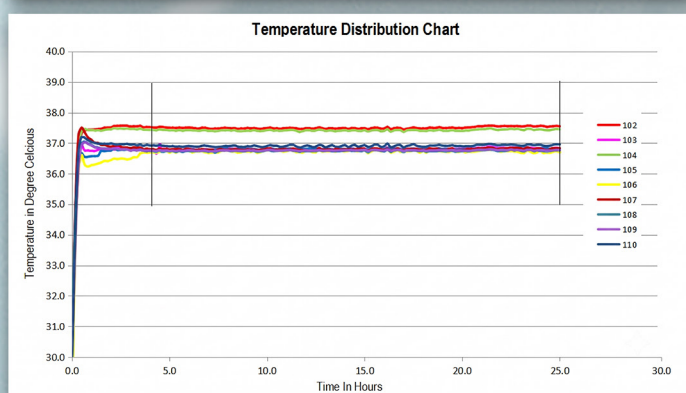
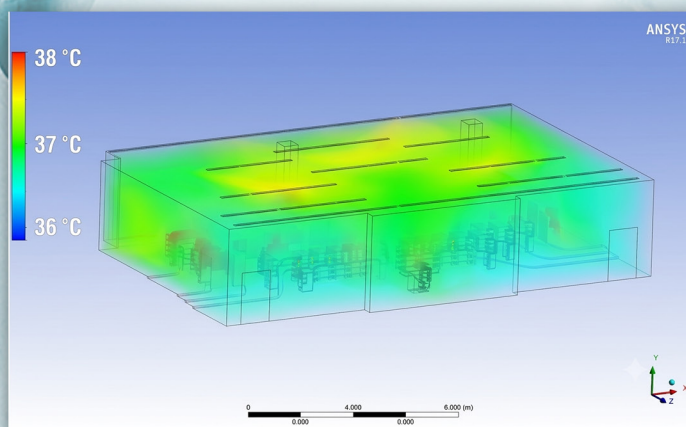
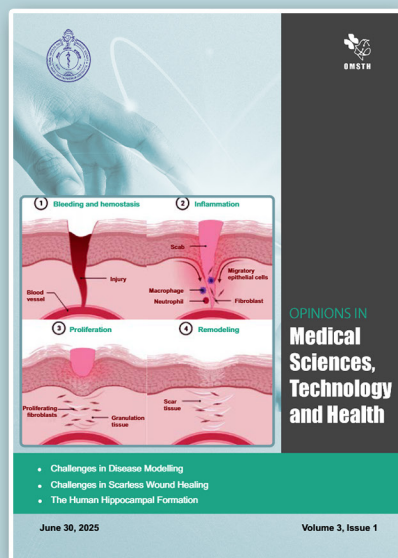




OPINIONS IN Medical Sciences, Technology and Health

- Temperature Distribution Measurement
- Therapeutic Algae in Cancer Therapy
- Lab to Market Transitions
- Post Neurosurgical Meningitis

PREVIOUS ISSUES OF OUR JOURNAL



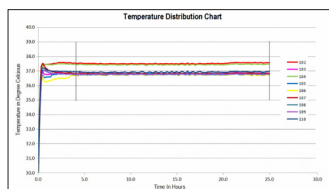
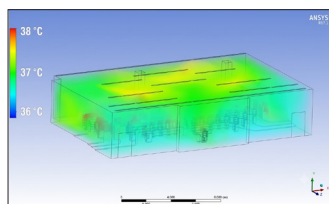


Cover Photos

Courtesy: Leena Joseph

Department of Technology & Quality Management,
Biomedical Technology Wing,
Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Thiruvananthapuram
Kerala, India – 695 012

The figures illustrate the comprehensive thermal mapping of the equipment. Figure A shows the temperature profiles mapped across the internal space of the chamber, where continuous logging at fixed intervals over a 24-hour period allows users to pinpoint critical hot or cold spots. Complementing this, Figure B illustrates how plotting these profile data points provides a clear, detailed understanding of the overall internal temperature distribution. These periodic verifications benefit the user by ensuring optimal equipment efficiency and consistent thermal performance.



Cover Design and Logo Credit
Aishwarya Nandkumar

OPINIONS IN Medical Sciences, Technology and Health

Chief Editor

Dr. Maya Nandkumar A, *SCTIMST, Thiruvananthapuram*

Executive Editor

Dr. Francis Boniface Fernandez, *SCTIMST, Thiruvananthapuram*

Editors

Dr. Roy Joseph, *SCTIMST, Thiruvananthapuram*

Dr. Biju Soman, *SCTIMST, Thiruvananthapuram*

Dr. Narayanan Namboodiri, *SCTIMST, Thiruvananthapuram*

Dr. Sapana Erat Sreedharan, *SCTIMST, Thiruvananthapuram*

Dr. Deepti A. N., *SCTIMST, Thiruvananthapuram*

Dr. Ganesh Divakar, *SCTIMST, Thiruvananthapuram*

Dr. Naresh K., *SCTIMST, Thiruvananthapuram*

Dr. Renjith P. Nair, *SCTIMST, Thiruvananthapuram*

Mr. Arumugham V., *SCTIMST, Thiruvananthapuram*

Guest Editor

Dr. Annie John (*Retd. Faculty*)

Editorial Assistance

Dr. Divya PV., *SCTIMST, Thiruvananthapuram*

Scope

Technology has been breaking boundaries in medical sciences. We here at SC-TIMST were the torchbearers of innovations in medical sciences in India by the amalgamation of engineering, basic science and public health and were responsible for the development of the first indigenous aortic valve in India. The Chitra blood bag is another success story. At this juncture, as we complete 46 years of dedicated innovations to society, the knowledge and expertise we possess on the development, validation, clinical trials, translation and commercialization of medical devices, and at the same time delivering high-end medical care in neuro-logical and cardiological disciplines and public health, we think it is time to share and hence this Journal.

The Journal will publish reviews in the field of medical sciences with a focus on cardiological and neurological sciences, biomedical technologies its translation and commercialisation and public health.

Published by The Research & Publication Cell, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram 695011, India



Contents

Volume 4, Issue 1, June 2026

- e26001 **Editorial:**
Maya Nandkumar A
- e26002 **Review Article:** Measurement Model of a Thermal Metrology System
Arumugham V, Rajesh RP, Ranjith G and Leena Joseph
- e26003 **Review Article:** Engineering Therapeutic Algae in Cancer Therapy through Synthetic Biology and Nanotechnology
Shai Shikha Rout, Jiban Jyoti Panda
- e26004 **Review Article:** From Lab to Market: Bridging Academia-Industry Gaps in MedTech Innovation
Subhash NN, Muraleedharan CV
- e26005 **Perspective:** Post Neurosurgical Meningitis: A Perspective on Laboratory Guided Management
Kavita Raja
- e26006 **Advertising Feature**
- Submission Guidelines** v



Editorial

A Maya Nandkumar

Scientist G (Sr. Grade), Division of Microbial Technology, Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram-695012, Kerala, India.

**anmaya@sctimst.ac.in*

In this first issue of the 4th Volume of Opinions in Medical Sciences, Technology and Health we have some interesting reviews and commentary. Scientific progress is often described as a journey from discovery to application. In practice, however, the path from laboratory to clinics is rarely linear. It depends on GLP (Good Laboratory Practices) to build robust, reliable, and acceptable data, biological understanding, engineering discipline, industrial collaboration, and clinical judgment. The topics assembled in this issue - from thermal metrology in enclosed chambers to engineered therapeutic algae, MedTech translation, and the laboratory-guided management of post-neurosurgical meningitis - illustrate a shared principle: innovation becomes meaningful only when it is measurable, reproducible, safe, and responsive to the real-world needs.

The measurement model of a thermal metrology system, particularly in studies of temperature distribution within enclosed chambers, provides a useful foundation for this broader discussion. Temperature is not a single value but a spatially and temporally variable phenomenon influenced by sensor placement, chamber geometry, airflow, heat sources, calibration, and environmental conditions. A robust measurement model must therefore account for uncertainty, traceability, repeatability, and the distinction between the quantity being measured and the instrument used to measure it. Such rigour is essential not only in thermal engineering but across biomedical research, where poorly characterized measurements can compromise experiments, obscure mechanisms, and produce irreproducible conclusions.

