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EDITORIAL

Appreciated

Research requires vocation, talent, time and synergies between a number of specialities. It also requires the resources to carry it out. Last September, a large proportion of these ingredients came together in Barcelona, where we provided an optimistic, realistic and innovative vision of the future with regard to the different challenges and scenarios, both from the Barcelona Macula Foundation: Research for Vision (BMF) and from the Institut de la Màcula, two institutions which have worked closely and actively for some years.

The B-Debate forum, *Fighting Blindness. Future Challenges and Opportunities for Visual Restoration*, was organised by Biocat (the entity that coordinates and promotes the life sciences and health sector in Catalonia) and “la Caixa” Banking Foundation. The event was led by the BMF, with the collaboration of the Centre for Genomic Regulation (CRG) and the Leitat Foundation. It drew thirty prestigious experts in each of its areas. Heterogeneous profiles, specialists in fields like nanotechnology, optogenetics and gene therapies among others. Internationally respected professionals together with those of us who are aware of the situation regarding research into degenerative retinal diseases and the proposals for approaching the different future scenarios.

The meeting provided the research sector with a wonderful opportunity and also served to reaffirm the BMF and the Institut de la Màcula’s research aims and commitments by introducing and setting out the different European projects in which our professionals are involved.

Research with international partners continues to form a cornerstone of our mission, together with the improvement of research in our country. Accordingly, the BMF in July became part of the community, RIS3CAT Nexthealth. This community will develop innovation projects with a view to resolving the health challenges of citizens and improving the Catalan health system. All this, in our case, is encapsulated in the ADVANCECAT project, a regenerative medicine initiative that also enjoys the participation of the Centre of Regenerative Medicine of Barcelona (CMRB), the Banc de Sang i Teixits (BST), the University of Barcelona and the August Pi i Sunyer Biomedical Research Institute (IDIBAPS), among others.

Excellence is sought by working and sharing knowledge with the best. In these challenges we strive to keep providing the best medical and diagnostic solutions and to shed new light on pathologies that each day we are nearer to knowing how to beat.

In collaboration with



INSTITUT
DE LA MÀCULA
Innovating Eye Care

IN DEPTH

INTERVIEW WITH FELIPE YAGÜE

“Medical literature compares the loss of sight to the loss of a relative”

Felipe Yagüe _ In charge of the Psychological Care Department of the Institut de la Màcula

Felipe Yagüe, who is in charge of the Institut de la Màcula's Psychological Care Department — a service that is offered to the institution's patients in collaboration with the Barcelona Macula Foundation — has been the subject of several interviews over recent months. Here is part of his conversation with the journalist, Àngela Lara. It appeared in La Razón newspaper on 15 July.

What are the main tools that help someone with visual deficit to move on with their life despite the disability they have acquired?

When someone suffers significant vision loss, they first need support and companionship because they are not going to want practical solutions for a while. Sometimes they suffer stress or emotional anxiety when they learn they are going to lose their sight. There are some people who, following diagnosis, cut themselves off from their social, working, sporting and leisure environments. They take a long time to accept this. This is perfectly understandable because it is sometimes easier to withdraw, isolate oneself or become inactive than to take the decision to face up to the situation, one that initially you tend to avoid because of how difficult it is. When the person has grown more used to their new visual and life reality then they do start to gradually open up and become ready to discover how to adapt to their work, mobility, access to culture and leisure, in order to interact with others. First, though, there is a period of withdrawal, self-denial or a rejection of everything.

Once this adaptation process is over, is it important to set yourself challenges?

In the second instance, yes, when you have become used to your new situation. Because initially there is rejection. First, you have to accept yourself and make a slight change to the concept you have of yourself, your self-esteem. Then you can set yourself challenges. First, you learn to accept and then you redirect the loss or damage to the challenge.

How are people like this treated at a psychological and emotional level?

