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IITs make giant strides in precision onco research

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Cancer has been a leading cause of death worldwide including in India. A study published in Asian Pacific Journal of Cancer Prevention projects that by 2026, new cancer cases in India annually would reach 0.93 million in male and 0.94 million in female patients. Cancers of oral cavity and lungs account for over 25 per cent of cancer deaths in males and cancers of breast and oral cavity account for 25 per cent cancer deaths in females. BioSpectrum India brings a-not-so exhaustive list of some significant cancer research developments made by leading Indian Institutes of Technology (IITs).

Indian cancer researchers are striving hard to bring about evidence-based and research backed potential treatment solutions that are mainly India-specific, accessible, and affordable. In recent years, most prominent cancer research centers have taken significant steps to translate research into improvements in cancer treatment outcomes and public health. Centers such as Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), the state of art of R&D wing of the Tata Memorial Centre are dedicated to onco-research and have really expanded the horizons of India's cancer research. The National Institute of Biomedical Genomics (NIBMG) has also made telling contributions to cancer research and is part of the International Cancer Genomics Consortium.

Among India's several cancer research institutes, IITs have been a major contributor to cancer research. In the past 10 months, researchers from IITs across the country have been consistent with their breakthrough announcements in cancer research. Hence, this is an attempt to put forward a concise compilation of select breakthroughs of this year.

Spearheading cancer R&D

Highlighted here are some indigenous research developments that are raising the bar of our country's cancer research prowess to meet global ranks. No doubt, the IITs have been instrumental in India's climb to 2 spots above and to be ranked 46th by the World Intellectual Property Organisation in the Global Innovation Index 2021 rankings. India has been on a rising

trajectory, over the past several years in the Global Innovation Index (GII), from a rank of 81 in 2015 to 46 in 2021. Undeniably, innovations from IITs have been a major contributor to the consistent improvement in the GII ranking along with scientific departments like the Department of Atomic Energy; the Department of Science and Technology; the Department of Biotechnology, and the Department of Space.

Before we begin on knowing the contributions of some of the IITs in cancer research it is important to understand why India needs indigenous cancer R&D? The main reason is that the majority of the cancer incidences are unique to Indian demographics and ethnicity. Given the heterogeneity of cancers across the world, and the increased prevalence of certain cancers in India, vis-a-vis the western world, a number of researchers focus on India-specific cancers. Due to the inherent genetic diversity, genome-wide association studies have been used to understand the risks and susceptibility of certain ethnic groups for higher cancer incidence. It is also the age of 'personalised medicine' or 'tailoring treatments' to individual patients for better treatment outcomes.

Dr Karthik Raman, Faculty Member, Robert Bosch Centre for Data Science and AI (RBCDSAI), IIT-Madras argues that the public policy reasoning behind cultivating a proper clinical research environment for cancer in India hinges on developing cost-effective solutions proportionate to the incidence rate or burden of the disease. He says, recent developments of national infrastructure across various domains such as clinical trials, tissue banks, and registries have prioritised cancer research for national cancer control.

Adding more insight into this, Dr Siddhartha Sankar Ghosh, Professor, Department of Biosciences and Bioengineering, IIT Guwahati, says, "The research on cancer is crucial to develop safe and efficient methodologies for the diagnosis, prevention, and treatment of cancer. It must be noted that breakthroughs in the prevention, detection, screening, diagnosis, and treatments are the result of extensive research by scientists of diverse fields for decades. Research has helped us acquire extensive knowledge about the biological processes that facilitate the onset, growth, and spread of cancer. This in turn has led us towards discovering novel strategies that include targeted treatments and combination therapies, which have proved to be efficacious in comparison to the conventional therapies."
Former Union Health Minister Dr Harsh Vardhan, in an event held in 2020 on cancer research, had said that it is important to create indigenous, open-source, comprehensive database of molecular profiles of all cancers prevalent in the Indian population. "Many developed countries have invested significant public resources in high-impact, multi-disciplinary cancer research specific to local contexts. India must adopt a similar approach," quoted the then Union Health Minister at that event.