The review on therapeutic algae through synthetic biology and nanotechnology examines algal systems as an intriguing platform for cancer therapy because of their versatility, biocompatibility and amenability to engineering to produce therapeutic molecules, deliver drug payloads, and facilitate targeted drug delivery. All this becomes feasible when characterizations are performed precisely, with calibrated equipments within the right framework, essentially on the GLP platform.

Scientists must be able to measure biological performance under defined conditions: growth kinetics, genetic stability, nanoparticle behavior, biodistribution, immune response, toxicity, and clearance. As in thermal



Citation: Nandkumar AM. Editorial. Opn. Med. Sci. Technol. Health. 2026; 4(1): e26001.

Copyright: © 2026 Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Corresponding Author Address:

Dr. A. Maya Nandkumar, Chief Editor,
Scientist G (Senior Grade) and Head,
Division of Microbial Technology,
Biomedical Technology Wing,
Sree Chitra Tirunal Institute for Medical
Sciences and Technology,
Thiruvananthapuram 695012, India
anmaya@sctimst.ac.in
ORCID ID: 0000-0002-8949-4953

metrology, the central question is not whether a system “works,” but under what conditions, with what uncertainty, and according to which validated endpoint. Differences in temperature, pH, oxygenation, light exposure, or culture conditions can alter algal behavior. Without standardized protocols and reliable measurement models, apparent therapeutic success may reflect uncontrolled experimental variation rather than a reproducible biological effect.

The transition from a promising laboratory technology to patient benefit also depends on addressing the persistent gap between academia and industry in MedTech innovation. Academic research often rewards novelty, publication, and proof of concept. Industry, by contrast, prioritizes manufacturability, regulatory compliance, quality systems, usability, and sustainable business models. These are not opposing priorities, but they need to be addressed for commercial success.

The need for a common platform becomes important when extrapolated to a clinical setting. Here we present a perspective on laboratory guided management of post-neurosurgical meningitis. Diagnosis and treatment are complicated by prior antimicrobial exposure, altered cerebrospinal fluid characteristics, blood contamination, indwelling devices, atypical clinical presentations, and the possibility of organisms with significant antimicrobial resistance. Laboratory data—including cerebrospinal fluid analysis, microbiological culture, molecular diagnostics, antimicrobial susceptibility testing, and relevant blood investigations—must be interpreted alongside surgical history, imaging, and the patient’s clinical history.

So, this issue with a wide repertoire of essays on various aspects of health-care delivery shows that the future of medicine will depend on technologies that can move confidently across boundaries: from physical measurement to biological function, from proof of concept (POC) to industrial production, and to clinical decisions. The studies represented here reinforce that a successful innovation is built through rigour, accurate measurement, transparent uncertainty, rigorous validation, and sustained collaboration.



Measurement Model of a Thermal Metrology System

A case study on temperature distribution in enclosed chambers

Arumugham V¹, Rajesh RP¹, Ranjith G² and Leena Joseph^{1*}

¹Calibration Cell, ²Division of Artificial Internal Organs,

^{1,2}Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala, India – 695 012.

Abstract

To maintain the accuracy and reliability of thermal processing through adherence to various regulations and standards for medical, pharmaceutical, food, and laboratory applications, it is essential to evaluate the temperature distribution within the enclosed chambers. Variations in temperature across a chamber and fluctuations over time can result in non-uniform processing conditions, potentially affecting chemical reactions, biological growth, product stability, experimental outcomes, and sterilization efficacy. Temperature distribution measurement, commonly performed through temperature mapping using calibrated temperature probes, provides a systematic means of assessing thermal uniformity within an enclosed chamber. It enables the identification of hot spots and cold spots, evaluation of temperature variations over time, and verification that the measured temperatures remain within predefined acceptance limits. Temperature mapping of enclosed chambers, such as ovens, incubators, stability chambers, refrigerators, and other controlled-temperature equipment, is therefore an important quality-assurance practice. It supports the reliability and reproducibility of experimental and processing conditions and contributes to compliance with applicable Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and relevant regulatory and quality standards.



Citation: Arumugham V, Rajesh RP, Ranjith G, Joseph L. Measurement Model of a Thermal Metrology System. *Opn. Med. Sci. Technol. Health.* 2026; 4(1): e26002.

Received: Jan 2, 2026

Accepted: May 5, 2026

Published: June 30, 2026

Keywords: temperature measurement; temperature distribution; thermal metrology, multi-channel logging, calibration

Copyright: © 2026 Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the manuscript.

Funding: Declared.

Competing interests: None declared.

***Corresponding Author Address:**

Leena Joseph,
Engineer G, Calibration Cell,
Department of Technology & Quality
Management
Biomedical Technology Wing
Sree Chitra Tirunal Institute for Medical
Sciences and Technology
Thiruvananthapuram, Kerala, India – 695 012
Email: leenaj@sctimst.ac.in
ORCID ID: 0009-0005-8525-9680

1. Introduction

Metrology, in the view of the scientific community, is the science of measurement made to validate the theories of the nature of the universe or to explore new theories. Calibration is such a measurement done under specified conditions in relation to a traceable standard equipment or reference material. Temperature is the average kinetic energy of a system, as defined by the zeroth law of thermodynamics. Thermal metrology is crucial since temperature measurement is required in various fields such as environmental monitoring, power plants, agro-industries, oil & gas refineries, medical sciences, and even more [1].

Temperature distribution measurement is a versatile procedure used to evaluate variations in temperature at different locations within an enclosed chamber over a specified period. This is achieved through temperature logging using traceable and calibrated temperature sensors positioned at designated locations within the chamber. The recorded data enable quantitative assessment

of both the spatial distribution of temperature (temperature uniformity) and the stability of temperature control over time [2,3].

An in-house temperature mapping setup, developed based on the requirements of relevant international standards, including ASTM E145 and ASTM E715, is available for carrying out temperature distribution measurements. Identification of sources of uncertainty elements and estimation of a standard uncertainty along with measurement results in carrying out the temperature distribution measurement procedures.

A case study is presented to demonstrate the methodology for temperature distribution measurement and uncertainty estimation in an incubation chamber. The study illustrates sensor placement, temperature data acquisition, analysis of spatial and temporal temperature variations, identification of uncertainty components, and estimation of the associated measurement uncertainty.

2. Temperature, it's measurement techniques and calibration

Temperature is a measure of the average kinetic energy of individual molecules of matter. In simple terms, temperature is often said to be the 'degree of hotness', but more scientifically, it is the potential for heat transfer by conduction, convection or radiation. The very first record of a temperature scale belongs to the Greek Galen (AD 130–200), who identified eight degrees of temperamentum, which he used to characterize the temperament of his patients and the effects of his medicines [4]. Temperature sensors belong to different categories based on their principle of measurement like resistance type, thermocouples, non-contact type, etc.

Temperature calibration determines the performance characteristics of temperature sensors or a measurement system by means of a direct comparison against reference temperature measurement standards [5]. Following are the main reasons for performing the calibration of an instrument [6].

- To establish and demonstrate traceability.
- To ensure readings from the instrument are consistent with other measurements.
- To check the accuracy of the instrument.
- To establish the reliability of the instrument.

3. Types of Temperature Sensors

Accurate temperature measurement is fundamental in medical device analysis. Accurate temperature measurement is crucial for evaluating Medical Devices, especially those used within a controlled-temperature environment such as incubators, sterilizers, blood, and stability chambers and environmental test chambers. Here, minor fluctuations in temperature can impact device performance, patient safety, and the dependability of test results. It is

mandatory therefore to have suitable temperature sensors and follow an internationally recognized temperature measurement scale, such as the International Temperature Scale of 1990 (ITS-90), as an integral component of thermal metrology system reliability.

Temperature Sensors: A temperature sensor is a device that measures changes in temperature and converts them to an electronic signal for display. The temperature sensors most frequently used when testing Medical Devices are referred to as Resistance Temperature Detector (RTD), Thermocouple, Thermistor, and Infrared (IR) Sensors. Each type of sensor operates on a different physical principle and is chosen based upon the choice of temperature sensor according to their desired temperature accuracy, measuring range(s), and response time(s), as well as other environmental factors.

