

From 'Second Skin' to 'Liquid Cornea'

Pandorum's journey into lab engineered tissues as regenerative medicine

Prologue: **Centre for Cellular and Molecular Platforms (C-CAMP) startup Pandorum Technologies**, one of the first Indian biotech startups to venture into tissue engineering with lab-engineered artificial human tissue and organoids such as liquid cornea and 3-D bio-printed livers, is gunning to address the colossal supply-demand gap in organ transplant in India, especially in low-resource settings.

From treating injury or infection led corneal opacity to single-gene metabolic disorders; lab-on-a-chip models to drug efficacy testing, Pandorum is India's soft tissue engineering pioneer both in clinical and medical research. The now ten-year old startup has raked up a whopping pre-Series B funding of 4.8 Million USD ~37 Cr INR from Sunil Munjal, Chairman, Hero Motocorp blazing a new trail for India's biotech startups and India's investment community to succeed in market with deep science.

This latest fundraising comes close on the heels of an investment of upto 41.5 Cr INR by

BTB Ventures, BTB Ventures, Capital Trust, IAN Fund, Kotak Investment and Karnataka Trustee Company in 2020 as its corneal tissue technologies and cell-free exosome therapies for lung fibrosis near clinical trials.

A team of academic entrepreneurs from IISc with backgrounds as diverse as Biophysics and Aerospace Engineering, Pandorum Founders Dr Tuhin Bhowmick and Arun Chandru's journey began with winning the ABLE and DBT organized All India Biotechnology Entrepreneurship Student Content BEST in 2010.

“Startup was not the keyword back in 2011 when we started Pandorum. We needed to build an entity to apply for Government grants which is how it all started. The actual beginning was being selected for first cohort of BIRAC BIG grant with C-CAMP as our BIG partner and incubator.” Says Co-Founder Chandru about the early inception days of Pandorum.

Although Pandorum's genesis was with a skin regeneration concept, the focus later shifted to platform technologies such as biomaterials and hydrogels that can encapsulate different cell-types and enable 3D tissue culture. The startup team of 26 incubated at C-CAMP and Bangalore BioInnovation Centre now spearheads one of India's front running bio-engineering R & D efforts, with 3-D bioprinting capabilities that are compatible with several tissue structures.

Pandorum's initial offering was 3-D differentiated liver micro tissues, only 10 million cells, no vasculature, no neural system. These early stage bio-printed organoids lent themselves easily to CROs, CMOs and assay developers including industry leaders Syngene and Jubilant for clinical trial, drug efficacy, dosing and toxicity studies. Early research collaborations at C-CAMP involved National Institute for Malaria Research, FNDR Foundation for Neglected Disease Research labs to explore

Functional 3-D hepatic spheroids suitable for hepatotoxicity, disease modelling and drug metabolism studies

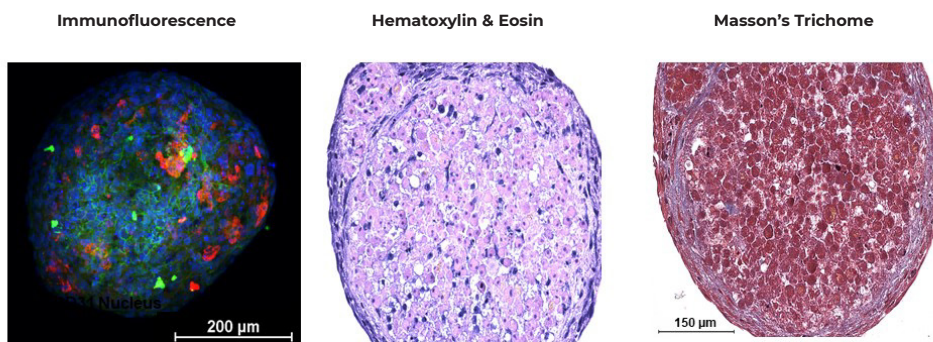


Figure 1: Pandorum's Liver organoids created for tissue regeneration and to mimic wound model for drug screening studies. Immunofluorescence staining of primary liver organoids (multi-lineage liver spheroids) consisting of hepatocytes (ALB), mesenchymal stem cells and vascular endothelial cells (CD31). Histology of organoids using H&E staining and Masson's Trichrome staining showing microarchitecture and distribution of extracellular matrix.

the hibernation capacity of microbes such as malarial parasite plasmodium vivax in livers.

