

Sapere Aude

Reflexión ante nuevos retos

hitos en las Terapias avanzadas e investigación en Oftalmología

Dr. Pastor-Idoate, PhD, FEBO





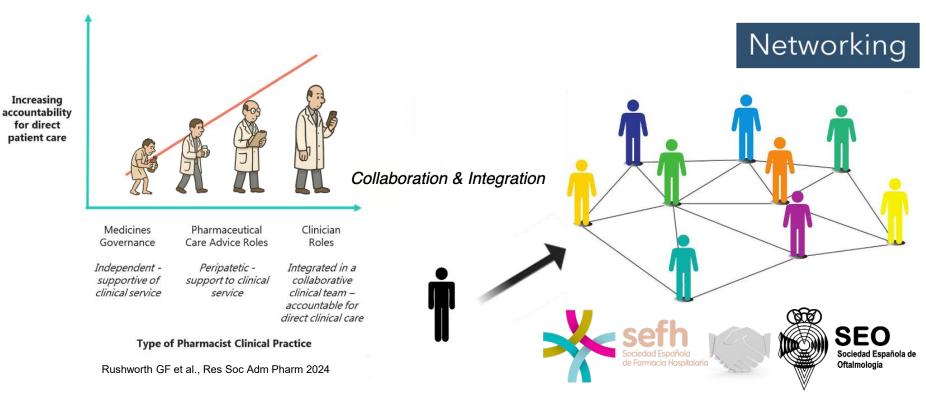




Apply the Law of Three

Do what you can, with what you have, where you are

FROM GOVERNANCE TO COLLABORATIVE CLINICAL CARE

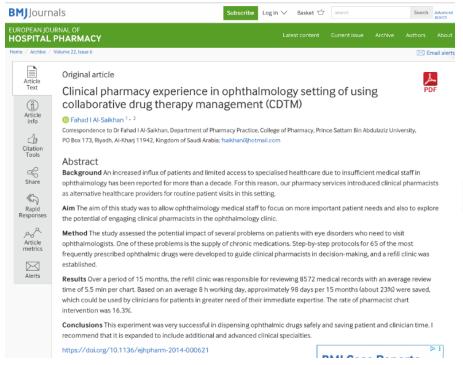


Evolving role: from governance to direct accountability in patient care

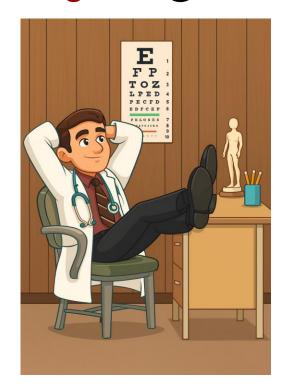
Objective: creating a collaborative network between pharmacists and ophthalmologists

Don't worry... we are not suggesting this (









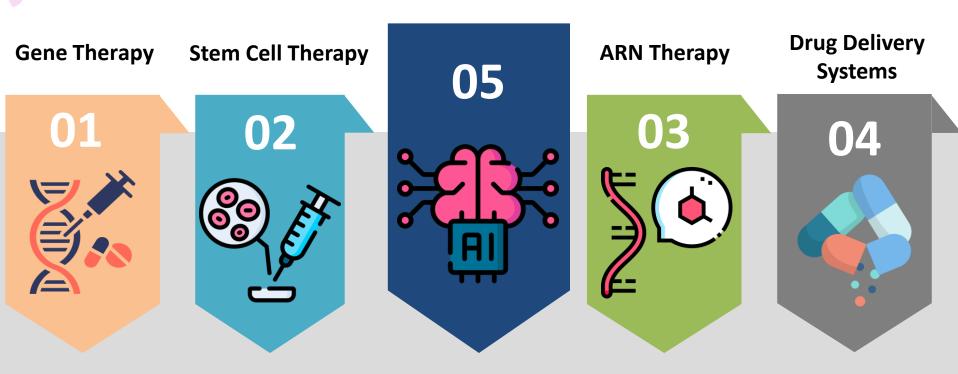
In Saudi Arabia, Clinical pharmacists even started running ophthalmology refill clinics!





05 - MILESTONES

Personalised Medicine



Importance of Gene Cell replacement therapy

World Health Organization

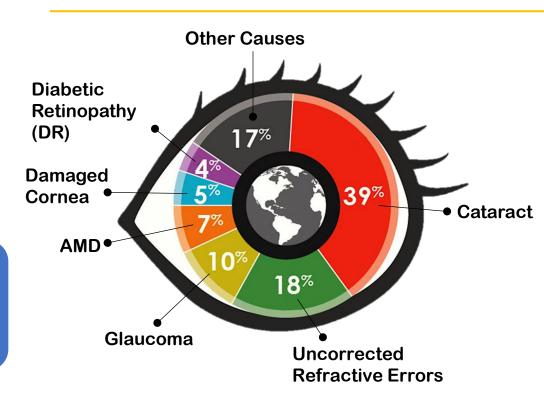
Leading Causes of Blidness Around the World

