammatory TLRs-induced activation in these cells, by western-blot/immunoblotting, confocal microscopy and flow cytometry of conditioned media. PI cytokines expression-secretion is induced in RPE cultures. Unravelling the regulated activities of TLRs in RPE cells and its plasticity in immune response, new therapeutic avenues to control retinal inflammation may be revealed. |
| <b>Scientific publications</b>   | - Puchades-Lanza L, Prieto-Chinchilla P, Pinazo-Durán MD, Jiménez-Santana P, Gallego-Pinazo R, Boscá-Gomar L. <b>Pro-inflammatory capacity of ARPE19 cells in response to toll like receptors challenge</b> . Ophthalmic Res 2013.   |
| <b>Institution</b>               | Ophthalmic Research Unit “Santiago Grisolia”, Faculty of Medicine, University of Valencia, Valencia  |

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| <b>Experimental Model</b><br><br>54 | <b>Development of the visual system</b>  |
| <b>Target Disease</b>               | Ocular Malformations   |
| <b>Species</b>                      | Rat ( <i>Ratus Norvegicus</i> )  |
| <b>Short Description</b>            | <p>Rat model of Chronic Ethanol Intoxication. The foetal alcohol syndrome.<br/>Rat model of Chronic Pre- and Postnatal Exposure to drugs.</p> <p>We have been studying the ocular development in normal and pathologic conditions. Our goal was to analyse the retinal and optic nerve development by morphologic, morphometric and molecular approaches.</p> <p>We have used control rats to study by scanning, light and electron transmission microscopy the characteristics of the pre- and postnatal eye and optic nerve development at key stages (prenatal day 19 and 21; postnatal days 5, 7, 10 14. 21. 28). The retinal cells and layering were examined and several developmental parameters were analysed (retinal thickness, each retinal layer thickness, number of cell profiles, neuronal axonal and glial cell markers (Neurofilament antibody, Glial fibrillary acidic protein antibody, myelin basic protein antibody).</p> |

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| <p><b>Scientific publications</b></p> | <ul style="list-style-type: none"> <li>- Pons-Vázquez S, Gallego-Pinazo R, Galbis-Estrada C, Zanon-Moreno V, García-Medina JJ, Vila-Bou V, Sanz-Solana P, Pinazo-Durán MD. <b>Combined pre- and postnatal ethanol exposure in rats disturbs the myelination of optic axons.</b> Alcohol Alcohol. 2011;46(5):514-22.</li> <li>- Melo P, Zanon-Moreno V, Alves CJ, Magalhães A, Tavares MA, Pinazo-Duran MD, Moradas-Ferreira P. <b>Oxidative stress response in the adult rat retina and plasma after repeated administration of methamphetamine.</b> Neurochem Int. 2010;56(3):431-6.</li> <li>- Melo P, Pinazo-Durán MD, Salgado-Borges J, Tavares MA. <b>Correlation of axon size and myelin occupancy in rats prenatally exposed to methamphetamine.</b> Brain Res. 2008;1222:61-8.</li> <li>- Pons-Vázquez S, Vila-Bou V, Zanon-Moreno V, Iborra FJ, Gallego-Pinazo R, Melo PM, García-Medina JJ, Pinazo-Durán MD. <b>Study of apoptosis and mitosis mechanisms in the eye. Experimental model of gestational toxic syndrome.</b> Arch Soc Esp Oftalmol. 2008;83(1):37-44.</li> <li>- Pons S, Zanón-Moreno V, Melo P, Vila V, Gallego-Pinazo R, Pinazo-Durán MD. <b>Optic neuropathy induced by prenatal drug or alcohol exposure.</b> Arch Soc Esp Oftalmol. 2007;82(1):21-6.</li> <li>- Pinazo-Durán MD. <b>State-of-the-art in ocular malformations. Human and animal model studies.</b> Arch Soc Esp Oftalmol. 2002 Sep;77(9):473-6.