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Serge Picaud, the Executive Director of the Paris Vision Institute outlines a bold vision to transform ophthalmology through cutting-edge research and innovation. From pioneering the first successful optogenetic vision restoration to advancing therapies for AMD, myopia, and diabetic retinopathy, the institute blends academic excellence with commercial impact supported by 15 spin-offs and global partnerships.

Could you provide an overview of the Paris Vision Instituteâ??s strategic research framework and core priorities?

The Paris Vision Institute operates through four fundamental research pillars that collectively address the spectrum of vision science and therapeutic intervention. Our primary focus centres on advancing fundamental understanding of visual mechanismsâ??a field where significant knowledge gaps persist regarding the precise mechanisms of human sight.

Simultaneously, we are developing sophisticated therapeutic strategies for ocular diseases, with particular emphasis on unmet medical needs. Our third pillar involves vision restoration programmes for blind patients, where we have achieved unprecedented success with optogenetic therapyâ??the worldâ??s first clinical demonstration of vision recovery through this approach.

The fourth pillar encompasses the development of advanced diagnostic tools designed to accelerate clinical trial timelines. This capability is particularly crucial for therapeutic development, as our diagnostic innovations enable demonstration of treatment efficacy within significantly compressed timeframes compared to traditional methodologies.

How does the institute position itself within the global ophthalmology research landscape?

According to our recent international review committee assessment, the Paris Vision Institute ranks among the global leaders in ophthalmology research. This positioning is substantiated by our exceptional grant acquisition success, including six active European Research Council grantsâ??a remarkable achievement that underscores our research excellence.

Our funding portfolio demonstrates truly international reach, encompassing European Research Council support, French national grants from institutions such as the ANR, and American funding from the National Institutes of Health and the Foundation Fighting Blindness. This diversified funding strategy enables us to pursue ambitious research objectives while maintaining financial resilience.

The instituteâ??s unique positioning stems from our integration with Europeâ??s largest ophthalmology hospital campus, the HÃ´pital de la Vision des XV-XX, facilitating seamless collaboration between clinicians and researchers. This proximity ensures that our research agenda remains closely aligned with genuine clinical needs and patient challenges.

What factors have contributed to the increased investment and industry attention in ophthalmology?

The ophthalmology sector has experienced significant capital influx following the emergence of several blockbuster treatments that demonstrated substantial commercial viability. This success has fundamentally altered industry perception regarding the therapeutic potential and market opportunities within ophthalmology.

The eye presents unique advantages for therapeutic development and clinical assessment. Its accessibility enables direct mechanical intervention through injection techniques, while its transparency allows real-time cellular monitoring and quantification. Specifically, we can directly observe and count photoreceptors at the retinal level, providing unprecedented capability to assess treatment efficacy through cellular preservation or recovery.

Furthermore, the contained nature of ocular interventions significantly reduces systemic risk profiles. Even with complete diffusion of therapeutic agents beyond the target tissue, the dilution effect ensures minimal systemic exposure, thereby substantially reducing both patient risk and investment risk for venture capital participants.

Which ophthalmological conditions represent the most significant unmet medical needs currently?

Age-related macular degeneration represents perhaps the most critical unmet need, particularly the dry form of the disease. While effective treatments exist for wet AMD, dry AMD therapeutic options remain limited in efficacy. Given the conditionâ??s prevalence in industrialised nations and the

demographic trends toward population aging, this represents a substantial public health challenge requiring innovative therapeutic approaches.

Myopia presents an equally pressing concern, particularly given its epidemic proportions in Asian populations, where approximately 90 percent of young adults are myopic compared to between 30 and 50 percent in Europe. Of particular concern, 10 percent of these individuals will progress to high myopia, carrying significant risk for retinal detachment, haemorrhage, and potential blindness. The scale of this challenge, affecting potentially nine percent of entire Asian populations, demands urgent prevention and therapeutic options.

Diabetic retinopathy constitutes the third major area of unmet need, representing the leading cause of blindness in adults under 50 years of age. As diabetes prevalence continues to increase globally, the associated retinopathy burden will expand correspondingly, necessitating innovative therapeutic strategies for this relatively young patient population.

Gene editing and gene therapy are rapidly evolving fields, particularly in oncology. How are these technologies now being applied to ophthalmology?

Ophthalmology is now emerging as one of the most promising frontiers for gene and cell therapies. The central idea is to either correct the faulty genes causing vision loss â?? potentially offering a curative approach â?? or to design therapies that can be administered more regularly and with greater control.

However, the field faces unique challenges. For instance, permanent expression of gene-editing proteins raises safety concerns, such as off-target genetic modifications. So, some researchers are favouring transient treatments, where the therapeutic protein is expressed only briefly â?? just long enough to be effective without lingering risks.

Weâ??re also seeing classical gene therapy using AAV vectors evolve rapidly. These therapies, designed to deliver genetic material to retinal cells, are already showing clinical potential. And ongoing work is now focused on developing more efficient viral vectors, which could significantly improve delivery, safety, and patient outcomes.

The Vision Institute recently achieved a world-first in optogenetic therapy. Could you walk us through this innovation and its implications?

At the Vision Institute, we have been working on vision restoration in blind patients using an approach known as optogenetic therapy. This is designed for patients whoâ??ve lost their photoreceptors but still retain other functional retinal cells.