RTDs (Resistance Temperature Detectors) are one of the most precise and stable types of contact-based temperature sensors in the market. RTDs work on the principle that the resistance of a pure metal (usually platinum) varies predictably and consistently with temperature, making it possible to accurately determine temperature using the measurement of resistance. The most common configuration for an RTD is a Pt100, which has a resistance of 100 ohms at 0°C, and the less common Pt1000 that has an equivalent resistance of 1000 ohms at 0°C. Due to their high accuracy, repeatability, and long-term stability, RTDs are extensively used in the medical field and in calibration labs and medical environment chambers (i.e., incubators, blood banks, pharma refrigerators, and stability chambers) [7]. The temperature ranges that can be measured by RTDs vary significantly depending on their design and intended application, with most RTDs measuring from -200°C to 850°C, providing exceptional accuracy when performing temperature mapping or validation testing.

Thermocouples are another type of widely used temperature sensors. Thermocouples utilize the Seebeck effect to create an electrical signal due to discrepancies in temperature found inside the sensor, or at the connection of the two dissimilar metals. Thermocouples can be grouped according to the thermoelectric junctions used, with Type K, Type T and Type J being the most predominant types of thermocouples found in laboratories and industry. Each of these thermocouples can function within specific temperature ranges, exhibit different degrees of sensitivity and can withstand varying degrees of environmental and mechanical stress during testing and operation [8]. Thermocouples have the ability to measure a wide range of temperatures (-200°C to 1600°C) depending on the types of metal used to manufacture the thermocouple. Although thermocouples are not as accurate as resistive temperature devices (RTDs), they are capable of being utilized for thermal profile analysis and thermal mapping of zones requiring multiple measurements throughout large chambers [9]. Thermocouples are also commonly used to measure temperature gradients, hot and cold zones, in medical devices.

Thermistors which are temperature-sensitivity resistors made from semiconductor materials (like metallic oxides), have a great increase in their resistance based upon a minimal increase in temperature, providing them

with an extremely high sensitivity and very fast response to change. The type of thermistor typically used for medical purposes is a Negative Temperature Coefficient Thermistor (NTC), which means that as the temperature increases, the resistance of the thermistor decreases. Thermistors may be used in patient monitor equipment, digital thermometers and localized temperature sensing applications. Long-term drift can occur, making them less than ideal for high accuracy standards as compared to an RTD (resistance temperature detector). They typically will function in the range of about -50°C to $+300^{\circ}\text{C}$ depending on the thermistor construction and materials used.

Infrared (IR) Sensors are classified as Non-contact temperature sensors because they detect infrared Radiation emitted by an object, rather than directly measuring the temperature. IR sensors can be used when there is no opportunity to physically touch the object to take a temperature reading or if you are trying to take a temperature reading from a moving or fragile object. The main applications of these devices are Thermal Imaging and Surface Temperature Measurement. However, the accuracy of an IR sensor is affected by many factors including the emissivity of the surface it is measuring, the distance from the object and the environmental conditions. Typically, due to the closed structure of medical chambers, IR sensors are only used for surface temperature measurements not for studying the temperature distribution of the air inside medical chambers.

4. International Temperature Scale of 1990 (ITS-90)

An internationally recognised Reference Temperature Scale is required to ensure temperature measurement uniformity and accuracy globally. The International Temperature Scale (ITS-90) of 1990 provides that reference standard [10]. ITS-90 is an internationally recognised standard that has been developed by the General Conference of Weights and Measures (CGPM) and is based on several fixed-point definitions and interpolation devices. There are several critical Fixed Points in the ITS-90 including the triple point of water (0.01°C) and freezing points for pure metals such as Indium, Tin, Aluminium, Silver, and Gold, or boiling points for gases such as Oxygen and Argon. These fixed points act as reproducible reference points to calibrate temperature sensor devices. Standard Platinum Resistance Thermometers (SPRTs) have been designated as the interpolation elements for the realization of the ITS-90 Standard by both national and international metrology laboratories [11].

In a thermal metrology system used for the evaluation of medical diagnostic devices, both the reference Thermometers and Working Thermometers must be traceable to the ITS-90 standard through national/metrological calibration standards. That is to say, temperature measurements obtained through various sources - including medical diagnostic devices - may be compared with confidence with one another, without the fear of introducing systemic error.

5. Temperature chambers and distribution measurement

Thermal parameters of medical devices cannot be neglected both during its

development stages and in routine use. Incubators, refrigerated centrifuges, ovens, deep freezers, etc., are equipment commonly used in biomedical device development or evaluation facilities, to provide controlled temperature environment for specific purposes. These temperature chambers are generally working on forced air convection principles, by means of a fan to assure uniformity. Excessive or low temperatures inside the chamber may cause unforeseen product failures. In such cases, availability of data from periodic calibrations can ascertain the temperature pattern inside. Hot or cold spots may get identified by analyzing the data patterns to prevent the loss of time and cost.

Built of thermal chambers are varied with material of construction, type of door sealing, air circulation equipment, and working principle of temperature controllers, etc [12]. Their thermal characteristics may vary with their design parameters selected to suit their end uses. Computational Fluid Dynamics (CFD) is being used to interpret and assess the temperature distribution patterns in the design phases [2]. Whereas during routine use, periodical monitoring or calibrations are required to ensure the performance of temperature chambers. Deterioration in performance with ageing or poor performance of feedback sensors or heating systems should be corrected based on such calibration results.

Multipoint temperature measurements as part of installation qualifications may help users to get proper understanding of thermal pattern inside the chambers. Based on end use requirements, distribution measurements may be performed at different load conditions like empty load, maximum load or simulated load conditions, to understand the thermal characteristics of chambers. By logging temperature at fixed time intervals, over a period, say 24 hours, and over the space inside, user could model temperature profiles (figure 1) to understand the hot points or cold points inside the chamber. User could get benefited with the efficient use of equipment with the periodic verifications.

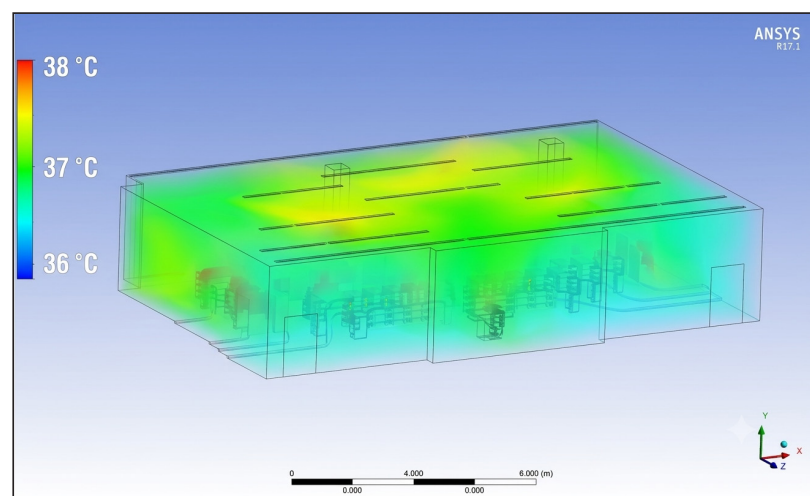


Fig. 1 Temperature distribution model

6. Sources of uncertainty in temperature distribution measurement

Measurement uncertainty is a parameter associated with the result of a measurement that characterizes the dispersion of the values that could reasonably be attributed to the measurand. It is evaluated as Type A (by statistical methods) and Type B (non-statistical) approaches, then combined and, expanded to give a final range within which the true value is believed to lie with a specified probability. It is always non-negative and is most often expressed as a standard uncertainty u (standard deviation-like) or as an expanded uncertainty $U = k \cdot U_c$ with a stated coverage factor and confidence level.

The major parameters [say x_i] considered for the estimation of uncertainty during the measurement of temperature in enclosed chamber are,

- Repeatability of measurement [x_1]
- Accuracy of data acquisition system [x_2]
- Calibration uncertainty of data acquisition system with RTD probes [x_3]
- Drift of RTD probes [x_4]
- Resolution of readout [x_5]
- Temperature Gradient/stability of temperature chamber [x_6]
- Uniformity of temperature chamber [x_7]

The Uncertainty from each parameter [x_1 to x_7] is estimated separately as U_1 to U_7 .