2.2 Billion people have vision impairments

In at least 1 billion could have been prevented

400 million people due to AMD, glaucoma, DR, Stargardt and RP

Global financial burden US\$

























THE EUROPEAN REFERENCE NETWORK DEDICATED TO RARE EYE DISEASES

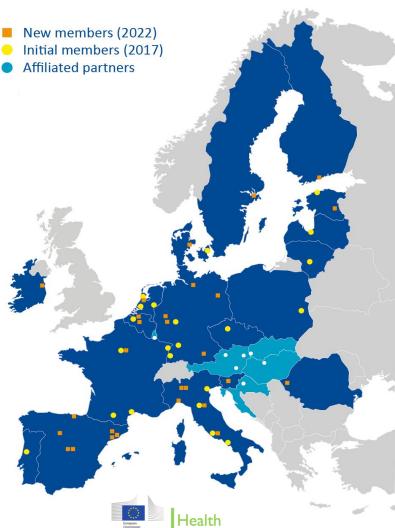






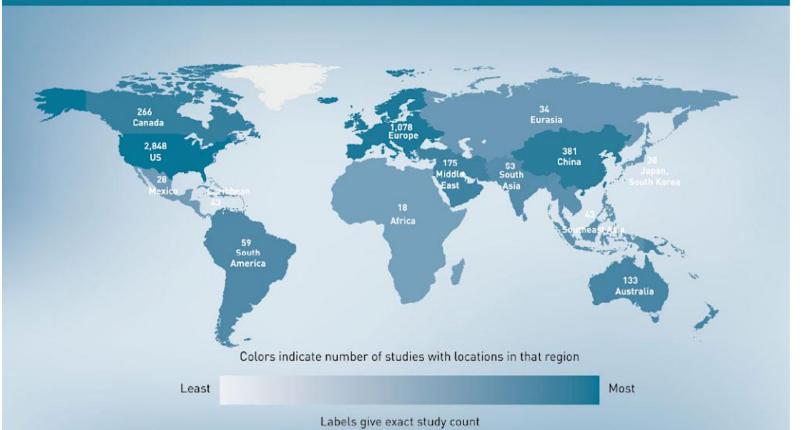


29 Hospitals 900 Rare Eye Diseases 24 000 patients in our centers



Who's Leading the Global Stem Cell Race?

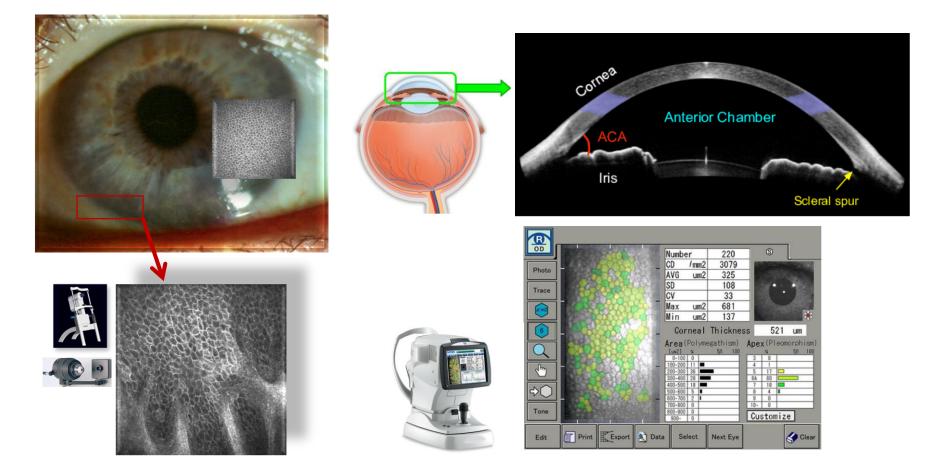
A global snapshot of which regions and countries house the most stem cell studies

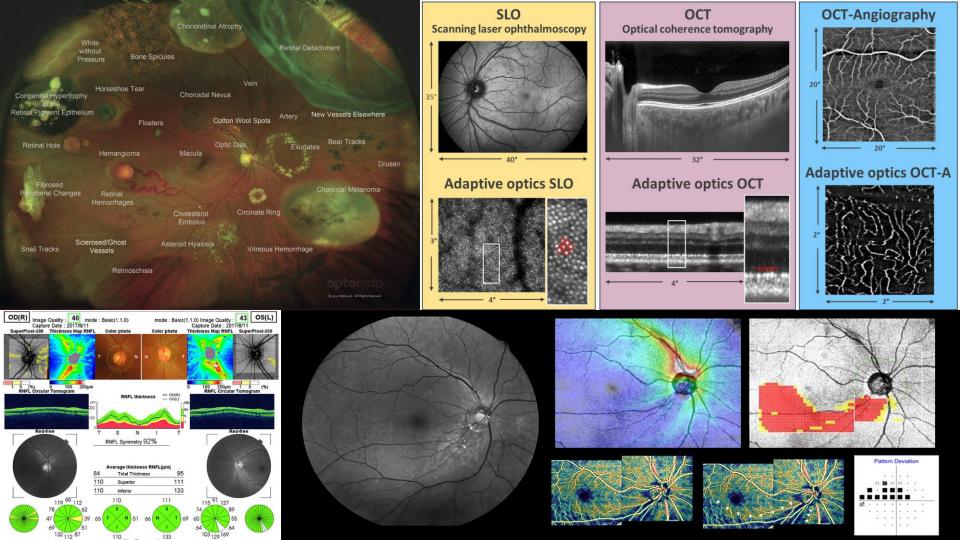


Source: UC Davis School of Medicine Professor Paul Knoepfler's blog

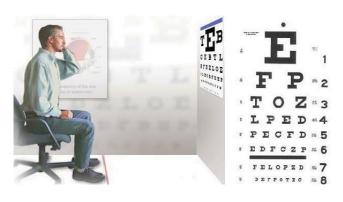


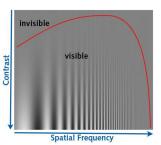
Non-invasive imaging of the ocular lesions

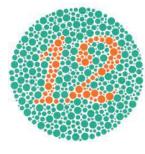


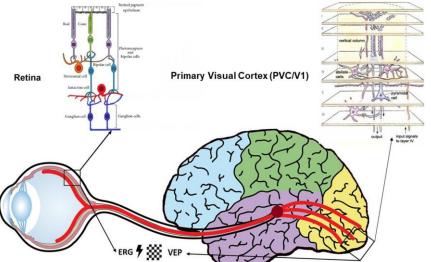


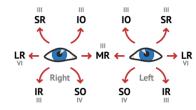
Non-invasive Functional Vision Assessment