We used gene therapy to introduce an opsin gene from green algae into these surviving retinal neurons. Opsins are light-sensitive proteins â?? and in algae, theyâ??re naturally linked to ion channels that directly trigger electrical activity in response to light. We took the genetic code for this algae opsin, packaged it into an AAV vector, and injected it into the retina.

What is remarkable is that these human retinal neurons, once treated, became light-sensitive, effectively acquiring the capacity to respond to visual stimuli again. In 2021, we published the first clinical evidence worldwide showing that a blind patient was able to perceive objects, count them, and even grasp them using this method. That was an extraordinary milestone.

One of the big unknowns had been whether the immune system would tolerate this algae-derived protein, which is completely foreign to the human body. Surprisingly, and fortunately, we observed no immune rejection. The cells remained stable, and the patient retained vision capabilities post-treatment.

To support the therapy, the patient uses special goggles that adapt light to the specific sensitivity of the opsin, allowing functional sight in everyday conditions.

This therapy was fully developed at the Vision Institute, a spin-off company, GenSight Biologics, was created to advance the therapy through clinical trials. While early trials demonstrated success, weâ??re now working on improving expression levels of the opsin and refining the light delivery system. GenSight is currently seeking funding to launch the next phase of clinical trials.

We are also exploring cortical vision restoration using sonogeneticsâ??a novel technique that aims to make brain neurons responsive to ultrasound instead of light, for patients having lost the optic nerve as in glaucoma. The idea is to project images directly into the visual cortex via ultrasound. Weâ??ve completed proof-of-concept studies and are now testing whether animals can perceive shapes and images this way before moving to human trials.

Beyond optogenetics, what other therapeutic areas is the Institute advancing?

Weâ??re developing a broad pipeline of ophthalmic innovations, many of which are targeting highly prevalent conditions with few current treatment options.

In age-related macular degeneration (AMD), for example, we have two research tracks: one focusing on preventing photoreceptor degeneration, and the other on modulating the inflammatory response, which is increasingly recognised as a driver of disease progression. Weâ??re also exploring myopia, particularly its underlying biology and how to slow or prevent its onset â?? which is especially relevant given its global rise among younger populations.

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What is the instituteâ??s approach to industry partnerships and commercialisation?

Our partnership strategy emphasises both established industry collaboration and entrepreneurial venture creation. As part of the National Institut Carnot (Voir et Entendre), we maintain strategic relationships with major industry players including EssilorLuxottica and ThÃ©a, while simultaneously fostering start-up development.

We have generated fifteen ophthalmology-focused start-ups, operating under the principle that when suitable partners do not exist, we create them. This approach ensures optimal alignment between research objectives and commercial development priorities.

One notable example is Sparing Vision, which is advancing rod-derived trophic factor therapy to preserve cone photoreceptorsâ??critical for high-acuity and colour vision. The company is currently

conducting clinical trials with promising preliminary results, demonstrating the viability of our translational research approach.

While weâ??ve built solid partnerships, thereâ??s still significant room to grow. Thatâ??s why weâ??re exploring the creation of our own instruments to help launch new companies. By enabling more start-up creation directly linked to the Vision Institute, we can expand our industrial collaborations and better bridge innovation with application.

How do you assess the current level of support for ophthalmology research and development?

While industry support continues to grow, ophthalmology lacks the focused attention accorded to oncology through national cancer programmes. Public awareness of vision loss risks remains insufficient, despite the universal threat that aging poses to visual function.

We are implementing comprehensive communication strategies to highlight the societal importance of vision preservation research, targeting both industry partners and philanthropic supporters. Our goal is to accelerate therapeutic development through enhanced funding availability, as we possess the scientific capabilities to deliver transformative treatments given adequate resource support.

The institute benefits from Franceâ??s exceptional educational infrastructure, including prestigious engineering schools and universities such as Sorbonne University. Our international attractiveness is evidenced by our diverse researcher population, including talent from Italy, Turkey, the US, and globally, drawn by our unique research ecosystem.

How is artificial intelligence transforming ophthalmology research and patient care?

Artificial intelligence has been integral to our research methodology for years, particularly through the work of colleagues like Olivier Marre from Ã?cole Polytechnique, who has applied machine learning to visual system modelling. The convergence of AI with ophthalmology occurs naturally, as both fields utilise neural network principles.

Our primary AI application focuses on disease progression modelling, enabling prediction of patient outcomes over months or years. This capability is revolutionary for treatment assessment, as it allows us to determine whether therapeutic interventions successfully alter disease trajectory and demonstrate clinical efficacy.

The availability of comprehensive ophthalmological data, combined with advanced AI modelling capabilities, positions us to solve fundamental questions regarding disease evolution and therapeutic intervention timing.

Looking ahead, what are your strategic priorities for the next few years?

Our fundamental commitment is the successful delivery of new therapies to prevent blindness. This represents a non-negotiable objective that demands collaborative effort across academic, industry, and philanthropic sectors.

We possess the scientific capability and innovative technologies necessary for success. However, the pace of therapeutic delivery will be directly proportional to the level of support we receive. The

choice facing the global community is not whether we will succeed, but how rapidly we can deliver these life-changing treatments to patients worldwide.

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