Combined standard uncertainty [U_c] in the temperature distribution is given by

$$u_c = \sqrt{U_1^2 + U_2^2 + U_3^2 + U_4^2 + U_5^2 + U_6^2 + U_7^2}$$

The expanded uncertainty, U is estimated by multiplying the combined standard uncertainty by a coverage factor $K=2$, which for a normal distribution corresponds to a coverage probability of approximately 95% confidence level. It can be estimated as, $U = U_c \times K$

7. A typical case study of temperature measurement inside an enclosed Chamber at 37°C

A sample temperature distribution measurement inside an incubator set at 37°C is described below. The measurement system is set up as shown in figure 2.



Fig. 2 Temperature distribution model

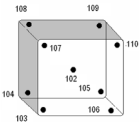
Nine platinum resistance (Pt100) temperature probes are positioned within the test incubator. Each probe is secured properly inside the incubator ensuring that no sharp bends are there in sensor cables. One Pt100 probe is placed in each of the eight corners of the measurement chamber, approximately 5 cm from the adjacent walls. The ninth Pt100 probe is positioned within 2.5 cm of the geometric centre of the incubator.

All Pt100 probes are connected to their respective channels on the data logger, and the functional parameters of each channel are appropriately configured. The incubator is then switched on, and its temperature is adjusted to the required set point. The system is allowed to stabilize for a minimum of three hours cut-in cycles (in the case of On-Off controllers) or for at least 30 minutes after the set temperature has been reached.

Once thermal stabilization is confirmed, continuous Pt100 sensor readings are recorded for a minimum of 24 hours in an interval of 10 minutes. Temperature readings from the incubator's indicator, the ambient room temperature, and the nine Pt100 probes are manually recorded for a minimum duration of three hours at 10-minute intervals in between these 24-hour logging.

Upon completion of data acquisition, the scanning process is terminated, and the recorded data from the data logger are transferred to a computer. The logged data are subsequently processed using Microsoft Excel to evaluate the temperature uniformity, stability, and uncertainty characteristics of the incubator.

Data in table 1 below provides the average temperature of each channel which are placed in various positions inside the incubator for minimum 24 hours. Plotting temperature profile as in figure 3, will give an understanding on distribution of temperature inside the chambers.

Table 1. Average temperature of 9 sensors in various positions inside Incubator over 24 hours										
	Channel ID	102	103	104	105	106	107	108	109	110
	(°C)									
	Average	36.1	36.2	36.1	36.2	36.0	36.3	36.3	36.2	36.3
	Expanded uncertainty $\pm U$	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7

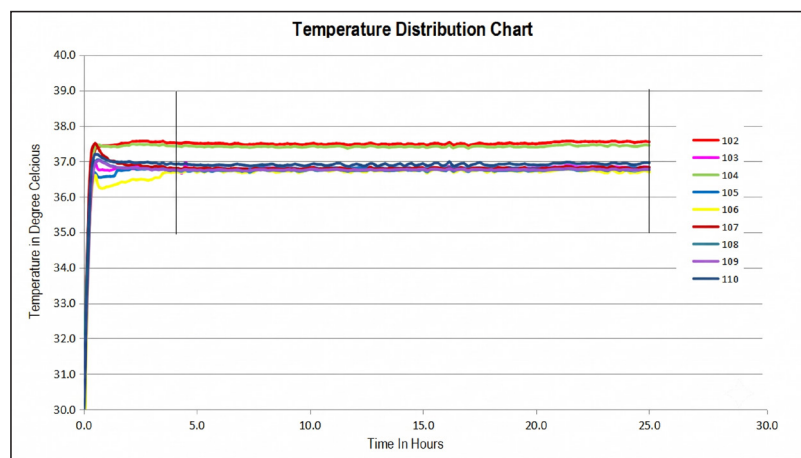


Fig. 3 Temperature distribution profile

Uniformity and stability parameters of temperature inside the incubator are calculated as,

- (1) Uniformity is the average of the maximum instantaneous temperature difference between 9 channels over the scan period (measure of spatial distribution of temperature).
- (2) Stability is computed as the half the difference between the maximum and minimum readings at the geometric centre of the chamber, during the scan period.

The table 2 below provides the uniformity and stability values of temperature inside the incubator

Table 2. Temperature Uniformity and Stability results over 24 hours	
Duration of Temperature logging	24 hours
Temperature Uniformity Parameter (1)	0.19°C
Control Stability Parameter (2)	0.26°C

From the measurement results, it is concluded that the maximum deviation of temperature is $+0.3^{\circ}\text{C}$ with an uncertainty of 0.7°C (in channel 105). In this case, temperature can vary from 36.4°C to 37.0°C in the specified position of incubator. As per manufacturer's accuracy specification of the incubator, temperature can vary from 36.0°C to 37.0°C . Temperature distribution measurement confirms that the incubator functions as per the manufacturer's specification. The temperature distribution chart clearly indicates that the incubator reaches the required temperature (37.0°C) in less than half an hour after switching it on.

8. Conclusion

Temperature distribution measurement inside enclosed chambers is essential for verifying temperature uniformity at different chamber locations and understanding thermal stability through monitoring of temperature variation with respect to time. This measurement method helps to identify hot and cold areas which may cause unintended process deviations. Such deviations cannot be observed by measurement with single sensors alone. Distribution measurement results confirms that the equipment performs well within the manufacturer's specification and act as a document proof for calibration, validation, and regulatory or quality audits. Such a measurement systems become essential in predicting developing maintenance problems with the equipment also.

9. Acknowledgments

Authors acknowledge the Dept. of Science and Technology, Govt. of India for supporting the facilities provided at Calibration Cell, SCTIMST.

10. References

1. Muhammad J, Krisman K. Improving homogeneous chamber temperature of biomass dryer by automatic air controlling system. *Sci Technol Commun J* [Internet]. 2021;1(3):95-100.
2. Mangeh III FC, Wu M, Xiao Y, Looh GA. Numerical assessment of temperature distribution in two hot air-drying chamber geometries (cuboid and cylindrical). *J Multidiscip Eng Sci Technol*. 2019;6(5):10096-102.
3. Nechaev AN, Dunaevskii GE. Temperature distribution in the phantom of limb in the microwave chamber with linear source of radiation. *J Phys Conf Ser*. 2021;1989(1):012035.
4. Webster JG. *Measurement, instrumentation, and sensors handbook*. Boca Raton: CRC Press; 2015.
5. ASTM International. *Standard guide for temperature measurement in medical and laboratory environments*. West Conshohocken: ASTM International; 2020.

6. Nicholas JV, White DR. Traceable temperatures: an introduction to temperature measurement and calibration. 2nd ed. Chichester: John Wiley & Sons; 2001.
7. Kako SA. A comparative study about accuracy levels of resistance temperature detectors RTDs composed of platinum, copper, and nickel. Al-Nahrain J Eng Sci. 2023;26(3):216-25.
8. Webster ES. A critical review of the common thermocouple reference functions. Metrologia. 2021;58(2):022001.
9. Kuş A, Işık Y, Çakır MC, Coşkun S, Özdemir K. Thermocouple and infrared sensor-based measurement of temperature distribution in metal cutting. Sensors. 2015;15(1):1274-93.
10. Bureau International des Poids et Mesures. The International Temperature Scale of 1990 (ITS-90). Sèvres: BIPM; 1990.
11. Preston-Thomas H. The International Temperature Scale of 1990 (ITS-90) Metrologia. 1990;27(1):3-10.
12. Bernstein DM, Drew RT. The major parameters affecting temperature inside inhalation chambers. Am Ind Hyg Assoc J. 1980;41(6):420-6.



