

Gene Therapy: New Ray of Hope in Vision Restoration

In recent years, gene replacement therapy has emerged as a successful treatment option in many inherited retinal diseases which were previously thought to be incurable.

About 1 in 4000 people suffers from an inherited retinal disease. Disorders like Leber's congenital amaurosis, Stargardt's disease, retinitis pigmentosa, choroidemia and other inherited dystrophies have poor visual outcomes with very few treatment options.

Recent researches on gene therapy have seen remarkable breakthroughs leading researchers and clinicians to believe that it is now ready to play a major role in the fight against inherited retinal problems.

The principle of gene therapy is based on the transfer of a therapeutic gene or a part of a gene into the eye through

viral or non viral vectors. There are several reasons why the eye can be an ideal organ for showcasing the success story of gene therapy. Firstly, the eye is an immunologically privileged site in the body, i.e. less likely to instigate a systemic immune response to injected gene vectors.

Secondly, taking into account the small volume of the eye, minute amounts of viral vectors are enough to achieve therapeutic effects without the risk of toxicity.

Finally, the localized nature of retinal pathology and advanced imaging techniques ensure that treatment effects in the retina are better observed by researchers

than anywhere else in the body. An excellent example of how successful genetic research has helped patients with retinal degeneration is a set of trials on



Leber's Congenital Amaurosis (LCA). About 18 different gene mutations are known to lead to different forms of LCA, one of the most common causes of inherited childhood blindness. The most common of these is

mutation of RPE 65 gene. A major breakthrough came in 2008 when three groups, two in the US and one in UK, reported success in RPE 65 associated

LCA using adeno associated viral vector. In all the three trials, patients recovered functional vision without side effects. These results helped trigger worldwide interest resulting in more trials on retinal degenerative diseases.

disease is the most common juvenile degenerative retinal disease and is caused by mutation of the ABCR gene.

Oregon Health and Science University of Portland, and Centre Hospitalize National



D'Ophthalmologie des Quinze-Vingts in Paris are jointly conducting a clinical trial assessing the safety and efficacy of Stargen™ gene therapy to deliver a corrected version of ABCR gene.

Similar trials are underway for choroideremia, an inherited disorder causing degeneration of choroid and outer retinal layers.

"All the evidence suggests that gene therapy will be a significant contributor to therapies for some of the hereditary blinding conditions that are currently incurable", said one of the researchers involved in the human trials of LCA.

Gene Therapy for Retinitis Pigmentosa

Recent experiments show Retinitis Pigmentosa can be treated with gene therapy

Researchers of the Columbia University Medical Center revealed the results of two treatments they have been



experimenting with, for Retinitis Pigmentosa. The first treatment involved the use of stem cells (iPSCs) while the second one involved gene therapy.

In the iPSCs study, researchers transplanted the cells via injection under the retina. After the injection, all stem cells managed to assimilate into the retina without problem and no tumours were reported.

Researchers observed that the iPSCs cells expressed certain markers indicating that they have the capacity to develop into normally functioning retinal cells.

Later, scientists tested for any visual improvements. The results were highly encouraging. Visual function had improved and it was shown that the effect was long lasting.

Stephen H. Tsang, leader of both studies, said: "We've never

seen this type of improvement in retinal function. We hope we may finally have something to offer patients with this form of

vision loss."

The second study involving gene therapy consisted of adeno-associated viruses (AAV) which transferred the correct copies of DNA into the retina cells. Once again the results were encouraging. All treated subjects showed great visual improvement.

"These results provide evidence that RP is likely to be treatable by gene therapy," said Tsang.

Tablet PCs May Help Those with 'Low Vision' Read Better

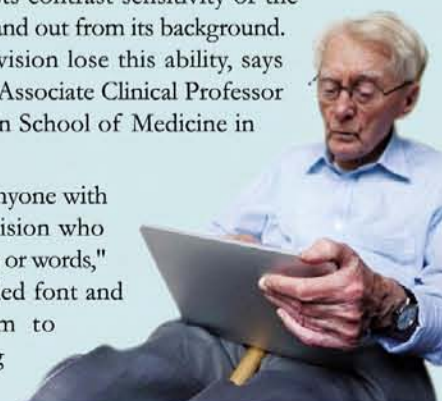
Tablet PCs with back-lit screens may allow millions of people with 'low vision' to read faster and easier, a new study suggests.

Low vision is an umbrella term for people who have trouble reading, watching TV, or performing other daily activities despite glasses, contact lenses, medication, or even surgery. For them only remaining options are magnifying glasses and low-vision aids which are bulky and difficult to use.

Enter backlit tablets. The new study shows that these devices may allow some people to read faster and more comfortably than printed materials.

The backlit device boosts contrast sensitivity or the ability to see an object stand out from its background. Many people with low vision lose this ability, says researcher Daniel Roth, Associate Clinical Professor at Robert Wood Johnson School of Medicine in New Brunswick, N.J.