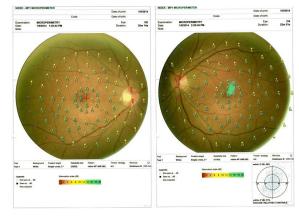


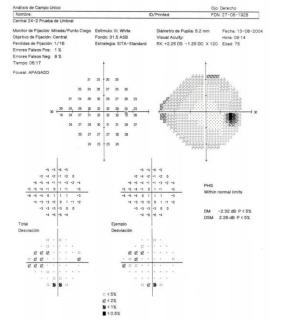












THE EYE: AN IDEAL TARGET FOR GENE AND CELL THERAPY

Accessible target organ

- √ Topical
- ✓ Intracameral
- ✓ Intravitreal
- ✓ Suprachoroidal
- ✓ Subretinal

Emerging therapies

- ✓ Gene Specific
- ✓ DNA editing
- ✓ RNA therapies
- ✓ Translational Read-through
- ✓ Stem Cell
- ✓ Optogenetics

Relative immune privilege

- ✓ Limits immune response to injected genetic material
- ✓ Blood Retinal Barrier limits systemic spread

Good progress Single gene defects / IRD's Leber's Congenital Amaurosis (Luxtuma)

(Luxturna) Retinitis Pigmentosa Stargardt Disease

Genetically heterogenous

Glaucoma
Age-related Macular
Degeneration
Diabetic Retinopathy

Direct observation

- ✓ Advanced imaging enables noninvasive monitoring of both efficacy and safety
- ✓ Can observe contralateral eye as an **in-vivo control**

Neuro-Regenerative potential

- ✓ Cell reprogramming
 - ✓ Photoreceptors
- ✓ Axon Regeneration
 - ✓ Optic Nerve

Genetic engineering and the eye. Eye 39, 57–68 (2025)

Limitations of current therapies in clinical use

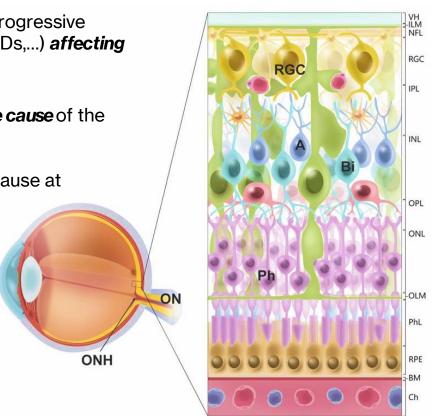
✓ The most common ocular causes of vision loss are progressive chronic eye diseases (LSCD, AMD, DR, Glaucoma, IRDs,...) affecting different types of cells at the Same time

Treatment options only treat the consequence, not the cause of the pathology

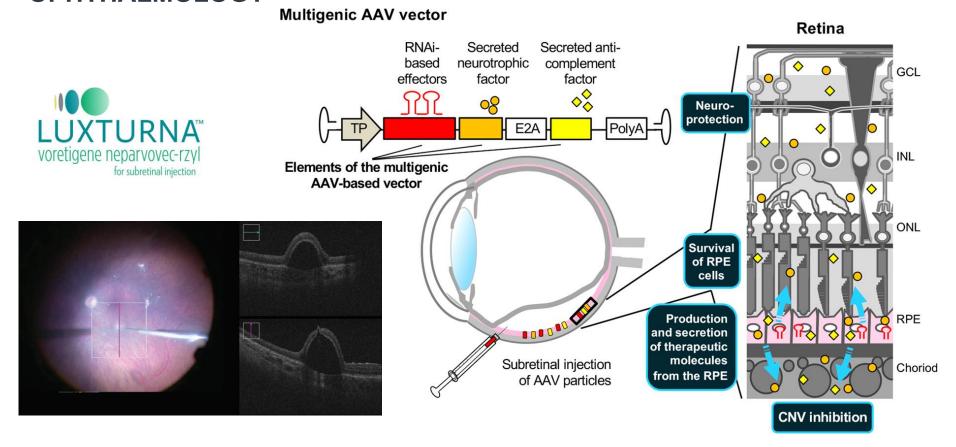
✓ There are hardly any treatment to restore vision, because at present, lost cells can not be replaced

✓ There's over 300 genes that are important for how the retina works and for which misspellings can cause retinal conditions