Engineering Therapeutic Algae for Cancer Therapy through Synthetic Biology and Nanotechnology

Shai Shikha Rout¹, Swapnil Srivastava¹, Jiban Jyoti Panda^{1*}

¹Brain and Supramolecular Nanotherapeutics Laboratory, Chemical Biology Unit, Institute of Nano Science and Technology, Sector-81, Knowledge City, Sahibzada Ajit Singh Nagar, Punjab, 140306, India

Abstract

Microalgae's rapid growth, simplicity of cultivation, photosynthetic activity, and rich reservoir of bioactive chemicals have rendered them flexible biological platforms for sustainable and effective cancer therapies. Thanks to recent developments in synthetic biology, therapeutic proteins, vaccines, and anticancer metabolites can now be produced by precisely modifying microalgae using CRISPR-based genome editing technologies, metabolic engineering, and programmable gene circuits. Furthermore, by aiding the synthesis of green nanoparticles, targeted drug delivery, and the creation of nanoparticle-algae hybrid nanosystems, nanotechnology has demonstrated significant potential to advance the biomedical applications of algae. Low therapeutic output, poor tumor selectivity, and delivery issues limit the use of microalgae in cancer therapy despite their promising therapeutic qualities. While nanotechnology enhances targeted delivery, imaging, and treatment efficacy, synthetic biology enables microalgae to generate more oxygen, produce therapeutic chemicals, and perform programmable cellular functions. This review demonstrates how combining these technologies can turn microalgae into multipurpose platforms for achieving precision cancer therapy and combating tumor hypoxia.



Citation: Rout SS, Panda JJ. Engineering Therapeutic Algae in Cancer Therapy through Synthetic Biology and Nanotechnology. *Opn. Med. Sci. Technol. Health.* 2026; 4(1): e26003.

Received: Feb 6, 2026

Accepted: June 11, 2026

Published: June 30, 2026

Keywords: Synthetic biology, Nanotechnology, Algae, Cancer

Copyright: © 2026 Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

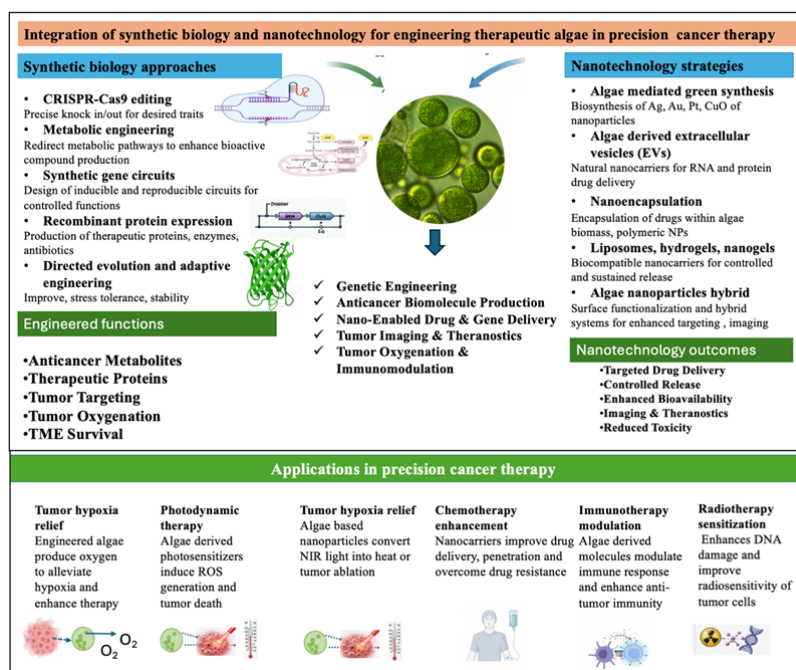
Data Availability Statement: All relevant data are within the manuscript.

Funding: Declared.

Competing interests: None declared.

***Corresponding Author Address:**

Dr. Jiban Jyoti Panda,
Brain and Supramolecular Nanotherapeutics
Laboratory,
Chemical Biology Unit,
Institute of Nano Science and Technology,
Sector-81, Knowledge City,
Sahibzada Ajit Singh Nagar, Punjab- 140306,
India
Email: jyoti@inst.ac.in
ORCID ID: 0000-0003-0350-7491



Scheme 1: Synthetic biology and nanotechnology approaches for precision cancer therapy (created using Biorender)

1. Introduction:

In 2020, cancer resulted in close to 10 million deaths globally and remains one of the foremost causes of morbidity and mortality despite significant advances in diagnosis and treatment. Conventional therapeutic approaches, including chemotherapy, radiotherapy, and surgery, have certain limitations. These include lack of specificity, systemic toxicity, tumour recurrence, and drug resistance [1]. The major issue results from tumor heterogeneity that can be intratumoral or intertumoral, which is explained by many mechanisms such as genotypic challenges, mutations, genetic manipulations, and also many adaptive mechanisms. These challenges have driven the search for innovative and sustainable platforms to refine treatment efficiency while reducing side effects. Recently, microalgae have emerged as promising candidate of biomedical importance due to their small size, photosynthetic capability, biocompatibility, and ability to produce a wide range of bioactive compounds with antioxidant, anti-inflammatory, and anti-cancer features [2]. To advance cancer therapies, scientists have created nanocarriers that are brilliant platforms to increase specificity through encapsulation or conjugation [3].

Algae, once regarded as an aquatic photosynthetic organism, are now redefining the future of medical science through their extraordinary reservoir of bioactive biomolecules [4]. Algal-derived metabolites and biomolecules are emerging as promising candidates in biomedical and pharmaceutical research because of their therapeutic potential, sustainability, and biocompatibility [5]. Recent research shows that microalgae and macroalgae encompass unique bioactive compounds such as sulphated polysaccharides, carotenoids,

phycobiliproteins, polyphenols, and omega-3 fatty acids that display unique antioxidant, antimicrobial, antiviral, anti-inflammatory, and anticancer activities [6]. Algal nanoparticles and alginate-based hydrogels enhance targeted drug delivery, enable precise drug release, and improves cellular uptake. In cancer studies, fucoidan extracted from brown algae has shown the ability to induce apoptosis through mitochondrial pathways and inhibit angiogenesis in tumor cells [7]. Additionally, spirulina-derived phycocyanin fractions have shown neuroprotective effects by reducing oxidative stress and inflammatory cytokine expression in neuronal models. These are used in regenerative medicine, where they support wound healing, tissue engineering, and stem cell proliferation due to their non-toxic and biodegradable nature [8]. Elsewhere, in therapeutics, algae-based nanoparticles are driving the fields of tissue engineering, biosensing, and vaccine development [9]. The blend of algal biotechnology with nanomedicine and synthetic biology has unlocked a new era of eco-friendly healthcare solutions, making algae a green powerhouse for next-generation biomedical advancements [10].

The recipe of nanotechnology and synthetic biology has further expanded the therapeutic potential of microalgae. Synthetic biology helps to precisely manipulate algal genomes through genetic engineering, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-mediated genome editing, and metabolic pathway optimization [11]. Concurrently, nanotechnology provides powerful avenues for enhancing drug delivery and effectiveness. They can serve as intelligent modalities for creating hybrid systems with algae for boosting cancer treatment [12]. In particular, targeted medication delivery, tumour oxygenation, photodynamic therapy (PDT), and photothermal therapy (PTT) effects are feasible with nano-engineered microalgae [13]. Therefore, the integration of these technologies will not only develop living therapeutic platforms but also address current limitations associated with cancer therapy [14]. This review highlights current developments in synthetic biology and nanotechnology for engineering therapeutic algae, highlighting the emerging applications in cancer therapy and precision medicine.

2. Algae commonly used for cancer therapy:

Algae have arisen as capable biological platforms for cancer therapy due to their unique ability to produce a wide range of bioactive composites, generate oxygen through photosynthesis, and serve as natural carriers for therapeutic agents [15]. Both microalgae and macroalgae have demonstrated significant potential in cancer treatment.

Blue-green microalgae (Cyanophyceae)

Blue-green microalgae (Cyanophyceae) have served as important source of many active bioproducts. For instance, Cryptophycin1, extracted from *Nostoc* GSV 224, exhibits anti-tumorigenic activity against solid tumors [16]. Moreover, Borophycin extracted from marine *Nostoc spongiaeforme* showed anti-cancerous effects against epidermoid carcinoma [17]. Another example of blue-green microalgae is *Lyngbya majuscula*; isolated Cucarin A can suppress

many types of tumor cells such as renal, colon, and breast cancer cell lines [18].

Microalgae

The most extensively researched microalgae species include *Dunaliella salina*, *Spirulina platensis*, *Chlamydomonas reinhardtii*, and *Chlorella vulgaris* [19]. *Chlorella* and *Chlamydomonas* can generate oxygen in the tumor microenvironment and are especially appealing as they can assist in overcoming hypoxia, a significant obstacle to successful cancer treatment [20]. *Spirulina* is abundant in phycocyanin, a natural pigment known to induce cancer cell death and avoid tumour growth [21], while *Dunaliella* is a valuable source of β -carotene, which possesses antioxidant and chemopreventive properties [22].