"The findings apply to anyone with compromised reading vision who has difficulty seeing letters or words," said Roth. "The magnified font and backlight allows them to improve their reading ability and comfort."



Cholesterol Control Key to Fighting Sight Loss



Dr. Rajendra Apte

A new study led by a scientist of Indian origin suggests that eye drops designed to lower cholesterol may be able to save sight in some people suffering from age related vision loss and Age related

Macular Degeneration (AMD).

The study supported by the National Institutes of Health, USA, showed that large cells called macrophages appear to play a key role in clearing cholesterol from the eye, and that with aging, these cells become less efficient.

Eye drops containing a type of drug known to promote cholesterol release from macrophages, called a liver X receptor (LXR) agonist, helped restore macrophage function and prevent AMD progression.

The study was led by Rajendra Apte, an eminent professor of **Ophthalmology and Vision**

Sciences at Washington University. In previous studies, Dr. Apte found that macrophages normally help limit the growth of new blood vessels in the eye, but with age, the cells lose this ability. The new study suggests that prior to these changes, old macrophages become less efficient at processing cholesterol.

A protein called ABCA1 is needed for macrophages to release cholesterol into the bloodstream. In these experiments, Dr. Apte and his team found that in old macrophages, there is a decrease in the level of ABCA1 protein. Next, the researchers tried treating old macrophages with an LXR agonist; a drug known to enhance cholesterol transport from macrophages by turning on the ABCA1 gene. Exposure to the drug rejuvenated the old macrophages and enabled them to inhibit blood vessel cell growth.

"This study points to a novel strategy for early intervention to prevent the progression of AMD to the severe neo-vascular form of the disease," said Grace Shen, Program Director at NIH's National Eye Institute.



Can Your Retina Predict the Risk of Dementia?

The width of blood vessels in the retina may indicate brain health years before the onset of dementia and other deficits, according to a new study published in the journal of the Association for Psychological Science.

To investigate the potential link between intelligence and brain health, the researchers borrowed a technology from ophthalmology.

Researchers used digital retinal imaging to gain a window into vascular conditions in the brain by looking at the small blood vessels of the retina. Retinal blood vessels share similar size, structure, and function with blood vessels in the brain and can provide a way of examining brain health in living humans.

Having wider retinal venules was linked with lower IQ scores at the age of 38, even after the researchers accounted for various health, lifestyle, and environmental risk factors that might have played a role.

Individuals who had wider retinal venules showed evidence of general cognitive deficits, with lower scores on numerous measures of neuropsychological functioning. Surprisingly, the data revealed that people who had wider venules at the age of 38 also had lower IQ in childhood, a full 25 years earlier.

"It's remarkable that venular caliber in the eye is related, however modestly, to mental test scores of individuals in their 30s, and even to IQ scores in childhood," the researchers observe.

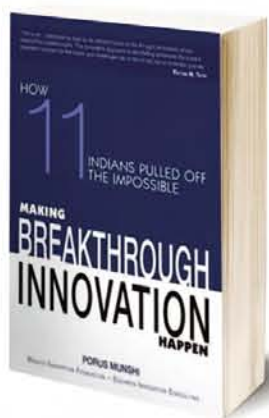
The findings suggest that the processes linking vascular health and cognitive functioning begin much earlier than previously assumed, years before the onset of dementia and other age-related declines in brain functioning.

"Increasing knowledge about retinal vessels may enable scientists to develop better diagnosis and treatments to prevent age-related worsening of cognitive abilities," they conclude.

OUR COLLABORATOR: ARAVIND EYE CARE SYSTEM

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BOOK EXTRACT



The book revolves around the idea of innovation and presents 11 ground-breaking stories across sectors and regions in India which are immensely inspiring. One such story is that Dr. V and his mission at the Aravind Eye Hospital to eradicate blindness to the extent possible.

Making Breakthrough Innovation Happen

by Porus Munshi

"Aravind Eye Hospital is internationally recognized as an institution best suited to make not just a dent, but a grand canyon in the world of blindness. There are nearly twenty-four million blind in the world. And nearly one-third of them are unnecessarily blind, which means that they don't have to stay blind; a medical intervention can treat them. But the intervention in many cases requires surgery. And there just aren't enough doctors to go around. Instead of increasing the number

of surgeons to cope with the problem of unnecessary blindness, Aravind decided to find ways to increase a surgeon's productivity. And it has perfected an assembly-line technique of surgery that increases this productivity by a factor of ten. It has also developed such a cost-effective revenue model that thousands of blind poor can be operated on for free or nearly free. Revenues are generated from a small percentage of paying patients."