IRDs: Heterogenicity and genetic variability



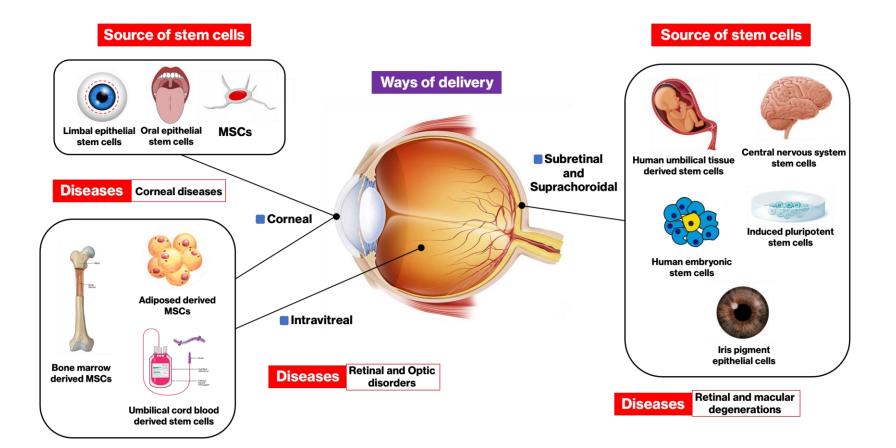
01. GENE THERAPY AS THE FIRST CLINICAL MILESTONE IN OPHTHALMOLOGY



02. OCULAR STEM CELL NICHES AND CURRENT CLINICAL STAGE

	Ocular región	Stem cells	Disease	Therapeutic/ experimental stage
	Ciliar body	Ciliar body stem cells	Ciliary body detachment	Still under study
/ /	— Iris	Iris pigment epithelial cells	Iritis/nAMD	Clinical application
	Lens	Lens stem cells	Cataractogeneis	Still under study
	— Sclera	Mesenchymal originated stem cells	Myopia	Still under study
	— Choroid	Mesenchymal originated stem cells	Ocular neurodegenerative diseases	Still under study
	Conjuntiva	Globet and epitelial cells	Conjuntival scarring, dry eye, cicatricial pemphigoid	Clinical application
	Fovea			
	Retina	Retina cells	Inherited retinal distrophy, Dry-AMD	Clinical application
	Vitreo			
	RPE	RPE cells	Inherited retinal distrophy, Dry-AMD	Clinical application
	Optic nerve			
	Cornea	Corneal stromal stem cells	Corneal scar-like disruption	Still under study
	— Pupil			
	Limbus	Limbal epithelial stem cells	Limbal stem cell deficiency	Clinical application
	Trabecular Meshwork	Mesenchymal and endothelial cells	Intraocular pressure	Still under study

Types of Stem Cells currently used for Eye?



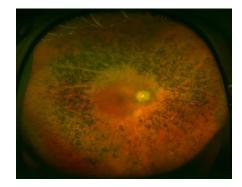
THE 8 EYE DISEASES CURRENTLY TARGETED FOR STEM CELL-BASED THERAPIES



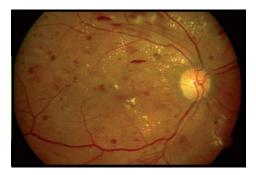
Corneal Disorders Limbal stem cell deficiency (LSCD)



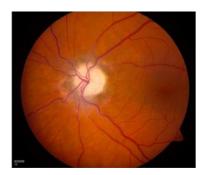
Macular Degeneration (nAMD, Dry-AMD)



Inherited Retinal Distrophy (RP, Stargardt)



Retinal Vascular Diseases (DR)



Optic Nerve Disorders (Glaucoma, optic neuritis)









Our experience: from bench to bedside

1-Stem cell-based therapy for corneal failure

2-Intravitreal MSCs for optic neuropathies















CLET: Cultured Limbal Epithelial Transplantation - 11 autologous, 9 allogeneic

Clinical Trial

> Biomed Res Int. 2015;2015:408495

Stem Cell Therapy for Corneal Epithelium Regeneration following Good Manufacturing and Clinical Procedures

Beatriz E. Ramírez, ¹ Ana Sánchez, ² José M. Herreras, ^{1,3} Itziar Fernández, ^{1,3} Javier García-Sancho, ² Teresa Nieto-Miguel, ^{1,3} and Margarita Calonge ^{1,3}

³Networking Center for Biomedical Research in Bioengineering-Biomaterials and Nanomedicine (CIBER-BBN), Carlos III National Institute of Health, Spain

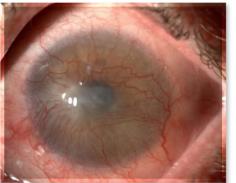




PRE Chemical burn alloCLET POST 12 m

SUCCESS

- *80% after 1 & 2 years
- •75% after 3 years
- ✓ No difference between autologous and allogeneic transplants





¹Institute of Applied Ophthalmobiology (IOBA), University of Valladolid, Campus Universitario Miguel Delibes, Pas 47011 Valladolid, Spain

²Institute of Molecular Biology and Genetics (IBGM), University of Valladolid, Valladolid, Spain

First clinical trial world-wide showing safety / efficacy of MSC in the eye

Calonge et al

AT A GLANCE COMMENTARY

Calonge M, et al.

Background

The current approach to corneal epithelial stem cell deficiency must be the replacement of stem cells. This randomized, controlled, and double-masked proof-of-concept clinical trial provides the first evidence that allogeneic bone marrow-derived mesenchymal stem cell transplantation (MSCT) to the ocular surface is as safe and as effective as allogeneic cultivated limbal epithelial cell transplantation (CLET), at facilitating recovery of potentially blinding corneal pathology due to limbal stem cell deficiency.

Translational Significance

This initial clinical success warrants the economic expenditure necessary for extensive evaluation of the mechanism of action of both CLET and MSCT before proceeding with multicenter clinical trials.

Clinical Trial

> Transl Res. 2019 Apr;206:18-40.

A proof-of-concept clinical trial using mesenchymal stem cells for the treatment of corneal epithelial stem cell deficiency

MARGARITA CALONGE, INMACULADA PÉREZ, SARA GALINDO, TERESA NIETO-MIGUEL, MARINA LÓPEZ-PANIAGUA, ITZIAR FERNÁNDEZ, MERCEDES ALBERCA, JAVIER GARCÍA-SANCHO, ANA SÁNCHEZ, and JOSÉ M. HERRERAS

VALLADOLID, SPAIN

SUCCESS 1st year

- CLET 78%
- MSCT 86%





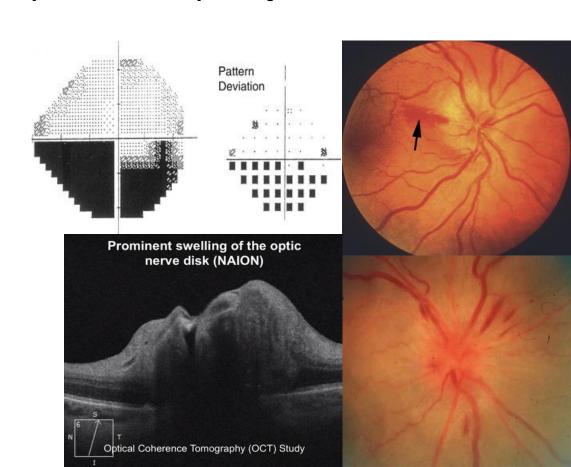
Non-Arteritic Ischemic Optic Neuropathy (NA-AION)