Significant cancer research findings from select IITs

IIT-MADRAS

Cancer is caused due to the uncontrolled growth of cells driven mainly by genetic alterations. In recent years, high-throughput DNA Sequencing has revolutionised the area of cancer research by enabling the measurement of these alterations. However, due to the complexity and size of these sequencing datasets, pinpointing the exact changes from the genomes of cancer patients is notoriously difficult.
Bringing a solution to this difficulty, IIT-Madras researchers have developed an Artificial Intelligence-based mathematical model to identify cancer-causing alterations in cells. The algorithm uses a relatively unexplored technique of leveraging DNA composition to pinpoint genetic alterations responsible for cancer progression. The main use of this technique is to tackle complexity and size of DNA sequencing datasets that can greatly help in pinpointing key alternations in the genomes of cancer patients, which is difficult using present methodologies.
This research was led by Prof. B Ravindran, Head, Robert Bosch Centre for Data Science and AI (RBCDSAI) and Mindtree Faculty Fellow IIT Madras and Dr Karthik Raman, Faculty Member, IIT Madras, and also the Coordinator, Centre for Integrative Biology and Systems Medicine (IBSE), IIT Madras. The results have been recently published in the reputed peer-reviewed *International Journal - Cancers.*

Commenting about this Dr Karthik Raman, Faculty Member, Robert Bosch Centre for Data Science and AI (RBCDSAI), IIT Madras, said, "Personalised medicine involves tailoring therapy based on the characteristics of an individual patient. Given their vital role in tumor progression and development, computational prioritisation of cancer driver (or pathogenic) mutations is an active area of research. Understanding the underlying mechanism of these alterations will help identify the most appropriate treatment strategy for a patient in an approach known as 'precision oncology.' There are many drugs that are known to 'NOT WORK' on patients with particular mutations/genetic backgrounds. Our focus on driver mutations is another step in this direction. Tailoring treatments to a specific illness and a particular person's genetic makeup is challenging and

requires extensive cataloging of the driver variants of interest.”

The other significant cancer research that has definitely placed India on par with global counterparts is IIT-M researchers’ breakthrough findings of a specific microRNA (miRNAs) called ‘miR-155’ that is over-expressed in tongue cancer. This finding is important in that molecular strategies can potentially be devised to manipulate miR-155 expression to develop therapeutics for tongue cancer.
miRNAs affect cancer growth through inhibiting or enhancing the functions of certain proteins. For example, it has been shown that a type of protein called ‘programmed cell death 4’ or phelps in stopping cancer cells from growing and spreading. Inhibition of this protein has been known to cause spread of oral, lung, breast, liver, brain and colon cancers.

A team led by Prof. Devarajan Karunagaran, Head, Department of Biotechnology, IIT-M, collaborated with researchers from Cancer Institute and Sree Balaji Dental College and Hospital at Chennai and Indian Institute of Science (IISc) Bengaluru for this research.

Apart from these research developments, IIT-M researchers in collaboration with Chennai's Adyar Cancer Institute are developing a kit for early ovarian cancer detection. Ovarian cancer, which is the seventh most common cancer in the world, is often known as "the silent killer" as most women do not show symptoms at an early stage. This results in patients seeking treatment only after the disease progresses. As of now, early detection of ovarian cancer has not been possible due to a lack of reliable markers or diagnostic tests. To address this need, IIT-Madras is collaborating with Chennai's Cancer Institute (WIA) for ovarian cancer detection to be a reality. Both institutions are developing low-cost diagnostic kits for early ovarian cancer detection.

In another research development, IIT-M researchers have developed an alternative source for anti-cancer drug Camptothecin. The researchers, led by Dr Smita Srivastava, Associate Professor, Department of Biotechnology, IIT Madras, have identified a sustainable and a high-yielding microbial strain as an alternative producer for the anti-cancer drug Camptothecin. This novel microbial fermentation process can be an economically-efficient method of production to fulfil the market demand at large scale.

Topotecan and Irinotecan are two widely used anti-cancer drugs, which are produced by using Camptothecin as the lead molecule. Camptothecin is an alkaloid isolated from the Chinese tree Camptotheca acuminata and the Indian tree Nothapodytes nimmoniana. Nearly 1,000 tonnes of plant material is required to extract just one tonne of Camptothecin. Due to extensive overharvesting to meet the market demand both these plants are now critically endangered. Owing to these issues, IIT Madras researchers have now developed an alternative method of Camptothecin production to meet the demand and conserve the natural sources.

Also, IIT-M and Massachusetts Institute of Technology (MIT) scientists have grown human brain tissues called ‘organoids’ with help of a 3D Printed Bioreactor that they developed. The objective was to observe the brain tissues while they grow and develop, a technology that can potentially accelerate medical and therapeutic discoveries for diseases such as cancer and neurological disorders like Alzheimer’s and Parkinson's.

Mid of 2021, IIT-M researchers published a deep learning-based AI framework that can perform digital pathology image analysis to diagnose cancer accurately and quickly. Last year, another team from IIT-M showed how reactive oxygen species (ROS) could be used to fine-tune anti-cancer therapies for better outcomes.

