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Expert Speak

Personalised Medicine: How Biobanks Enable Healthcare Advancements

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Experts have been proclaiming that the healthcare industry is on the verge of technology disruption, but any material changes depend on a number of factors such as the rate of technology adoption and consistency in public health spending. Personalised delivery of healthcare innovation and services is one way to help improve both lifespan and the quality of life. Dr Jugnu Jain, Co-founder and CEO of Sapien Biosciences, writes how biobanks can prove useful in this regard.

Telehealth has been a saviour since the COVID-19 pandemic broke out. People were able to get information and treatment in mild cases without having to go to the hospital. Several companies came up to offer matchmaking for people who needed help at home, heralding the evolution of home-based care, because it was better to be sick at home with COVID-19 than to risk getting sicker in a hospital with critically infected patients. With neighbours offering cooked meals or grocery runs, the crisis also brought communities together.

On the one hand, it was commendable how individuals and communities helped one another during this catastrophe; but on the other hand, healthcare systems, in India and around the world, crumbled under the pressure. With barely 1 to 1.5% of GDP spending on healthcare,[1] the abysmal state of India's caregiving machinery, especially during the pandemic, was there for all to see.

At Sapien Biosciences, our intent is to help develop new diagnostics, which could help detect a disease early and distinguish between two diseases that may superficially look the same, such as a fever. Such research studies are long-term and can take several years. For instance, after a decade of operations and rigorous work, we have developed two diagnostic tests. Sustained research in the life sciences—in research laboratories, think tanks, and biobanks—will prove beneficial in this pursuit, and help us comprehend the heterogeneous nature of diseases.

The Concept of Personalised Medicine

Advances in healthcare improve lifespans and quality of life. But diseases affect individuals differently. Detection or diagnosis of a disease and its treatment, therefore, must be customised and personalised to the specific complaints of the patient, their metabolism and their tolerance to various treatment options.

Here is an example from our work at Sapien Biosciences. During our second year of operations, one of our doctors wanted to test a patient's genes for colon cancer. On doing so, we found a major mutation in their genes, which is causally linked with colon cancer, meaning that those who had the said mutation, developed colon cancer. Armed with this information, the doctor counselled the patient and proceeded with simple blood tests for her sibling—the reason being that

[1]Sinha, D. (2021, February 2). Explained: Despite Govt Claims, India's Health Budget Only Around 0.34% of GDP. The Wire Science. https://science.thewire.in/health/union-health-budget-nirmala-sitharaman-covid-19-pmasby-allocation-gdp-expert-analysis/

hereditary diseases can be detected in the DNA made from blood.

The sibling was found to have the same gene mutation but no symptoms at that point. On a preventive basis, the doctor advised the sibling for a colonoscopy, and found a benign growth; it was caught at the stage where it had not yet become malignant. The patient was advised to get a colonoscopy every two to three years; and we are hopeful that they will most likely never develop colon cancer. Since they know of their disease tendency, if and when there is a manifestation of the cancer, it will be caught in time. And if better treatments that can block the growth of even benign tumours become available, the patient will be able to benefit. In the same way, the patient's children could be monitored early on, and in all likelihood, go on to lead normal lives.

Genomics has been useful in the identification of many such diseases and conditions. It ensures that once something about the human body becomes known, it is not limited to the patient, but becomes a holistic concept that encompasses members of their family. This resultant information can help modify behaviour, particularly in diseases like diabetes, which are also highly influenced by diet, exercise regime, stress levels, etc.

> Therefore, our concept of personalised medicine is giving the right treatment or the right test to the right person at the right time, at the right dose, and at the right regimen.

This can mean understanding that the same drug sometimes split into two doses in the day can be better tolerated by some people rather than giving them all of it once in the day. There are lots of tweaks like these and we should not hesitate to become knowledgeable and involve the doctor in our treatment and health.

Here is another example from a therapy point of view. Temozolomide is one of the only approved drugs for brain cancer. Yet, it works only for about 25% of brain cancer patients.[2] Until 2016, there was no particular reason to understand why it worked for some people, and not for others. But slowly we started to realise that we should give the drug only to the patients who would respond to it. By doing this, those who would not respond to the drug could be saved from exposure to its toxicity. This is personalised care in more general terms.