Optic nerve head infarct followed by inflammation

Clinical features:

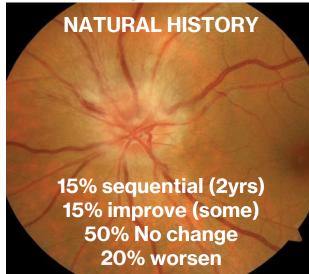
- Acute, painless monocular visual loss
- Visual field defects
- Dyschromatopsia

≥50 yo (61±12.3yo) (Hayreh SS et al., 2007)



Why alternative therapeutic approaches?

- Up to 30% spontaneous improvement (limited)
- 5-29% deterioration continues
- Recurrence in affected eye 6% (2 yrs), 8% in 3 yrs
- Fellow eye: 15-25% at 5 years (Beri et al. 1987; Newman et al. 2002)
- Treatments (No effective treatments and no prevention for fellow eye):
- Antiplatelet agents (Aspirin®) (Kupersmith MJ et al. 1997; Beck RW et al. 1997)
- Corticosteroids (Hayreh SS & Zimmerman MB, 2008)
- Fenestration (Ischemic optic neuropathy decompression trial research group, 1995)
- Diphenylhydantoin (Ellenberger C et al. 1974)
- Levodopa (Beck RW et al. 2000; Hayreh SS, 2000)
- Brimonidina (Wilhelm B et al. 2006)
- Oestrogen (Bernstein SL et al. 2007)
- Erythropoietin (Modarres M et al. 2012)







Preclinical *in vitro and ex vivo* testing

Preclinical in vivo testing

Clinical testing

From *in vitro* research to clinical trials







Organotypic neuroretinal cultures





Invest Ophthalmol Vis Sci. 2022 Apr; 63(4): 27. Published online 2022 Apr 29, doi: 10.1167/jovs.63.4.27 PMID: 35486068

Retinal Neuroprotective Effect of Mesenchymal Stem Cells Secretome Through Modulation of Oxidative Stress, Autophagy, and Programmed Cell Death

Ricardo Usategui-Martín, III 1, 2, 3, 4 Kevin Puertas-Neyra, 1 Nadia Galindo-Cabello, 1, 5 Leticia A. Hernández-Rodríguez, ¹ Fernando González-Pérez, ⁶ José Carlos Rodríguez-Cabello, ² · ⁶ Rogelio González-Sarmiento, 7,8,9 José Carlos Pastor, 1,2,3,4 and Ivan Fernandez-Bueno 81,2,3,4 ▶ Author information ▶ Article notes ▶ Copyright and License information PMC Disclaimer

> Exp Eye Res. 2019 Aug:185:107671. doi: 10.1016/j.exer.2019.05.011. Epub 2019 May 17.

Mesenchymal stem cells provide paracrine neuroprotective resources that delay degeneration of co-cultured organotypic neuroretinal cultures

Sonia Labrador-Velandia 1, Maria Luz Alonso-Alonso 1, Salvatore Di Lauro 2, Maria Teresa García-Gutierrez 1, Girish K Srivastava 3, José Carlos Pastor 4, Ivan Fernandez-Bueno 5

Affiliations + evpand PMID: 31108056 DOI: 10.1016/j.exer.2019.05.011

> Mol Ther Methods Clin Dev. 2020 May 13:17:1155-1166. doi: 10.1016/j.omtm.2020.05.003. eCollection 2020 Jun 12.

Human Mesenchymal Stem Cell Secretome Exhibits a Neuroprotective Effect over In Vitro Retinal **Photoreceptor Degeneration**

Ricardo Usategui-Martín 1, Kevin Puertas-Neyra 1, María-Teresa García-Gutiérrez 1, Manuel Fuentes 2 3, José Carlos Pastor 1 4 5 6, Ivan Fernandez-Bueno 1 5 6

Affiliations + expand PMID: 32514411 PMCID: PMC7267685 DOI: 10.1016/j.omtm.2020.05.003





> Graefes Arch Clin Exp Ophthalmol. 2018 Jan;256(1):125-134. doi: 10.1007/s00417-017-3842-3. Epub 2017 Nov 22.

Biocompatibility of intravitreal injection of human mesenchymal stem cells in immunocompetent rabbits

Sonia Labrador Velandia 12, Salvatore Di Lauro 12, Maria Luz Alonso-Alonso 1, Soraya Tabera Bartolomé 3, Girish Kumar Srivastava 1 4 5, José Carlos Pastor 1 2 4 5, Ivan Fernandez-Bueno 6 7 8

Affiliations + expand

PMID: 29168045 DOI: 10.1007/s00417-017-3842-3

ClinicalTrials.gov NCT03173638







Clinical Trial > Stem Cell Res Ther. 2023 Sep 21;14(1):261. doi: 10.1186/s13287-023-03500-7.