Firstly, with time and companionship and then beginning a process of adaptation or adjustment. In the literature on this, there are even analogies to the loss of a relative. In fact, you lose the version of yourself that you have had up to then and you have to reinvent another. In this painful situation, you can't wait for someone else to react and see a positive side because there isn't one. Subsequently, you start to get moving and arouse your interest in how to do the things you used to do, or other different things,

by incorporating personal attitudes that you are bound to need, such as adopting a different communicative attitude to interact with people, becoming more extrovert etc. Sight and capacities in general are over-estimated. Sight is a luxury. With 50% of your sight you lose nothing of what you used to do, you can still do it. If you have no sight you lose certain things but you still have a multitude of things; what happens is that sometimes your mind, your thoughts, are on what you can't do, on what you have lost.

Does the fact that you have gone through this process yourself, have experienced this situation at an emotional and psychological level, enable your message to get through to people who have suffered significant vision loss? Is it a useful tool for working with them?

Yes, it is not essential but it is a very useful tool because when there is significant vision loss there is a feeling of solitude. It is very hard to feel understood. In my case, as well as the theory and the professional practice, I have possess the experience and this broadens my knowledge as a concept.



NEWS

Dr. Lucia Ferraro joins the IM and BMF

The ophthalmologist Lucia Lee Ferraro MD has joined the Retina Department of the Institut de la Màcula and the BMF. Ferraro has a postgraduate degree in retinal diseases at the Hospital de Sant Pau (Barcelona) and is a Fellow of the European Board of Ophthalmology (FEBO). She is currently a co-researcher in international clinical trials and European research projects, such as EYE-RISK and LITE together with the CHROMA, HARRIER, OPH 1003 and OPH 1004 (FOVISTA), COLUMBUS, PROXIMA A and PROXIMA B studies. She is a member of the European Society of Cataract and Refractive Surgeons (ESCRS) and the Societ  Oftalmologica Italiana.



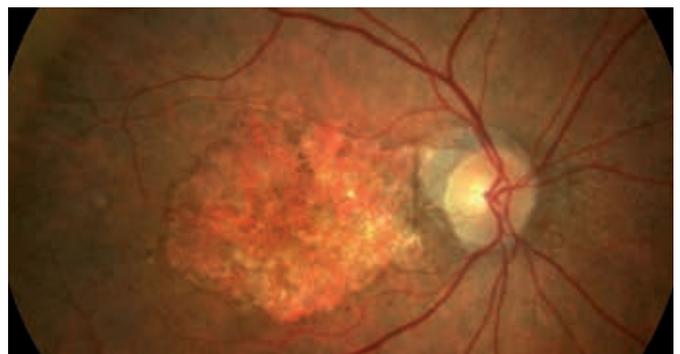
Dr. Sala answers queries on eye problems associated with diabetes

Dr. Anna Sala took part in the Twitter debate organised by the Spanish Diabetes Federation (FEDE) with the hashtag #TuiteaDiabetes5. The event sought to resolve internet users' doubts about the ophthalmic complications associated with the pathology. Anna Sala reiterated that the establishment of an intensive control of glycaemia during the first five years after diagnosis of the disease reduces the appearance of diabetic macular oedema by 23%. She also stressed that early diagnosis, combined with good multidisciplinary monitoring, can often prevent the progression of diabetic retinopathy.



Jordi Mon s addresses EURETINA 2016

Dr. Jordi Mon s spoke on 11 September at the Congress of the European Society of Retina Specialists (EURETINA), held in Copenhagen. He focused on therapeutic approaches to the atrophic form of AMD during the session on the new perspectives in atrophic AMD, a form of the disease for which there is still no treatment.



Starting shot sounds for the RIS3CAT strategy

The BMF is part of the Nexthealth community of the RIS3CAT strategy for implementing the project ADVANCECAT: Accelerator for the development of advanced therapies in Catalonia. Nexthealth aims to promote a competitive, sustainable health system, fostering excellence in research, development and innovation. Coordinated by Biocat, it also comprises the University of Barcelona (UB), the Centre of Regenerative Medicine of Barcelona (CMRB), the August Pi i Sunyer Biomedical Research Institute (IDIBAPS), and the Banc de Sang i Teixits (BST) among others.