Aravind Eye Hospital is internationally recognized as an institution best suited to make not just a dent, but a grand canyon in the world of blindness



Aravind Pays Tribute to Swami Vivekananda

Ramakrishna Math and Mission organized a "Ratha Yatra" in commemoration of the 150th birth anniversary of Swami Vivekananda. The "Ratham" reached Aravind on July 20. The entire Aravind staff assembled to pay tribute. A motivational session followed at the Dr. G. Venkataswamy Research Institute.

Dr. Joseph Gnanadickam Memorial Oration Award for Dr. Ramakrishnan

Dr. R. Ramakrishnan was awarded the **Dr. Joseph Gnanadickam Memorial Oration Award** at the 61st Annual Conference of the Tamil Nadu Ophthalmic Association held at Chennai. We congratulate him on receiving this prestigious award.

International Retinoblastoma Awareness Week

Retinoblastoma(RB) is a fast-growing, often fatal type of eye cancer, affecting primarily children. To create awareness about this serious sight-threatening disease, Aravind Madurai arranged several programmes on the occasion of **International Retinoblastoma Week**.



PBA Eye study analyzes safety and benefits of the popular makeup item

Doctors of **PBA Eye** collaborated with researchers at IIT Kharagpur, in a study to analyze the safety of kaajal, the popular eye makeup. Published in the September, 2013 issue of **Analyst**, the research journal of the Royal Society of Chemistry, UK, the study demonstrated that kaajal prepared from leaves of *phanimanasa* (*Euphorbia nerifolia*) is not only safe for use as eye makeup, but possesses antifungal and antibacterial properties as well.

Whether use of kaajal is safe or not has long been a controversial issue. Previous studies have indicated commercial preparations of kaajal contain high concentration of lead, a potentially toxic element. Conflicting reports have been found on whether kaajal application to eye actually causes higher lead concentration in blood or not. In January 2010, French researchers reported that, at low levels, lead compounds of the eye makeup of ancient Egyptians

actually boosted the immune system, thereby having a beneficial effect in the body.

The **PBA Eye**- IIT team analyzed the structural composition as well as the biological compatibility of



"We found that the sample demonstrated the presence of two types of dispersed and spherical carbon nanoparticles" says Dr. Suman Saha, microbiologist at **PBA Eye**.

The study also demonstrated that fibroblast cell lines, when supplemented with kaajal did not show any morphological changes. Neither did it cause any hemolysis (breakdown) of red blood cells which confirmed the biocompatibility of kaajal.

"We also tested the behavior of kaajal on two pathogens associated

with corneal infections: *pseudomonas aeruginosa*, a bacteria and *candida albicans*, a fungus. By electron microscopy



we found that the carbon nanoparticles of kaajal adhered to the bacterial and fungal cell surfaces causing drastic damage to the cell walls and cell membranes," commented Dr. Jayanshu Sengupta, Chief of Cornea services at **PBA Eye** and a co-author of the study. "But a word of caution: excessive use of kaajal can block the glands present on the eyelids and cause complications" he added.

"Not the commercial preparations, but traditional kaajal made from soot on *phanimanasa* leaf does have a protective effect against microbial contamination," Dr. Saha rounded off.

The M.P. Birla Group: A vision for philanthropy

The **M.P. Birla Group** is a multi-product, multi-location Group dedicated to growth, with a keen awareness of its social responsibilities. The Group also has a significant presence in the fields of education, healthcare and scientific research, all of which are run on a philanthropic and non profit basis.



Apart from **PBA Eye**, it runs leading hospitals like Bombay Hospital in Mumbai and Indore, M.P. Birla Hospital and Priyamvada Birla Cancer Research Institute in Satna and Belle Vue Clinic, Kolkata. South Point School and the M.P. Birla Foundation Higher Secondary School in Kolkata are two notable educational institutions managed by the Group. It has established and also manages the M.P. Birla Planetarium in Kolkata.

PBA Eye has been established in collaboration with Aravind Eye Hospitals, the largest eye care provider in the world, and collaborating centre for World Health Organisation (WHO). **PBA Eye**, a not-for-profit hospital, ensures all revenues earned are retained and redeployed to expand its services to society and to continuously improve the quality of treatment for its patients. The associated M.P. Birla Eye Clinic operates an eye bank and also regularly holds eye camps as part of its outreach programme in keeping with the philanthropic philosophy.

Outpatient Department

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A memorable case

A difficult thyroid ophthalmopathy related strabismus treated successfully by a multidisciplinary approach



Dr. Alokesh Ganguly
MBBS, DO, MS, DNB, FICO, FELLOW
(ANT.SEGMENT, GLAUCOMA &
PAEDIATRIC), AEH

“
Why would most ophthalmologists not touch such a patient? Because the surgery in the fibrosis laden field is very difficult and the dissection is challenging.
”

When Mr. Shah (name changed) visited our hospital in January 2012, he complained of watering, redness and swelling of his left eye over a period of two weeks. Dr. Alokesh Ganguly took up the case.