Intravitreal allogeneic mesenchymal stem cells: a non-randomized phase II clinical trial for acute nonarteritic optic neuropathy

Jose C Pastor ¹ ² ³ ⁴, Salvador Pastor-Idoate ⁵ ⁶ ⁷, Marina López-Paniagua ¹ ² ³ ⁸ Marta Para ¹, Francisco Blazquez ¹ ³, Esther Murgui ¹, Verónica García ³ ⁹ ¹⁰, Rosa M Coco-Martín ¹ ² ³

Affiliations + expand

PMID: 37735668 PMCID: PMC10512539 DOI: 10.1186/s13287-023-03500-7







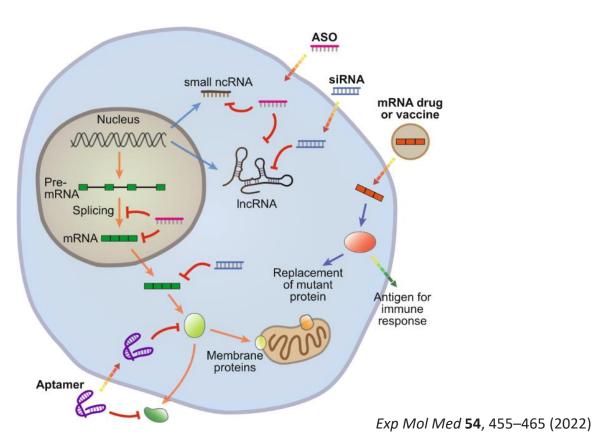


Table 1. Demographic Characteristics and BCVA Data (Letters)

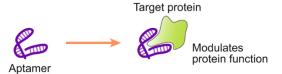
Patient	Age	Gender	Eye	Date of Onset	Date of	Systemic	Basal	BCVA	BCVA	BCVA	BCVA	Lens
	Range				Injection	Risk Factors	BCVA	1 Month	3 Months	6 Months	12 Months	status
1	80s	Female	RE	25/11/2020	3/12/20	HBP, cardiopathy	17	26	25	23	27	Cataract progression from C1N1 to C1N2PSC1
2	60s	Male	LE	28/01/2021	8/2/21	No	0	35	54	63	54	Cataract progression from C1N1 to C1N2PSC3
3*	70s	Female	RE	8/03/2021	23/03/21	HCh	24	33	1	2	0	Pseudophakia needed
4	60s	Female	RE	19/02/2021	8/03/21	HBP, HCh	25	73	80	80	67	Cataract progression from C1N1 to C2N2PSC1
5	50s	Male	RE	15/03/2021	29/03/21	НВР	14	36	51	48	57	Pseudophakic

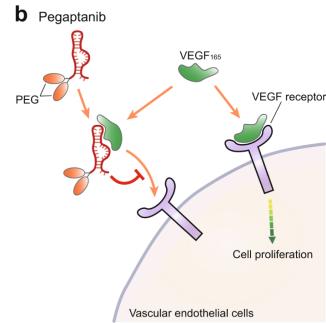
03. RNA-BASED THERAPEUTICS IN OPHTHALMOLOGY:

OPPORTUNITIES & CHALLENGES



a Mechanism of action for aptamer





√90

01 -OCULAR BARRIERS

- Topical limitations
- Posterior segment targeting: IRD
- Invasive delivery: i.e, intravitreal

02 - DEGRADATION

- Need for repeated treatments
- Short duration of action
- Patient burden

03 -INNATE IMMUNITY

 Activation of the innate immune system

04 - UNINTENDED EFFECTS

- Unintended silencing: unwanted gene silencing and cell death
- Potential off-target effects on non-targeted cells

About Us
Faculty Clinical Care Education and Training Research Calendar

Academic Departments (+) Ophthalmology (+)About Us (+) News Welcome from Bennie Jeng, MD and **Departmental News Articles RNA Therapy Reverses Blindness in Patient** After One Dose

RNA Therapy Reverses Blindness in Patient After One Dose



From left to right: Samuel G. Jacobson, MD, PhD, Artur V. Cideciyan, PhD

By Rebecca Salowe Scheie Vision Annual Report 2021

In a recent publication in *Nature Medicine*, Scheie researchers showed that a patient with a genetic form of childhood blindness gained vision that lasted for more than one year after receiving a single injection of an experimental RNA therapy. This study was led by *Artur V. Cideciyan*, *PhD* and Samuel G. Jacobson, MD, PhD, Professors of Ophthalmology and co-Directors of the *Center for Hereditary Retinal*Degenerations.

The patient was a participant of a larger international clinical trial for patients with Leber congenital amaurosis due to a

CEP290 mutation, which is a commonly implicated genetic cause for this disease. Patients with this mutation typically have severe visual impairment that begins in infancy.

CLINICAL PHARMACISTS IN GENE THERAPY & ATMPS



EDUCATION & COUNSELING

Educate patients, caregivers, and healthcare staff on complex gene and cellular therapies



TOXICITY MANAGEMENT

Monitor and manage acute (CRS, neurotoxicity) and longterm toxicities (cytopenias, immune dysfunction)



OPERATIONAL OVERSIGHT

Ensure safe product handling, system onboarding, and coordination across treatment centers



PHARMACOVIGILANCE

Contribute to evolving standards in follow-up, vaccination, and long-term safety registries



FINANCIAL & ACCESS CHALLENGES

Navigate ultra-high therapy costs, insurance barriers, and support cost-effectiveness evaluations



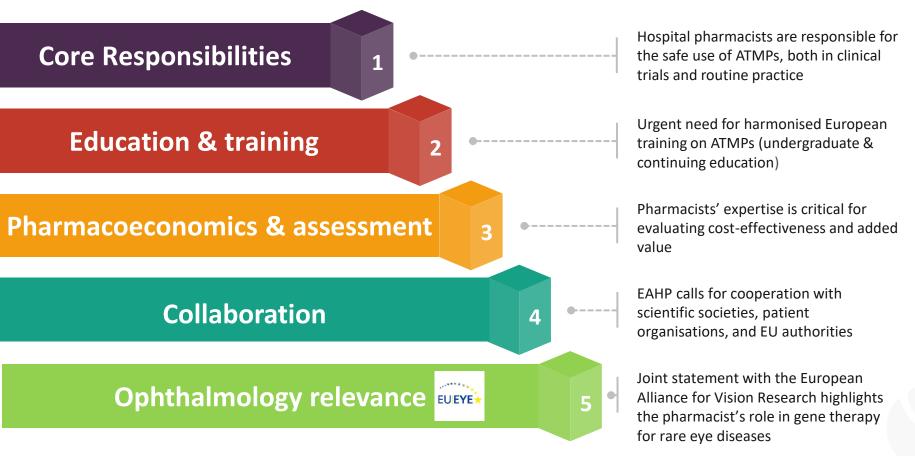
COLLABORATION

Act as a bridge across multidisciplinary teams: physicians, nurses, finance, case managers, and regulators