The Regional Minister for Business and Knowledge of the Government of Catalonia, Jordi Baiget, and the Director General of Industry and CEO of ACCI  (Catalan Agency for Business Competitiveness), N ria Betriu, together with the leaders of the five RIS3CAT communities. Photo: ACCI .

Paula Verdaguer speaks at the ESCRS Congress in Copenhagen

Dr. Paula Verdaguer presented the paper entitled "Unilateral iris-claw intraocular lens implantation for aphakia: a paired-eye study" at the Congress of the European Society of Cataract & Refractive Surgeons (ESCRS) in Copenhagen.

RESEARCH

Atrophy models that makes it possible to work with regenerative therapies on near-real examples



Research has created an atrophy model of the retina's external layers that is the same as in human atrophic AMD

This result will help to research and discover solutions to eye diseases that even today are incurable

In advanced cases of geographic atrophy (GA), there is a need to perform regenerative treatment to try and stop its progression

Despite the recent advances in the treatment of the wet form of AMD, the great challenge to which the scientific community is committed today is to discover a treatment that slows the inexorable progression of the atrophic form of the pathology, together with other focusses that restore or regenerate the affected part of the tissue of diseased retina.

At present, the advanced form of dry AMD with geographic atrophy (GA) is a leading cause of legal blindness in elderly patients in the industrialised world and represents up to a third of cases today.

As we try to find models with which the origins and treatments of pathologies like these may be researched, it has been detected that the pig eye model possesses very similar characteristics to those of the human eye, and likewise with regard to its retina. The study's aim has been to create an atrophy model for the external layers of the retina that is the same as in the atrophic AMD we find in humans, one that will help us to research and work to discover solutions to eye diseases that even today are incurable.

To work on the processes that must lead us to find a solution to the many questions raised by AMD, the prestigious scientific journal *Investigative Ophthalmology & Visual Science* (IOVS) has published an article whose principal author is the Medical Director of the Barcelona Macula Foundation: Research for Vision and Director of the Institut de la Màcula, Dr. Jordi Monés MD, PhD, together with a team of researchers including Dr. Marc Biarnés and the optometrist Míriam Garcia, who are both from the BMF. The study also enjoyed the support of the Department of Medicine and Animal Surgery of the Veterinary Faculty of the Autonomous University of Barcelona, the Miguel Hernández University of Alicante and CIBER-BBN of Madrid.

The research they conducted discovered which methods and materials can produce initial atrophy scenarios that are extremely similar to those suffered by humans. This scientific success will then make it possible to commence

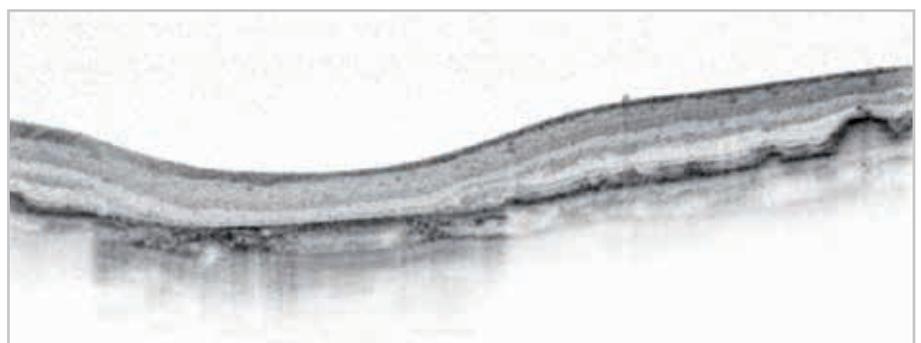
treatment processes with regenerative therapies on the basis of pathologies that are very similar to human ones.