Marine macroalgae (seaweeds)

Marine macroalgae, usually known as seaweeds, also contribute significantly to cancer research [23]. Brown algae such as *Sargassum*, *Laminaria*, and *Fucus* contain fucoidan, a sulphated polysaccharide that shows anticancer activities by promoting apoptosis, defeating angiogenesis, and reducing metastasis [24]. Red algae, including *Porphyra* and *Gracilaria*, produce bioactive sulfated polysaccharides with immunomodulatory and antiproliferative effects [25]. Green algae such as *Ulva lactuca* contain ulvan, a polysaccharide that has shown antioxidant and tumor-suppressive properties [26].

Currently, advances in synthetic biology and nanotechnology have additionally enhanced the therapeutic potential of algae by enabling genetic engineering, targeted drug delivery, production of therapeutic proteins, and development of algae-based theranostic systems [27] as mentioned in **Table 1**. These unique characteristics make algae an innovative and sustainable platform for next-generation precision cancer therapies.

Table 1: Various algae with anti-cancerous, anti-viral effects

Algae	Usage	References
<i>Ulva lactuca</i> (Green algae)	Antifungal and anticancer	28
<i>Sargassum fusiforme</i> (Brown algae)	Antiviral, antidiabetic, improves insulin sensitivity, improves liver & kidney function in diabetic animal models	28
<i>Sargassum fulvellum</i>	Antipyretic, antimicrobial, antioxidant, neuroprotective, anticoagulant, anti-inflammatory activities. Inhibits growth of pathogenic bacteria, protects neurons from oxidative stress & glutamate toxicity	29
<i>Ulva intestinalis</i> (extracted from seaweed)	Cytotoxic activities against cancer cells	30

<i>Gracilaria spp.</i> (general genus)	It has Antibacterial, antiviral, antifungal, anti-inflammatory, cytotoxic, and other biological activities	31
Red algae (general)	Antiviral potential, anticancer activities	32
<i>Ulva fasciata</i> / <i>Ulva reticulata</i>	Anticancer & antioxidant properties	32
Marine macroalgae	Antioxidant, antimicrobial, anti-inflammatory, antitumor properties	33
Mixed algae bioactives	Antimicrobial, anti-inflammatory, antioxidant activities seen	34
<i>Neorhodomela aculeata</i>	Generally Neuroprotective, anti-inflammatory (acts on neuronal cells and also on microglial cells)	35
<i>Ecklonia cava</i> (Brown algae)	It has dental protective activities and is also used in the treatment of neurodegenerative and periodontal disorders and anti-inflammatory and antioxidant properties as well	35
<i>Pelvetia siliquosa</i>	Enhances antioxidant enzymes (SOD, CAT), maintains mitochondrial membrane potential, neuroprotective & antioxidant	35
Red, green & brown algae (groups)	It will produce antibacterial, antiviral, bioactive compounds used in respiratory illnesses, gout, helminthiasis	36
<i>Gracilaria corticata</i>	Reduces lipid peroxidation, apoptosis & inhibits proliferation of cancer cells. Inhibits growth of <i>E. coli</i>	37

3. Use of nanotechnology-based approaches to improve algal therapeutics:

Algae-spanning microalgae (*Chlorella*, *Spirulina*, *Chlamydomonas*, diatoms) and macroalgae (seaweeds) are increasingly recognised not only as sources of bioactive compounds but also as active partners in nanotechnology. The convergence of algal biology and nanoscience has opened several complementary avenues: algae as bio-factories for nanoparticle synthesis, algae-nanoparticle hybrids as functional therapeutic systems, and genetically or chemically engineered algae as living drug-delivery vehicles for cancer therapy. Each is discussed below, along with the remaining translational challenges.

3.1 Algae-based green synthesis of nanoparticles

Algae offer an eco-friendly, low-cost, and scalable alternative to chemical and

physical methods of nanoparticle synthesis, which often rely on toxic reducing agents, high energy input, and generate hazardous byproducts.

Mechanisms involved are:

1. *Extracellular Synthesis*- Cell-free algal extract (aqueous or solvent) is mixed with metal salt precursors (AgNO_3 , HAuCl_4 , ZnSO_4) under ambient or mild conditions; biomolecules reduce metal ions to zero-valent nanoparticles, which are then capped by biomolecules that confer colloidal stability.
2. *Intracellular/ biogenic synthesis*- Living algal cells or biomass sequester metal ions, which are enzymatically or biochemically reduced within or on the cell surface, sometimes visualized as NP deposition on cell walls [38].

Such nanoparticles are biocompatible, and the inherent bioactive coating can impart additional anticancer, antimicrobial, or antioxidant activity. Size, shape, and surface charge can be tuned by varying algal species. Collectively, algae-mediated green synthesis provides a sustainable NP production platform whose products often show enhanced or synergistic bioactivity due to the co-presence of algal phytochemicals on the nanoparticle surface.

3.2 Hybrid Algae- nanoparticle systems

Beyond using algae merely as a synthesis platform, researchers have developed hybrid systems in which nanoparticles are conjugated to, embedded within, or grown on algal cells or algae-derived materials, combining the innate biological functionalities of algae with the physicochemical tunability of nanomaterials.

Some methods by which Hybrid Algae nanoparticle systems can be made are:

1. Surface-decorated algal cells- NPs are attached to the algal cell wall via electrostatic interaction, covalent conjugation, or biomineralization, creating “cyborg” microalgae with new functions such as magnetic steerability or enhanced light absorption [39].
2. Microalgae as micro-robotic carriers- Motile microalgae (*Chlamydomonas reinhardtii*, diatoms) functionalized with drug-loaded NPs exploit the cells’ natural motility (flagellar movement) and phototaxis/chemotaxis to achieve active, directed transport of therapeutic payloads- a concept sometimes termed “biohybrid microrobots” [40].
3. Algal-derived nanocarriers- Polysaccharides extracted from algae (alginate, fucoidan, carrageenan, ulvan) are used to fabricate nanoparticles, nanogels, or nanofibers that serve as drug delivery vehicles. These matrices are inherently biocompatible, Biodegradable, mucoadhesive, and in some cases possess intrinsic anticancer/ immunomodulatory activity (fucoidan’s known antitumor and anticoagulant properties) [41].

4. **Diatom-based silica scaffolds-** The naturally porous, bio-silica frustules of diatoms are exploited as ready-made mesoporous nanostructures for drug loading, offering high surface area, tunable pore size, and biocompatibility without the need for complex synthetic silica nanoparticle fabrication [42].

These hybrid platforms effectively convert algae from a passive biomass source into an active component of the therapeutic nano-system, capable of navigation, targeting, and drug delivery in one integrated unit.

3.3 Nanoengineered algae for combination cancer therapy

The most translationally significant application lies in engineering algae as multifunctional platforms for combination cancer therapy, where the goal is to integrate several therapeutic modalities to overcome the limitations of monotherapy- poor tumor penetration, drug resistance, and systemic toxicity. Strategies that can be followed are:

1. *Drug-loaded microalgae-* chemotherapeutic agents (e.g., doxorubicin, paclitaxel) are loaded onto NP-decorated algal cells, which are then administered locally or systemically. The motile, often magnetically or optically guidable, algal carrier improves tumor accumulation while its natural degradation profile limits off-target toxicity [43].
2. *Photothermal/photodynamic + chemotherapy combinations:* Algal pigments (chlorophyll derivatives, phycocyanin) and/or conjugated metallic NPs (gold, silica-coated iron oxide) act as photothermal or photodynamic agents, enabling light-triggered, on-demand release of co-loaded chemotherapeutics- a spatiotemporally controlled combination therapy that reduces systemic drug exposure [44].
3. *Immunotherapy integration:* Some algal-nanoparticle constructs are engineered to co-deliver immune adjuvants or checkpoint inhibitors alongside cytotoxic agents, exploiting the immunomodulatory properties of algal polysaccharides (e.g., fucoidan, β -glucans) to potentiate anti-tumor immune responses [45].
4. *Oxygen-generating algal systems:* Because live or semi-live microalgae can perform photosynthesis, some designs exploit in-situ oxygen generation to relieve tumor hypoxia, thereby enhancing the efficiency of oxygen-dependent treatments such as radiotherapy and photodynamic therapy — a distinctive advantage unique to algae-based systems [46].
5. *Magnetically guided/theranostic constructs:* Iron oxide NP-functionalized algae enable MRI-based tracking alongside magnetically directed tumor targeting, combining diagnosis and therapy (theranostics) with treatment delivery [47].