The role of hospital pharmacists in supporting the appropriate and safe use of CGT/ATMPs: a scoping review of current insights., BMC Health Serv Res (2025)



EAHP POSITION ON ADVANCED THERAPY MEDICINAL PRODUCTS (ATMPs)





OME ABOUT ARCHIVE EU DOSSIER EU RESEARCH & INNOVATION CONTACT US

EU Trans Reg ID: 221589017973-83

EUROPEAN ALLIANCE FOR VISION RESEARCH & OPHTHALMOLOGY

Inspiring the next generation of ophthalmologists















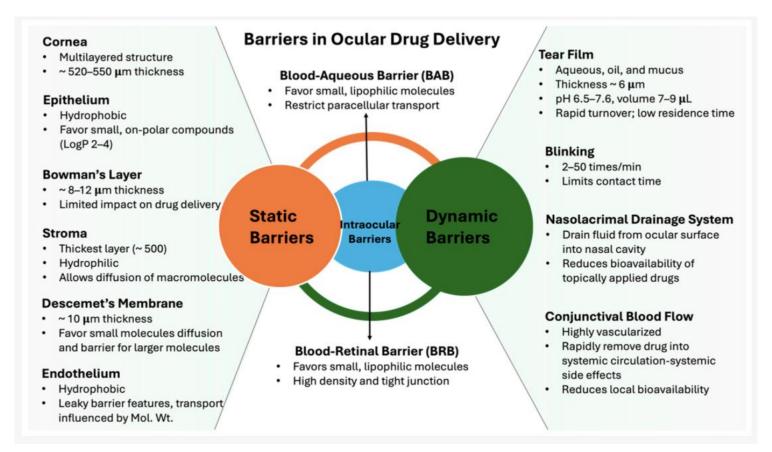


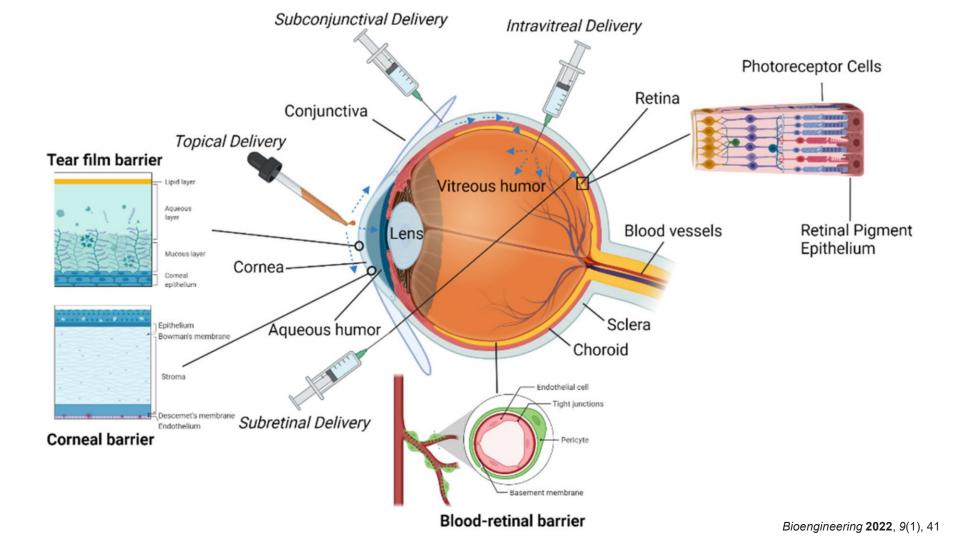
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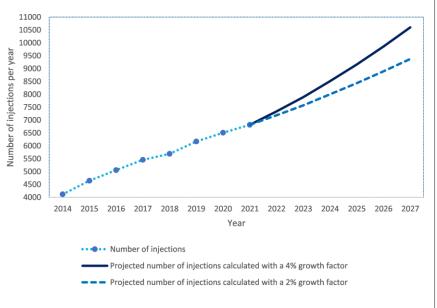