National Cancer Tissue Biobank (NCTB) is a state-of-the-art, non-profit community- based cancer tissue storage facility located at the Department of Biotechnology, Indian Institute of Technology Madras, Chennai. This facility is jointly funded by the Department of Sciences & Technology (DST), Government of India, IIT-M, and initiated in collaboration with Cancer Research and Relief Trust (CRRT), Chennai. Biobank collects the cancer tissue samples with consent from patients diagnosed with cancer and information about the previous medical history and treatment of the donors is also documented. Tissue samples collected following surgery are in excess of what is required for diagnosis and would otherwise be discarded. All the different types of cancer tissue samples collected from cancer hospitals will be stored. It is a first-of-its-kind facility in India that aims to provide researchers with high quality of cancer tissues and the patient data in order to facilitate cancer research discoveries that will lead to improvements in cancer diagnosis and treatment.

Apart from the NCTB at IIT-M, Tata Medical Centre Biorepository (TiMBR) in Kolkata, collects and stores tissue, blood, and other samples from cancer patients for future investigations and biomarker discovery.

IIT-GUWAHATI

Significant breakthroughs in cancer research have been demonstrated by IIT-Guwahati researchers too in recent years. A team led by Dr Siddhartha Sankar Ghosh has been working on cancer research since 2003, primarily focusing on cancer gene therapy systems. They have also been working on nanotechnology-based solutions for combating cancer. The team is also into understanding of the aggressive circulating tumor cells in the flow channel. At present, his group is working on nano-theranostic devices for early cancer detection and signaling of EMT dynamics in drug resistant cancer. Outcome of their research has been published in 175 peer-reviewed journals, and documented for several national and international patents.

Dr Ghosh said, “There is always a possibility to scale up the research studies in different aspects of cancer and cancer types, and it will only be fruitful if more researchers are inclined and dedicated to deciphering the mystery behind this complex disease. From what he says, it is clear that there is an increasing need for more Indian researchers to work on indigenous cancer related discoveries.
IIT-Guwahati has also signed an MoU with the North East Cancer Hospital and Research Institute (NECHRI), Jorabat, Assam, to undertake research to identify the cancer-susceptible population from North East India. Also, IIT-Guwahati researchers have developed AI models to detect colorectal cancers from colonoscopy images.

IIT-JODHPUR

In India, the incidence of central nervous system (CNS) tumors ranges from 5 to 10 per 100,000 individuals and accounts for 2 per cent of malignancies. High-grade gliomas (glioblastomas) account for 59.5 per cent of CNS tumours in India. Glioblastomas are associated with high mortality of fewer than 14 months even after chemotherapy, radiotherapy and surgery. A key challenge for clinical management of glioblastoma (GBM) is its highly heterogeneous nature, with heterogeneity between patients and within a single tumor representing important barriers for current therapies. Preclinical GBM models are limited by the lack of a ‘normal’ human microenvironment and the inability of many tumor cell lines in the laboratory to accurately reproduce GBM biology. To address these limitations, an interdisciplinary research team has created a model system to retro-engineer patient-specific GBMs using patient-derived cells into patient-derived GBM tumor spheroids.

Patient-derived xenografts (PDXs) are models of cancer where the tissue or cells from a patient's tumor are implanted into an immunodeficient or humanised mouse. Speaking about the viability of this research in the Indian context, Dr Sushmita Jha, Associate Professor, Inflammation, Immunity & Tumor Biology Lab (IITBio Lab), IIT-Jodhpur, says, “Our model is a viable option for personalised cancer medicine in the Indian subcontinent. We believe our efforts will provide an enhanced understanding of recalcitrant glioblastoma pathology allowing for better identification of histological markers, and therapeutic targets that, in the long run, may aid in the development of better strategies for diagnostics and/or development of therapeutics for improved survival and/or delayed disease progression. This will also provide a cost-effective and rapid method for disease diagnosis and treatment prediction.”

OTHER IITs

Recently, IIT Bombay researchers patented an indigenous CAR-T cell technology that leverages a patient’s immune system to treat cancer. A first-of-its-kind clinical trial of this indigenously developed therapy started in Mumbai’s Tata Memorial Centre last June. IIT Indore has developed a cost-effective drug with lesser side effects, M-ASPAR, to treat patients suffering from Acute Lymphoblastic Leukemia. They are also planning to start Phase I and II drug clinical trials in collaboration with the Advanced Centre for Treatment, Research, and Education in Cancer, Tata Memorial Centre, Mumbai. IIT Roorkee researchers have developed a new non-invasive method of detecting breast & ovarian cancer. The researchers got a breakthrough in identifying certain proteins present in the saliva that act as potential biomarkers indicative of breast & ovarian cancer metastasis.
As noted by M Venkaiah Naidu, Vice President of India, premier institutions like IITs are the knowledge capitals of the country and they must share their expertise and best practices with other educational institutes to boost innovation and pledge to

make India self-reliant in research and development and bring cost-effective treatments closer to the citizens of India.

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