A major difficulty in the research of GA therapies is the lack of good models. GA possesses its own characteristics when it is treated and, in advanced cases, there is a need to perform regenerative treatment beyond that of halting the progression of the atrophy.

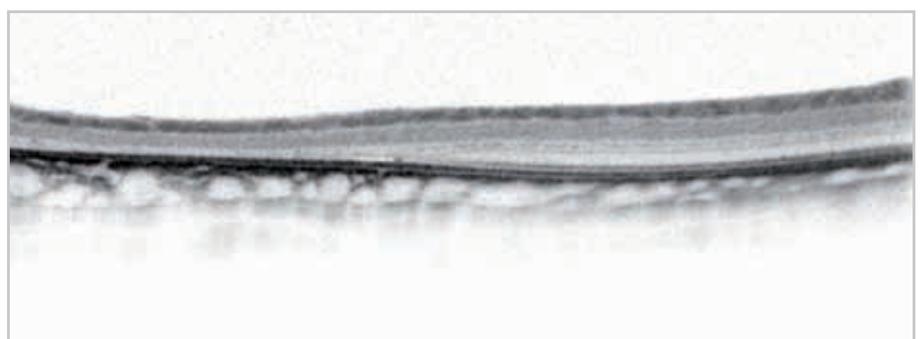
Pathologies like Stargardt's disease, another type of atrophy of the retina's external layers, have a major economic and social impact both on patients, who are often young people, and on their families.

For all these reasons, it should be noted that there is a need for an animal model that imitates the characteristics of GA in order to test the efficacy of the new emerging regenerative therapies that aim to restore visual function, such as stem cell transplantation or optogenetics.

**Dry AMD with geographic atrophy
in a human eye**



**Dry AMD with geographic atrophy
in a pig eye**



RESEARCH

Latest perspectives on research against blindness

The B-Debate promoted by the BMF analysed the latest developments in visual restoration



The forum *Fighting Blindness. Future Challenges and Opportunities for Visual Restoration* formed part of the B-Debate series, which was instigated by Biocat and “la Caixa” Banking Foundation to promote scientific debate. Experts came to Barcelona from all around the world to set out and discuss the main developments in fields like optogenetics, gene therapy and nanotechnology with regard to the new therapies against eye degeneration.

AMD is a problem of the first magnitude and is approached from multiple perspectives. A significant part of research is directed towards genetic studies. Marius Ueffing, the Director of the Institute for Ophthalmic Research (University of Tuebingen, Germany) points out that the pathology does not depend on genetics solely: «it is complex and interdependent with the environment; with luck, even». The studies presented by Caroline Klaver, professor of epidemiology and genetics at the Erasmus Medical Center (Netherlands) show that variants in the genes associated with AMD are highly complex and of very variable expression. She says that in order to predict whether a person will develop the pathology age,

gender, whether they smoke, weight relative to health and up to 26 genetic variants must all be taken into account. And, despite everything, around a third of the population at most risk would not be detected.

This is why research is focused on many aspects of this pathology. Patients who receive treatment also include those who develop resistance to drugs, fibrosis or atrophy. For these cases, there is work on new molecules like anti-PDGFs, a growth factor derived from the platelets that increase the indices of visual efficiency and anatomical response, impacting on the reduction of fibrosis in the long term. Working on this is Samir Patel, the co-founder of the Ophthotech Corporation, which has implemented a number of clinical trials to assess their effectiveness.