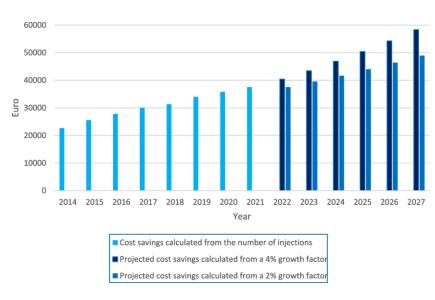
04. EMERGING DRUG APPROACHES



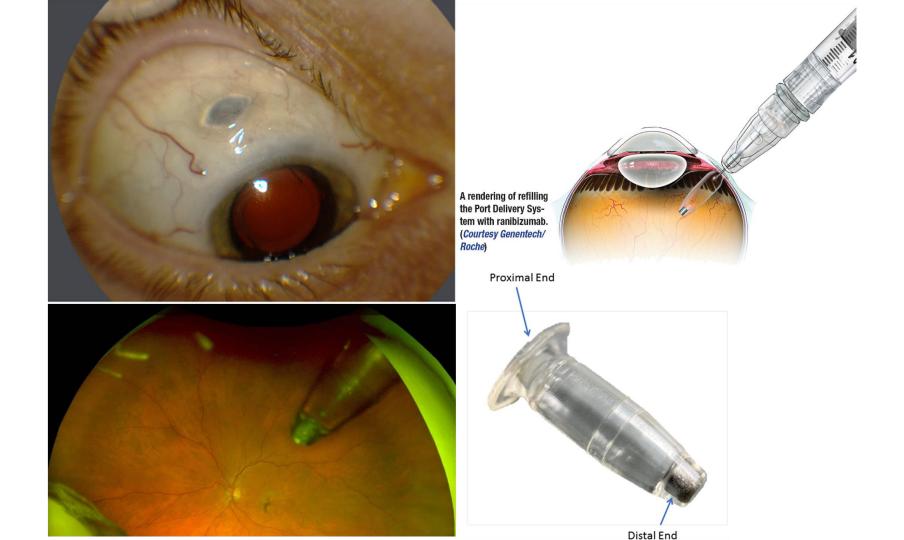


COST CONSEQUENCES OF TASK-SHIFTING INTRAVITREAL INJECTIONS IN A NORWEGIAN TERTIARY HOSPITAL

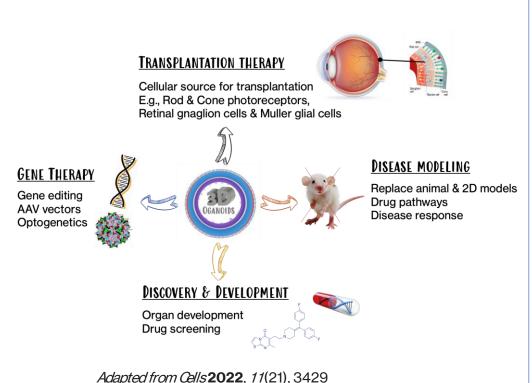


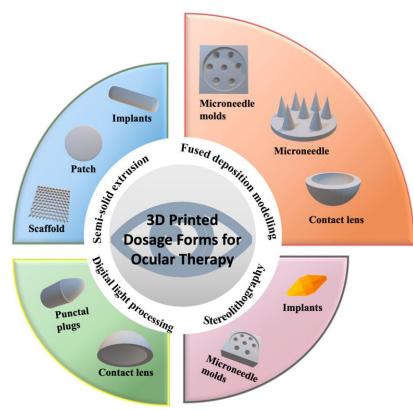


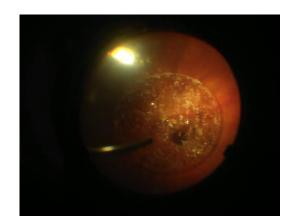
. BMC Health Serv Res 23, 229 (2023). https://doi.org/10.1186/s12913-023-09186-0



04. EMERGING BIOTECH SOLUTIONS FOR PERSONALIZED OCULAR DRUG DELIVERY







TOXICITY SCREENS IN HUMAN RETINAL ORGANOIDS FOR PHARMACEUTICAL DISCOVERY

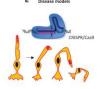














FINANCIACIÓN

Proyecto PID2020-114585RA-I00

PROYECTO RETINA -4

Proyecto RD21/0002/0017
 Grupos relacionados: GR10, GR11, GR14, GR32, GR41, GR52









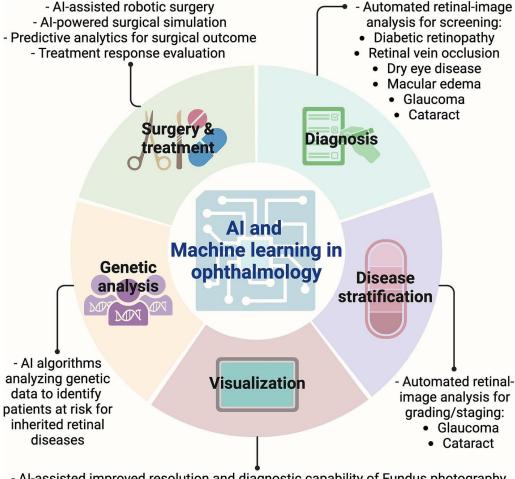








05. AI



- Al-assisted improved resolution and diagnostic capability of Fundus photography
- Deep learning-assisted OCT angiography for better visualizing vascular structures



PRESCRIBING THE FUTURE: THE ROLE OF ARTIFICIAL INTELLIGENCE IN PHARMACY AND HEALTHCARE MAIN THEME

Key Areas of Allmpact:

- **Drug Discovery:** Faster new drug development.
- Clinical Trials: Optimized recruitment & analysis.
- Medication Management: Better dosing & tracking.
- Personalized Care: Tailored treatments.
- Efficiency & Innovation: Improved workflows & decisions.





Challenges & Considerations:

- Data Privacy & Security
- Algorithmic Transparency
- Regulatory Compliance
- Adoption Resistance



- Al in healthcare drives innovation, reduces costs, and better dosing
- Pharma, regulators, and tech developers need to collaborate.
- Standardized AI frameworks ensure fairness, reliability, and compliance.



CHI PO NON VO, CHI VO NON PO CHI SA NON FA, CHI FA NON SA ET COSÌ IL MONDO MAL VA

~Ascoli Piceno- A.D. 1529 ~

En definitiva, las terapias avanzadas en oftalmología **no solo** requieren innovación científica, sino también *integración real entre especialidades*

El farmacéutico hospitalario y el oftalmólogo *no pueden actuar en paralelo,* sino como engranajes de un mismo sistema terapéutico

CONGRESO NACIONAL

SOCIEDAD ESPAÑOLA DE FARMACIA HOSPITALARIA

MÁLAGA 15-17 OCT 25









Gracias

Salvador.pastor@uva.es