</li> <li>- Melo P, Rodrigues LG, Pinazo-Durán MD, Tavares MA. <b>Methamphetamine and lipid peroxidation in the rat retina.</b> Birth Defects Res A Clin Mol Teratol. 2005;73(6):455-60.</li> <li>- Pinazo-Durán MD, Cervera R, Pons S, Zanón-Moreno VC, Gallego-Pinazo R, Guerri C. <b>Mechanisms of protein expression in the rat optic nerve. Modifications by alcohol exposure.</b> Arch Soc Esp Oftalmol. 2005;80(2):99-104</li> <li>- Melo P, Moreno VZ, Vázquez SP, Pinazo-Durán MD, Tavares MA. <b>Myelination changes in the rat optic nerve after prenatal exposure to methamphetamine.</b> Brain Res. 2006;1106(1):21-9.</li> <li>- Pons S, Zanón-Moreno V, Melo P, Vila V, Gallego-Pinazo R, Pinazo-Durán MD. <b>Optic neuropathy induced by prenatal drug or alcohol exposure.</b> Arch Soc Esp Oftalmol. 2007;82(1):21-6.</li> <li>- Strömland K, Pinazo-Durán MD. <b>Ophthalmic involvement in the fetal alcohol syndrome: clinical and animal model studies.</b> Alcohol Alcohol. 2002;37(1):2-8.</li> <li>- Gamborino MJ, Sevilla-Romero E, Muñoz A, Hernández-Yago J, Renau-Piqueras J, Pinazo-Durán MD. <b>Role of thyroid hormone in craniofacial and eye development using a rat model.</b> Ophthalmic Res. 2001;33(5):283-91</li> <li>- Pinazo-Duran MD, Renau-Piqueras J, Guerri C, Strömland K. <b>Optic nerve hypoplasia in fetal alcohol syndrome: an update.</b> Eur J Ophthalmol. 1997;7(3):262-70</li> <li>- Pinazo-Duran MD, Valles S, Guerri C, Renau-Piqueras J. <b>Gestational ethanol-induced changes in protein expression during the morphogenesis of the rat optic nerve.</b> Int J Dev Biol. 1996;Suppl 1:141S-142S.</li> <li>- Strömland K, Pinazo-Durán MD. <b>Optic nerve hypoplasia: comparative effects in children and rats exposed to alcohol during pregnancy.</b> Teratology. 1994;50(2):100-11.</li> <li>- Pinazo-Duran MD, Renau-Piqueras J, Guerri C. <b>Developmental changes in the optic nerve related to ethanol consumption in pregnant rats: analysis of the ethanol-exposed optic nerve.</b> Teratology. 1993;48(4):305-22.</li> </ul> |
| <p><b>Institution</b></p>             | <p>Ophthalmic Research Unit "Santiago Grisóla", Faculty of Medicine, University of Valencia, Valencia; and Institute of Cytological Research/Principe Felipe Research Center, Valencia</p>  |

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| <b>Experimental Model</b><br><br>55 | <b>Development of the visual system</b>   |
| <b>Target Disease</b>               | Ocular malformations and retinal diseases.  |
| <b>Species</b>                      | Rat ( <i>Ratus Norvergicus</i> )  |
| <b>Short Description</b>            | <p>Rat model of Thyroid hormone deprivation. The congenital-neonatal hypothyroidism. Hormonal neurodevelopment.</p> <p>We have been studying the ocular development in normal and pathologic conditions. Our goal was to analyse the retinal and optic nerve development by morphologic, morphometric and molecular approaches.</p> <p>We have used control rats and pre- and postnatally thyroid hormone deprived animals to study by scanning, light and electron transmission microscopy the characteristics of the pre- and postnatal eye and optic nerve development at key stages (prenatal day 19 and 21; postnatal days 5, 7, 10 14. 21. 28). The retinal cells and layering were examined and several developmental parameters were analysed (retinal thickness, each retinal layer thickness, number of cell profiles, neuronal axonal and glial cell markers (Neurofilament antibody, Glial fibrillary acidic protein antibody, myelin basic protein antibody).</p>  |