The optogenetic route. Trials are now taking place on optogenetics-based treatments for patients with retinitis pigmentosa (RP). This involves an attempt to insert algae genes that cause cells to recover the capacity to capture light. In this way, ganglion or bipolar cells that only transmit electrical impulses — and that are usually

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preserved in many types of retinal degeneration — would also become light receptors, adopting the role of the photoreceptors that the pathology has damaged. This involves, says Jordi Monés, the Medical Director of the BMF, the cell «becoming a receptor, as well as a cable». The therapy, applied to blind patients, will not allow them to recover normal nor colour vision but they are expected to be able to recognise shapes, read large letters and find their way around. Meanwhile, as explained by Marco Zarbin, a professor in the Department of Ophthalmology & Visual Sciences, New Jersey Medical School, work is taking place on more sophisticated methods that enable the results to be improved.

Gene therapy and stem cells, the big hopes. Up to now, gene therapy in the most advanced phase and already proven against blindness is targeting a type of hereditary disease, Leber Congenital Amaurosis. The investigator at the Andalusian Center for Molecular Biology and Regenerative Medicine (CABIMER), Francisco J. Díaz Corrales, says that this treatment «has shown itself

to be safe and effective». Only one gene is affected in this pathology so the therapy is of a clear design. Similarly, there is much hope for Stargardt's disease. It is believed that this task will be more difficult in pathologies where there are more factors involved, such as AMD.

There are now a number of trials with stem cells in progress to treat various forms of blindness. Therapies of this type have yet to be approved for any visual deficit. However, as pointed out by the Director of the Stem Cell Bank at the Centre of Regenerative Medicine in Barcelona, Anna Veiga, many trials are now in progress, most of which use embryonic stem cells. There is also study on the use of iPS cells, which come from reprogramming adult cells to turn them into stem cells. The investigator at the University of Barcelona, Michael Edel, explained that there are still difficulties, among which are «the possibility of them becoming tumorous, knowing whether they cause an immune response and standardising and optimising their production protocols».

DISSEMINATION OF PROJECTS

Some of the international research projects in which the BMF and the Institut de la Màcula participate have figured prominently in the space devoted to posters.

Identification of phenotypes in geographic atrophy using cluster analysis

Alexis Blaud, CD, MPH, PhD; Clara Ramon, CD, MSc; Jordi Monés, MD, PhD
Barcelona Macula Foundation, Barcelona
Institut de la Màcula, Barcelona

Phenotype	n	P	Q	Median
Normal	100	0.05	0.05	0.05
Small	100	0.05	0.05	0.05
Large	100	0.05	0.05	0.05
Very large	100	0.05	0.05	0.05
Very very large	100	0.05	0.05	0.05
Very very very large	100	0.05	0.05	0.05

EYERISK Project
Identification of phenotypes in geographic atrophy using cluster analysis.
Funded by the EU's Horizon 2020 (GA No 634479)

Images of the microscopic in-vivo human retina acquired using AGSLO

David García, MSc; María Bernal, MSc; Albert Sanjaume, MSc; Ferran Llorens, MSc
Institut de la Màcula, Barcelona

LITE Project
Development of Advanced Laser Imaging Techniques for the anterior and posterior Eye.
7ª PM. EM. ACCIÓ, Generalitat de Catalunya.

Innovative procurement for visually impaired people: Introducing the PRO4VIP project

Vicent A. Vella, researcher at AQUAS - GENCAT
for the PRO4VIP Consortium

PRO4VIP Project
Innovative Procurement for Visually Impaired People.
Funded by the EU's Horizon 2020 (GA No 645584)

PRESS



The media give the B-Debate wide coverage

In September, the Spanish media provided wide coverage of the B-Debate *Fighting Blindness. Future Challenges and Opportunities for Visual Restoration*. From La Vanguardia newspaper to Diario Médico, the general and specialised

press in their paper and digital versions led above all on the possibility of reversing certain types of blindness over the next decade.



The voice of patients, on TVE

The news programmes of TVE-Catalunya also focused on the Forum promoted by the BMF. In doing so, they sought out the voice of those who are affected by some of the pathologies covered by the experts who gathered at CaixaForum Barcelona. This included an interview with Anna Morancho, from the Associació Discapacitat Visual de Catalunya, who is pictured here.



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