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The then 6-year old Pandorum began its

migration to artificial tissue regeneration. The prime candidate was cornea, a 800 micron thick membrane that is immune-privileged, sans blood vessels and neural networks and a million times less complex to design and develop in petri dishes than vasculated organs.

More importantly, corneal opacity is one of the top three reasons for blindness. And in India alone, there are more than a million people awaiting corneal transplant! Transplants again come with their own set of disadvantages such as 10-20% rejection rate or else ageing, pre-damaged donor tissue. "Cornea donors are usually dead which leaves a narrow window before the tissue degenerates. Only 30% of donated corneas are eventually used for transplants." Adds Bhowmick.

With bio-engineered cornea being globally recognized as a clinically viable option, Pandorum is leading the race from India with two unique solutions- Liquid Cornea and Sutureable Cornea

Pre-clinical study performed with Pandorum's Bioengineered cornea

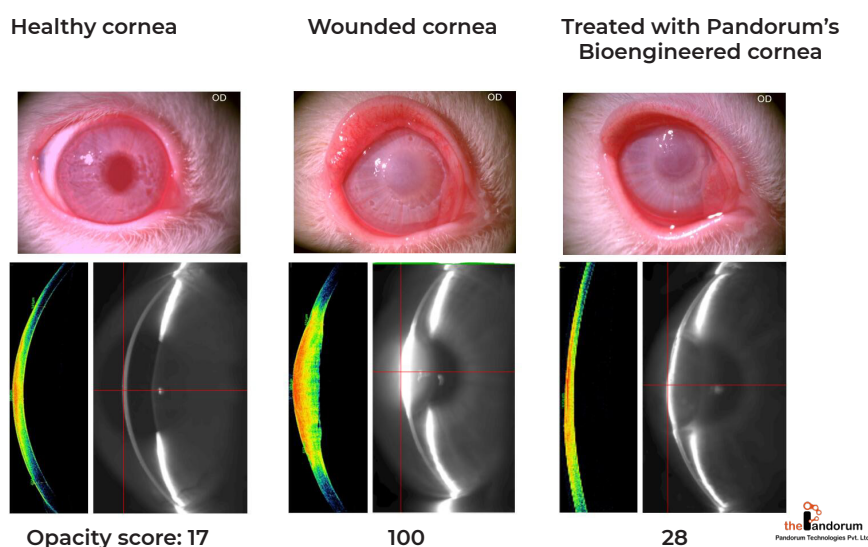


Figure 2: Pandorum's Bioengineered Cornea restoring near-normal vision in alkali-burn wound model in NZ white rabbits.

A cornea is the topmost transparent coat of the eye with a specific refractive index that transmits and partially focuses light into the eye chamber for vision. It comprises of 3 layers: epithelium, stroma and the endothelial layer. Injuries usually occur in the two top layers: epithelium and the stroma both being completely avascular. In case of injuries like acid burn, foreign bodies etc healthy cells from the limbal crypt in the periphery of the cornea migrate to the injury spot as response to the shock. Typically, these cells are from fibrosis regime that results in fibrosed, scarred healing of damaged area.

Pandorum's Liquid cornea, or as they call it "bio-ink" is a photosensitive hydrogel matrix that contain cell modulators, collagen, protein, proteoglycans and other biomolecules that help healing without scar tissue formation. It gelates instantly on shining a blue light and begins cross-linking in situ with neighboring cells. These in turn remodel the temporarily inserted matrix and build back tissue in a controlled manner leading to scar-less regeneration.

"Scars are a result of panic response by the cellular matrix to injury. Our liquid cornea promotes a slower, more organic healing process." explains Chandru. Interestingly there are two versions of the bio-ink, with and without cells. The bio-ink if functionalized with allogenic stem cells can also trigger the regrowth of cellular architecture even in absence of native cell migration. Their pre-clinical data on liquid cornea was presented to a rousing response at the annual meeting of Association for Research in Vision and Ophthalmology, ARVO 2019 in Canada.

The second technology from the same pipeline is the 3D bio-printed cornea. Their

proprietary 'bio-ink' can be used to print transparent, hard and suturable corneal lenticules embedded with live corneal cells. The 3D print is a pre-solidified version with stronger material properties than the liquid cornea allowing surgeons to perform artificially keratinized intra-lamellar transplants, a first in the field of corneal tissue engineering.