[2]Bae, S. H., Park, M.-J., Lee, M. M., Kim, T. M., Lee, S.-H., Cho, S. Y., Kim, Y.-H., Kim, Y. J., Park, C.-K., & Kim, C.-Y. (2014, July). Toxicity profile of temozolomide in the treatment of 300 malignant glioma patients in Korea. Journal of Korean medical science. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4101787/

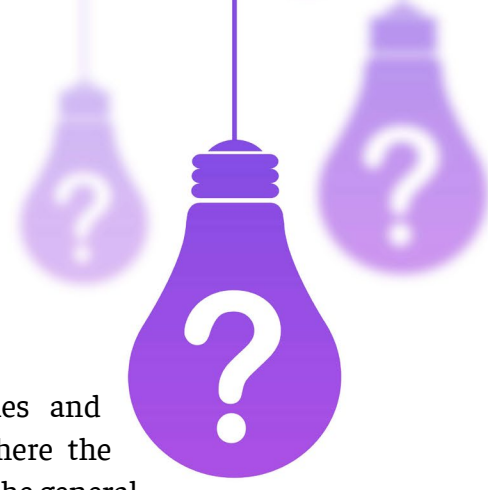
How Biobanks Can Help

A biobank is like a library, a repository of human tissue samples of many kinds. These can be solid and liquid biological tissues like blood or tears; saliva for tuberculosis; urine for kidney-related functions; and nasopharyngeal samples in the case of COVID-19. The collected tissue has the corresponding data associated with the sample like the patient's name, sex, age, history of disease, height, weight, BMI, whether they smoke or drink and the test for which the sample was taken.

Let's say a blood sample was taken for a thyroid test. The result shows the patient's thyroid levels; this information from a large number of people across age groups and genders, can help to understand the genetic basis of hypothyroidism. Furthermore, it makes it possible to compare the findings with people who may not have thyroid problems but display many of the same risk factors. Through this process, we can identify the risk factors, and arrive at a possible cure, or treatment.

So, a biobank at its heart, enables the research and development of personalised medicine by using patient samples to experiment on, rather than the patients themselves, as is done in clinical trials. Let me explain this with an example. When somebody has a fever during the monsoon season, a mosquito bite could be the cause, but a targetted test can help determine if the fever is due to malaria, dengue, Zika infection, or the seasonal flu. Only when enough samples from patients with different mosquito bites are studied, that appropriate tests, diagnosis and treatment plans can be derived.

This is also where a biobank like Sapien comes in—collecting data and samples in a harmonious manner (by utilising 'medical waste') and digitalising it for research in different kinds of studies. The sample and patient data would be safe, secure, and private in this process, ensuring the optimal use of the patient's sample for R&D (Research & Development) into better medicines, diagnostics, and treatments.



The Question of Ethics

Working with human tissue involves clear guidelines and ethical regulations. This is especially true in India where the exploitation linked with organ transplant contributes to the general distrust regarding tissue repositories. A lack of awareness and the fact that organ transplants are not always done in the right moral settings contribute to the disinformation. So, the question of ethics is very relevant in biobanking.

While organ transplant immediately benefits a patient, biobanks enable longer-term research and do not give an immediate benefit to the person who donated the sample. The information gathered from studying the sample may not help the donor directly, but can help many more long after it has been given.

However, it helps to understand that a biobank comprises mostly leftover medical waste. For instance, if three millilitres of blood were drawn for a test, approximately half a millilitre would be used and the remaining 2.5 millilitres would be discarded. But the case for biobanks is that they take the leftover sample instead of letting it be discarded, thus negating the question of exploitation of the human body or its tissue samples. Hence, there is no testing on patients, no trials, and minimal risk as per the guidelines of the Indian Council of Medical Research (ICMR).

For instance, even after a decade as India's first commercial biobank, Sapien is still working on educating its stakeholders and potential clients, like hospitals. This is a challenge for a pioneer in the life sciences industry. But we, at Sapien, are proud that our work caused the addition of a chapter on biobanking to the ICMR guidelines[3] in 2018.

Utility > Innovation

A pandemic year or not, India is not known for new drugs, but for being the pharmacy to the world. We can dispense processes, products, and services for all, and so, we must capitalise on this capability fully. An example of this can be seen in India's efforts towards miniaturising the medicines for HIV/AIDS through the triple treatment combination which was adopted by the World Health Organization (WHO) and provided to the world. Innovation, here, was

[3]Tayal, J., Mehta, A., & Kumar, A. (n.d.). Revised Ethical Guidelines In Indian Biobanking: Do We Need To Downregulate the Proposed Frameworks? https://cdn.ymaws.com/www.isber.org/resource/resmgr/isber_2020/anaheim_eposters/pf19.pdf.

in the process and the way the service was delivered, and not necessarily in the discovery of the drug.

Despite being a country where lakhs of students enroll in the sciences each year, at 1:1456, we have one of the lowest doctor-to-patient ratios in the world.[4] Moreover, there is a tremendous lack of good service companies in India that make scientific equipment or reagents.[5] When you visit any government, private life sciences or healthcare lab in India, you will see that most equipment—from simple deep freezers to microscopes to PCR (Polymerase Chain Reaction) machines—is imported. This is valuable forex that is going outside the country. I also take umbrage on the word innovation, because innovation for the sake of innovation is useless. Indians publish countless papers but barely anything from that research is created or manufactured into something practical, for the use of a lay Indian. So, a blind chase for innovation does not help our industry or our people. In fact, there is a tremendous lack of good service companies in the life sciences that can make reliable equipment.