3.4 Challenges and Future Perspectives

Even with these inspiring developments, there are still issues that need to be

resolved before nanoengineered algal treatments may be used in clinical settings. Standardization and reproducibility, which are crucial for regulatory approval, are difficult due to batch-to-batch variability in algae-mediated nanoparticle synthesis, which results from variations in algal species, growing conditions, extract composition, and seasonal variation. Scaling up from lab cultures to industrial biomanufacturing remains technically challenging, especially for hybrid systems that require precise control over cell viability, surface functionalization, and nanoparticle size. Concerns regarding chronic toxicity and off-target sequestration in organs like the liver and spleen are raised by the incomplete characterization of the long-term biocompatibility, biodegradation kinetics, and potential immunogenicity of algal cell-wall components and residual metal nanoparticles in vivo. Maintaining motility, phototaxis, and photosynthetic oxygen-generating capacity under physiological conditions (body temperature, serum proteins, immune clearance), and ensuring the carriers don't proliferate uncontrollably or cause unwanted immune activation, are major challenges for living or semi-living microalgal carriers. Additionally, the clinical usefulness of photothermal/photodynamic-triggered release techniques is limited by deep tissue light penetration, and it is still challenging to obtain precise magnetic or chemotactic guiding in the complex tumor microenvironment with the same effectiveness observed in vitro. In the future, creating algae with customized surface receptors, increased payload capacity, or inducible drug-release mechanisms through the integration of genetic engineering and synthetic biology techniques presents a possible route toward more accurate and manageable systems. Crucial next steps will include combining these platforms with cutting-edge imaging modalities for real-time tracking, creating biodegradable and stimuli-responsive coatings, and conducting thorough pharmacokinetic, biodistribution, and long-term safety investigations in relevant animal models.

4. Synthetic biology-based approaches for algal engineering:

Algae, including prokaryotic cyanobacteria and eukaryotic microalgae and macroalgae, have emerged as versatile vehicles for synthetic biology, combining rapid, low-cost, photoautotrophic growth with a eukaryotic secretory and post-translational machinery⁴⁸. Model species such as *Dunaliella*, *Chlamydomonas reinhardtii*, *Salina*, and the cyanobacterium *Arthrospira platensis* now serve as programmable biofactories for therapeutic proteins, high-value bioactive metabolites, and increasingly serve as living carriers that deliver drugs and biologics directly to diseased tissue [49,50]. Synthetic biology offers a transformative toolkit to address different challenges by enabling the rational design and precise engineering of microalgae tailored for therapeutic applications. It has greatly advanced the engineering of microalgae through the Design-build-test-learn (DBTL) framework (Figure 1a), which is a systemic approach to enhance the optimization of metabolic pathways for the invention of valuable biomolecules. First, in the design phase, transcriptomic, genomic, and metabolic data are analysed using bioinformatic tools to identify the target gene. Second, the build phase involves the introduction of

genetic modifications by using synthetic biology tools (CRISPR, TALENS). In the test step, the modified microalgae are evaluated through biochemical and molecular analyses, including metabolite profiling and gene expression studies. In the final step of the learning phase, experimental data are merged with the computational models to refine or improve engineering strategies and repeat the design step. The repetitive nature of this framework increases strain improvement and increases the production of therapeutically relevant compounds such as polyunsaturated fatty acids, carotenoids, and terpenoids [51]. Overall, the DBTL platform is helpful in developing engineered microalgae with enhanced therapeutics.

The key components required for engineering microalgae by using synthetic biology include genetic manipulation, genome integration, targeted genome editing, and strain improvement (Figure 1b). Genetic elements, or the fundamental components of a plasmid vector used for microalgae transformation, are the origin of replication (ori), promoters, reporter genes, multiple cloning sites (MCS), and antibiotic-resistant genes. The second step is gene integration by electroporation, conjugation, transposition, and biolistics. Genome engineering can be done using CRISPR-Cas9, which uses guide RNA to direct Cas9 nuclease to a specific DNA sequence, generating double-stranded breaks for precise genome modifications [52]. TALENs (Transcription Activator-Like effector nucleases) use engineered DNA-binding proteins fused to nucleases that introduce site-specific DNA cleavage. These tools provide a comprehensive framework for engineering microalgae as platforms for producing pharmaceuticals, bioactive compounds, vaccines, biofuels, and nanoparticle-based therapeutics [53].

5. Genetic engineering of therapeutic algae

Genetic transformation of algae for therapeutic ends builds on nuclear and chloroplast expression systems first optimised in *Chlamydomonas reinhardtii*, which remains the principal model organism owing to its well-annotated genome and generally regarded as safe status [48].

A major obstacle to using algae as biofactories for human biopharmaceuticals has been the divergence between algal and human glycosylation pathways, since N- and O-linked glycans strongly influence the immunogenicity, stability and efficacy of therapeutic proteins. Barolo and colleagues provided comprehensive microalgal glycosylation machinery to produce humanised recombinant microalgae for pharmaceuticals [48].

Genome-editing precision has advanced markedly with the adoption of CRISPR-Cas systems. Antonacci and co-workers at the Italian National Research Council reviewed how CRISPR-Cas9, delivered either as a stably expressed transgene or as preassembled DNA-free ribonucleoprotein (RNP) complexes, has enabled targeted gene knockout and, more recently, efficient knock-in of foreign DNA in *C. reinhardtii*, overcoming earlier reliance on inefficient, error-prone non-homologous end joining [49]. Beyond *Chlamydomonas*, genetic tool development has diversified across algal taxa relevant to human

therapy. The diatom *Phaeodactylum tricornutum* and the cyanobacterium *Spirulina platensis* have both been engineered to express recombinant antigens and antibodies, exploiting their intrinsically high biomass productivity and, in the case of *Spirulina*, a long history of human dietary consumption that eases downstream regulatory and safety considerations [50].

Collectively, these advances establish algae as a genetically tractable, GRAS-compatible framework for expressing therapeutic proteins, setting the stage for their application in bioactive-molecule production and living drug delivery discussed below.

Engineering Algae for Therapeutic Molecule Production/ Bioactive compounds

Synthetic biology has been applied both to increase the titre of these native compounds and to introduce entirely heterologous biosynthetic pathways for recombinant biologics.

Carotenoid Pathway engineering-

Baek and colleagues used DNA-free CRISPR-Cas9 ribonucleoproteins to inactivate the zeaxanthin epoxidase gene in *C. reinhardtii*, generating a mutant with 56-fold higher zeaxanthin content and 47-fold greater productivity than the wild type without loss of lutein — a proof of concept later extended to producing lutein- and zeaxanthin-enriched eggs by feeding the mutant biomass to laying hens [54].

Recombinant Protein and Antibody Production-

Beyond native pigments, algae have been engineered to synthesise entirely heterologous therapeutic proteins, including monoclonal antibodies, immunotoxins, cytokines, hormones, clotting factors, and vaccine antigens, primarily in *C. reinhardtii*, *Phaeodactylum tricornutum*, and *Chlorella* sp.

Lipid and fatty acid engineering-

CRISPR-Cas9-mediated knockout of lipid catabolism genes has been used to boost the accumulation of triacylglycerols and long-chain polyunsaturated fatty acids in *C. reinhardtii* -for example, Nguyen and colleagues reported a 28% increase in dry-biomass lipid content relative to wild type by knocking out genes involved in lipid degradation, without compromising growth. While much of this work targets biofuel applications, the same pathway-engineering logic underlies efforts to enhance omega-3 fatty acid and essential amino-acid content in algae intended for nutraceutical and precision-nutrition use [55].