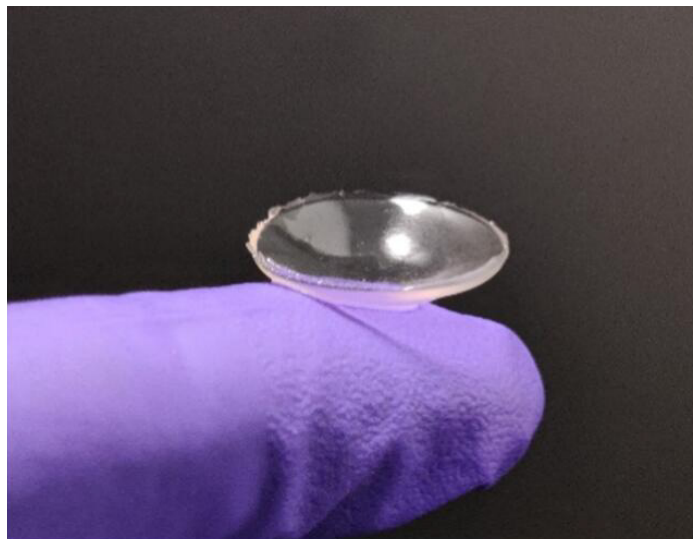


Figure 3: Corneal lenticule bioprinted using Pandorum's proprietary bioink.

Pandorum has already conducted biocompatibility, safety, efficacy, biostability, animal studies of their first product and is currently conducting pilot studies in collaboration with Dr. Virender Sangwan (Shanti Swarup Bhatnagar Awardee) of Dr Shroff's Eye Hospital in New Delhi, an eye surgery heavyweight in India. Over here, their bioengineered cornea is undergoing further trials under DCGI guidance. The biomaterials backbone of their 'Bio-Ink' are all either human-derived or US-FDA approved which is expected to ease the regulatory pathway both in India and abroad.

"While the first 5 years of Pandorum went into perfecting and optimizing our technology platform, as a company we have progressed from basic R&D, animal studies, and are moving towards regulatory approvals and clinical application. Internationally there are a few groups in this area but we are ahead in the race by at least 2-3 years" observes Bhowmick

Naturally media spotlight hasn't been far away. Pandorum was selected as a Economic Times Top Innovator across categories in 2017 and one of top 50 Disruptive Startups in 2019

according to YourStory. Co-Founder Arun Chandru was nominated as Forbes Asia 30 under 30 in 2016. They have won the BioExcellence Award' in Biopharma and

Healthcare sector by the Department of IT-BT and S&T, Govt. of Karnataka, and Association of Biotech Led Enterprises in 2016 and secured 1st place at the 2019 India leg of the Entrepreneurship World Cup becoming the only biotech company from India to compete at the global pitch event in Riyadh in November, 2019.

Apart from corneas, Pandorum is currently focusing on creating extracorporeal bio-engineered livers to treat single gene metabolism disorders which require only

5-10gm of tissue transplant. Having a platform technology with proven resilience, means bio-engineered cardiac tissues, skin cells and pancreas are on the cards as well.

Building on its experience with biopolymers, exosomes, MSC stem cells, it is looking to expand also in the area of cell-free therapies for tissue repair and regeneration. An immediate application is a cell-free treatment to cure COVID-related lung fibrosis which is sitting at the cusp of clinical development.

"In 2011, it was difficult to raise investment for deep-science ideas with an unclear route to market. BIRAC funding through C-CAMP helped us convert our ideas into Proof-of-Concept. Now, Pandorum has a strong IP portfolio, formidable team and exciting pre-clinical data" signs off Chandru

Indeed, one of the earliest BIG awardees at C-CAMP, Pandorum's success story has been the quintessential example of how a deep-science technology despite being extremely high-risk, can capture investor and market imagination. With an arm in the Mission Bay Capital MBC Biolabs in Bay Area,

USA and a clutch of collaborations in South Carolina, Series B capital, two revolutionary corneal tissue engineering products in clinical stage, and several more in pipeline Pandorum is poised to become India's numero uno tissue technology company.



Pandorum Technologies Pvt. Ltd. team working at Bangalore and at Dr. Shroff Charity Eye Hospital, New Delhi



Pandorum International Inc., MBC BioLabs, San Carlos, CA