One way to curtail this chasm is to emphasise to the industry that academia may be better at innovation, and that the industry itself can focus on personalised services, so that these may help the common person. Consider the example of Bharat Biotech's COVID-19 vaccine, Covaxin.[6] It was made in the traditional manner, where the active pathogen was killed but it still had all the proteins that elicit the immune reaction. The human body mounts an immune response to the injected killed pathogen proteins and becomes resistant to its infection. So, for all purposes, Covaxin is not a highly innovative vaccine, but it is a very useful one. And it may be beneficial to the Indian population if we aspire for usefulness and efficacy, as opposed to innovation alone.

Similarly, we must change our mentality to improve India's record with drug discovery and commercialisation of innovative products, beyond publication.

[4]Goel, S. (2020, January 31). The doctor-population ratio in India is 1:1456 against WHO recommendation. Deccan Herald. https://www.deccanherald.com/business/budget-2020/the-doctor-population-ratio-in-india-is-11456-against-who-recommendation-800034.html.

[5]According to Oxford Dictionary, a reagent is a substance or mixture used in chemical analysis or other reactions.

[6]Robertson, S. (2020, September 14). India's whole-virion inactivated SARS-CoV-2 vaccine shows promise. News. https://www.news-medical.net/news/20200913/Indias-whole-virion-inactivated-SARS-CoV-2-vaccine-shows-promise.aspx

Our preference for quick gains, willingness to compromise on quality to reduce cost, and aversion to risk, impacts scientific work negatively. *Jugaad* (a makeshift solution) is the enemy of excellence. If we are constantly bargaining and ready to take the lowest denominator—whether drugs or lab equipment—the government intervenes by fixing prices for things that should cost more, bringing us to an ecosystem in which things will not prosper.

The Case for a Symbiotic Ecosystem

Starting a venture in the life sciences is a very expensive affair. This was a major concern for us when we were ideating Sapien ten years ago. Initially, we thought it would be a not-for-profit or a nonprofit, so that others may access the biobank's samples. But we realised that it needed to be a private and for-profit venture that can support itself. Moreover, there is uncertainty with government funding, and the sad reality is that most academic biobanks the world over are not financially stable. The National BioBank of Singapore, for instance, closed down in 2014 due to lack of funds and utilisation. The same is the case when a biobank is founded for philanthropic reasons.

A private enterprise usually plans ahead with contingency and is motivated to make the venture sustainable. At the same time, public-private partnerships are the way to go for real and long-term change because it is essential that the public, the patients, the hospitals, and the government, all work harmoniously towards the same goal. Government bodies like the Department of Science and Technology (DST), Department of Biotechnology (DBT), Council of Scientific and Industrial Research (CSIR), and ICMR should promote public-private partnerships with biobanks. These arrangements would make more funds available to researchers as well as benefit patients.

At the start of the pandemic, we knew that having good quality data would be essential, because nobody seemed to know why some people in a house were getting infected with COVID-19, while others were not, and why certain individuals in an affected family were asymptomatic while others developed severe symptoms. And

then when plasma transfusion started, there were no guidelines about the level of antibodies for plasma treatment or what drugs were working at which stage; there was no real database. There were several gaps in the healthcare system which led to a tremendous loss of life in the second COVID-19 wave. To fill these gaps for a safer future, industry experts need to be made a part of the discussion and strategy for such public health matters. Otherwise, what academia thinks the world needs and what the world actually needs, may remain exclusive of each other.

Even small advances and measures can help address the gaps. For instance, the DBT's Institute of Life Sciences at Bhubaneswar was recently initiated as the nodal centre for COVID-19 biobanking. Digitalising this data from public and private hospitals into a common pool would help understand the etiology or the cause of the disease, thereby contributing to appropriate and cost-effective diagnosis. In the case of the COVID-19 pandemic, this would be useful in arriving at optimal treatment at a large and organised scale.

In addition to these challenges, India is not seen as a hub in international biobanking, and there is a sense of general wariness in the government regarding private enterprise. Lack of access to expensive lab equipment, ignorance of regulatory guidelines and traditional record-keeping practices among ethics committees or hospital administrators are also contributing factors. Constantly changing tax and corporate laws, especially around the financial year, go against the 'ease of doing business' in India. Thankfully, some of this has changed for the better in the last decade.

There should be a discernible push towards public-private integration, where all parties have a complementary expertise and role. And that, I think, is the key to making innovation come to the market in a manner that is useful for India and the world.

Dr Jugnu Jain *is Co-founder and CEO of Sapien Biosciences, India's pioneer commercial biobank. She is a molecular geneticist and cell biologist by training. On obtaining her PhD from Cambridge University, UK, she pursued a post-doctoral degree and Instructorship at Dana Farber Cancer Institute and Harvard Medical School at Boston, USA. She led multiple drug discovery projects at Vertex Pharmaceuticals in Boston, Massachusetts, before co-founding Sapien Biosciences with scientist-entrepreneur Sreevatsa Natarajan. In 2020, Dr Jugnu Jain won Niti Aayog's 'Women Transforming India' Award.*