| <b>Scientific publications</b>      | <ul style="list-style-type: none"> <li>- Pinazo-Durán MD, Pons-Vázquez S, Gallego-Pinazo R, Galbis Estrada C, Zanón-Moreno V, Vila Bou V, Sanz Solana P. <b>Thyroid hormone deficiency disrupts rat eye neurodevelopment.</b> Brain Res. 2011;1392:16-26.</li> <li>- Pinazo-Durán MD, Iborra FJ, Pons S, Sevilla-Romero E, Gallego-Pinazo R, Muñoz A. <b>Postnatal thyroid hormone supplementation rescues developmental abnormalities induced by congenital-neonatal hypothyroidism in the rat retina.</b> Ophthalmic Res. 2005;37(4):225-34.</li> <li>- Sevilla-Romero E, Muñoz A, Pinazo-Durán MD. <b>Low thyroid hormone levels impair the perinatal development of the rat retina.</b> Ophthalmic Res. 2002;34(4):181-91.</li> <li>- Bort AR, Sevilla-Romero E, Gamborino MJ, Muñoz A, Pinazo-Durán MD. <b>A study on developmental characteristics of optic nerve in a rat model of materno-foetal hypothyroidism.</b> Arch Soc Esp Oftalmol. 2002;77(2):73-80</li> <li>- Pinazo-Durán MD. <b>State-of-the-art in ocular malformations.</b> Human and animal model studies. Arch Soc Esp Oftalmol. 2002;77(9):473-6.</li> <li>- Bort AR, Sevilla-Romero E, Gamborino MJ, Muñoz A, Pinazo-Durán MD. <b>A study on developmental characteristics of optic nerve in a rat model of materno-foetal hypothyroidism.</b> Arch Soc Esp Oftalmol. 2002;77(2):73-80.</li> <li>- Gamborino MJ, Sevilla-Romero E, Muñoz A, Hernández-Yago J, Renau-Piqueras J, Pinazo-Durán MD. <b>Role of thyroid hormone in craniofacial and eye development using a rat model.</b> Ophthalmic Res. 2001;33(5):283-91.</li> <li>- Pinazo-Duran MD, Renau-Piqueras J, Guerri C. <b>Developmental changes in the optic nerve related to ethanol consumption in pregnant rats: analysis of the ethanol-exposed optic nerve.</b> Teratology. 1993;48(4):305-22.</li> </ul> |
| <b>Institution</b>                  | Ophthalmic Research Unit "Santiago Grisolia", Faculty of Medicine, University of Valencia, Valencia; and * Institute of Biomedical Research Alberto Sols, CSIC, Madrid  |

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| <b>Experimental Model</b><br>56 | <b>Preclinical safety of intravitreal docosahexaenoic acid in a rabbit model</b>  |
| <b>Target Disease</b>           | Retinopathies   |
| <b>Species</b>                  | Rabbit ( <i>Oryctolagus cuniculus</i> )   |
| <b>Short Description</b>        | <p>We try to evaluate the retinal toxicity of a single dose of intravitreal pure docosahexaenoic acid (DHA) in rabbit eyes over a short-term period.</p> <p>We set up an experimental model of pre-clinical toxicity in New Zealand albino rabbits. Six concentrations of DHA were used and injected intravitreally in the right eyes. Vehicle solution was injected in the contralateral eyes. Retinal safety was studied by slit-lamp examination, electroretinography and morphologic/morphometric histological examination. Aqueous humor samples were taken to quantify the concentration of omega-3 acids by gas chromatography.</p> <p>Our results indicate that administration of intravitreal DHA is safe in the albino rabbit model up to the maximum tolerated dose of 25µg/50µl. Further studies should be performed in order to evaluate the effect of intravitreal injection of DHA as a treatment, alone or in combination, of different retinal diseases.</p> |
| <b>Scientific Publications</b>  |   |
| <b>Institution</b>              | Universitary and Polytechnic Hospital La Fe, Valencia   |