The patient had moderate drooping of left eyelid, protrusion of the eye, and conjunctival chemosis with almost total restriction of elevation of the left eye. His best corrected visual acuities were 6/6 in BE.

The presumptive diagnosis was Thyroid Related Ophthalmopathy and the patient was admitted for intravenous steroid therapy.

Three cycles of intensive intravenous methyl prednisolone therapy were followed by a course of oral steroids. This halted the severe inflammatory process and the proptosis, along with conjunctival chemosis markedly decreased. After about three months, when the course of treatment was completed, the patient was much better.

Rising Discomfort

However, despite treatment, there was no lasting relief for the patient. He started having severe double vision due to the infiltrative fibrosis of the inferior rectus muscle in the left eye. His binocularity was lost and it took the shape of a physical deformity. But as the old adage goes, "fools rush in where angels fear to tread". We knew



Pre-Op: LE Restricted Upgaze



Post Operative: well-balanced eyes

that we could not surgically correct his squint till the inflammation subsided for at least a period of six months. We explained to him the grave consequences of losing patience and put him on glass correction and lubricant eye drops.

The D Day Approaches

After about a year from the time of onset of the disease, the orbit surgeon was confident that we could take the surgical plunge. Most ophthalmologists hesitate to operate on such a patient because the surgery in the fibrosis laden field is very difficult. Predictability of accurate results in such squints is almost nil and secondary surgeries on the other eye are almost universal. We decided to take up the challenge. After thorough explanation to the patient, we did a squint surgery of inferior rectus recession with absorbable sutures in the left eye.

All's Well That Ends Well

The post operative results were gratifying for us. The patient had a perfectly balanced eye with no angle and good binocularity. Cosmetically it was a no angle and there was no retraction of the lower lid. The patient is very comfortable and has gone back to his normal life. That's the magic of surgery combined with understanding of the disease.



DOCTOR'S PROFILE

Dr. Abhijit Chattopadhyay

MBBS (Calcutta Medical College), MS in Ophthalmology (Banaras Hindu University), Fellow (Vitreous & Retina) AEH

Dr. Chattopadhyay is currently Senior Consultant in the Retina & Vitreous Department and Surgical Retina Consultant at Priyamvada Birla Aravind Eye Hospital. He has been associated with the organization for over six years.

RETINOPATHY OF PREMATURITY: TWO VIEWS

PATIENT'S STORY

My wife gave birth to twin babies at one of the reputed hospitals of South Kolkata. Both the babies were premature as they were born in the 7th month of pregnancy. The elder twin, who weighed 1208 gm at birth, was released from NICU within 25 days of birth. As per the pediatrician's

advise, we came to **Priyamvada Birla Aravind Eye Hospital** for her eye checkup.

Dr. Abhijit Chattopadhyay informed me that my baby was suffering from severe retinopathy of prematurity and she underwent laser procedure on the same day. Today at 2 years of age, she has excellent vision in both eyes. The younger twin, who weighed 900 gm at birth, was more ill and stayed at the NICU for about two and a half months. Dr. Chattopadhyay insisted that the eyes of the younger twin should be examined as well. Once the baby was released from NICU, we took him to **PBA Eye**. We were shocked to hear that the baby had already become blind due to severe ROP in both eyes. I ran from pillar to post to do something for his vision but it was all in vain.

--- Mr. Nikhilesh Gupta

DOCTOR'S SPEAK

For a premature baby the timing of screening of the eye is of utmost importance. It is mandatory that the first screening should be done within the first month of birth (30 day policy).

Retinopathy of prematurity develops within 2 to 3 weeks of birth. Mr. Gupta brought the older of his twin children to us at the right time and though the eyes were in bad condition, timely treatment restored her vision successfully. Unfortunately the younger twin came to us so late that we could not salvage his vision.

In fact, we do not wait for babies to come to us. If and when a pediatrician calls us for an eye checkup, we go to the NICU and examine the baby there. Unfortunately, in case of Mr. Gupta's baby we were not called and by the time the baby came to us, it was too late.

--- Dr. Abhijit Chattopadhyay

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CUTTING EDGE TECHNOLOGY

Heidelberg Spectralis HRA-OCT

The Spectralis HRA-OCT is the latest state-of-the-art retinal and optic nerve imaging system available. It incorporates high resolution spectral domain OCT with confocal scanning laser ophthalmoscopy to deliver sharp, detailed, high-speed real-time digital angiographic images with high resolution OCT images. Compared to other machines, with Spectralis, we now have a much better way of having simultaneous high quality retinal fluorescein angiography and retinal indocyanine angiography along with OCT.

Spectralis Angiography and OCT of **PBA Eye** Diagnostic Services are available not only for our own patients but also for patients referred from other hospitals and consultants.



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