6. Future directions in Synthetic Biology for Therapeutic Algae

Although microalgae possess inherent advantages such as biocompatibility, photosynthetic oxygen generation, and the ability to produce diverse bioactive compounds, their direct application in cancer therapy is limited by low

therapeutic yield, insufficient tumor specificity, poor control over biomolecule production, and challenges associated with efficient delivery to tumor sites [56]. Synthetic biology addresses these limitations by enabling precise genetic and metabolic engineering of microalgae to enhance oxygen production, increase the synthesis of anticancer molecules, express therapeutic proteins, and develop programmable, tumor-responsive systems [57]. Simultaneously, nanotechnology overcomes delivery-related barriers by improving drug loading, targeted tumor accumulation, enabling controlled release, improving imaging capabilities, and heightening therapeutic efficacy. Therefore, the integration of synthetic biology and nanotechnology creates multifunctional engineered algal platforms capable of overcoming major challenges in conventional cancer treatment, including tumor hypoxia, systemic toxicity, drug resistance, and poor therapeutic specificity [58]. This review explores how these complementary technologies can transform microalgae into next-generation living therapeutics for precision cancer therapy.

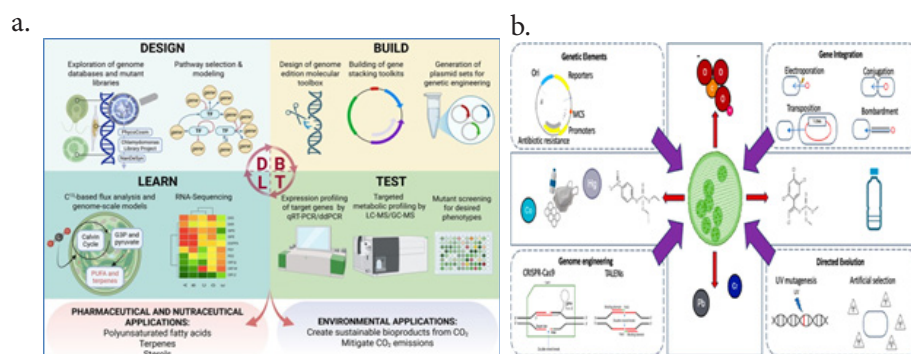


Figure 1: (a) The figure illustrates the *Design-Build-Test-Learn (DBTL) cycle*, a systematic synthetic biology framework used to engineer microalgae for enhanced production of valuable biomolecules. The cycle integrates computational design, genetic engineering, experimental validation, and data-driven optimization to improve strain performance for pharmaceutical, nutraceutical, and environmental applications, reproduced with permission [59]. (b) Illustrates the synthetic biology toolkit for microalgal engineering, encompassing genetic elements, gene integration methods, genome-editing technologies, and directed evolution strategies for developing enhanced therapeutic and biotechnological algal platforms, reproduced with permission [53].

Synthetic biology can further enhance the tumor oxygenation potential of photosynthetic microalgae by empowering precise genetic modifications that improve photosynthetic efficiency, oxygen production, and tumor-targeting capabilities [60]. Through CRISPR-mediated genome editing and metabolic engineering, microalgae can be engineered to produce higher oxygen levels under low-light conditions, enhancing their effectiveness in overcoming tumor hypoxia [61]. Synthetic gene circuits can also be incorporated to create stimuli-responsive systems that activate oxygen production, therapeutic protein secretion, or anticancer molecule release specifically within the

tumor microenvironment [62]. Furthermore, engineered microalgae can be programmed to express targeting ligands, cytokines, immune-modulating molecules, or therapeutic enzymes, thereby combining oxygen generation with immunotherapy, radiotherapy sensitization, and targeted cancer treatment [63]. When integrated with nanotechnology-based delivery systems, these synthetic biology approaches can transform photosynthetic microalgae into multifunctional living therapeutics for precision oncology.

7. Algae-based theragnostic systems currently used for pre-clinical studies-

Silver nanoparticles produced from the microalgae *T. erythraeum* inhibited the growth of MCF-7 and HeLa cell lines, while gold nanoparticles created from the microalgae *D. salina* were cytotoxic to cancer cell lines like MCF-7 [64]. Additionally, whereas the AgNPs were neutral to normal cells, they were deadly to breast cancer cell lines. Dextran-coated titanium dioxide nanoparticles were created utilizing 18S rDNA PCR and the microalgae *Chlorella vulgaris* in an environmentally responsible manner. After 48–72 hours of treatment, the produced TiO₂ NPs demonstrated up to 99% cytotoxicity against MCF-7 cell lines. The presence of bioactive algal metabolites, the dextran coating, and the smaller nanoparticle size all contribute to the increased anticancer effect [65].

Numerous chronic human diseases, including cancer, heart disease, diabetes, and neurodegenerative conditions like Parkinson's and Alzheimer's, have been linked to reactive oxygen species (ROS) and oxidative stress [66]. The effective use of sodium oligomannate, an oligosaccharide derived from algae, in the treatment of Alzheimer's disease highlights the growing significance of marine algae in drug discovery. Carrageenan and porphyrin improve the expression of brain-derived neurotrophic factor, balance mitochondrial activity, and reduce NF- κ B-mediated neuroinflammation. Red algae's sulphated polysaccharides have demonstrated a viable strategy for protecting neurons from oxidative stress, reducing neuroinflammation, and promoting neuronal regeneration [35]. Phycobiliproteins exert different mechanisms, thereby mitigating oxidative damage by activating antioxidant pathways. Bioactive compounds derived from red algae exhibit significant potential for amyotrophic lateral sclerosis (ALS) as they can simultaneously regulate oxidative stress and neuroinflammatory pathways [67]. Studies have shown that *Sargassum fusiforme* polysaccharides could regulate the immune response in a positive manner, thereby inducing apoptosis and promoting the expression of tumor suppressor genes [61]. Extracts from the brown alga (*Dictyota dichotoma*) have shown significant anticancer activity, driven by non-polar cytotoxic constituents rather than antioxidant mechanisms [68].

Microalgae-based microrobots have been shown to serve as promising platforms for enhancing photodynamic therapy (PDT) by overcoming tumor hypoxia and improving targeted cancer treatment [69]. *Chlorella vulgaris*-driven oxygen-supplying microrobots generated oxygen under near-infrared light, significantly increasing ROS-mediated tumor destruction and PDT efficiency [70]. Diatomaceous silica nanoparticles in combination with chlorophyll-

functionalized nanoplateforms and PDT, along with chemotherapy, enhance immune responses and antitumor activity [71]. Living *Spirulina platensis*-based magnetic microbots coated with Fe₃O₄ and CaCO₃ nanoparticles demonstrated targeted cancer therapy through combined Ca²⁺ overload and ROS generation. These cells are guided magnetically to tumor sites and release the ions in the acidic tumor microenvironment, while photosynthetic oxygen production reduced hypoxia and increased PDT effect [72]. This synergistic activity reduced off-target effects, emphasizing a novel biohybrid approach for advanced cancer treatment. Biohybrid microbots developed using *Chlamydomonas reinhardtii* enabled targeted chemotherapy delivery for lung cancer. In lung metastasis, these microbots significantly reduced tumor growth and improved median survival by 40%, demonstrating a safe and biodegradable strategy for precision cancer therapy [73]. Combinatorial therapies with algae increase oxygen generation with localized PDT effect, exhibiting strong synergistic anticancer effects. *Volvox*-based microbots and cyanobacteria modified with black phosphorus nanosheets produced oxygen and singlet oxygen under laser irradiation, thereby inducing oxidative stress and apoptosis in tumor cells. Also, magnetic nanoparticles with polydopamine coatings enable targeted heat generation under near-infrared light, destroying heat-sensitive tumor cells [74].

Since oxygen-deprived tumor cells show resistance to radiation-induced damage, tumor hypoxia is a significant obstacle to effective cancer treatment, particularly in radiotherapy. Through continuous in situ oxygen synthesis, photosynthetic microalgae have emerged as novel biological oxygen producers that can increase tumor oxygenation. According to recent research, biomineralized *Chlorella vulgaris* covered with calcium phosphate, as illustrated in Figure 2, can efficiently aggregate inside the tumors and produce oxygen when exposed to light, increasing the sensitivity of hypoxic tumors to radiation. Under 650 nm laser irradiation, the chlorophyll produced from the nanoparticles served as a photosensitizer to produce lethal ROS. Thus, in addition to improving cancer theranostics, the modified photosynthetic microalgae-based biosystem would offer a fresh approach to overcoming tumor hypoxia [75].

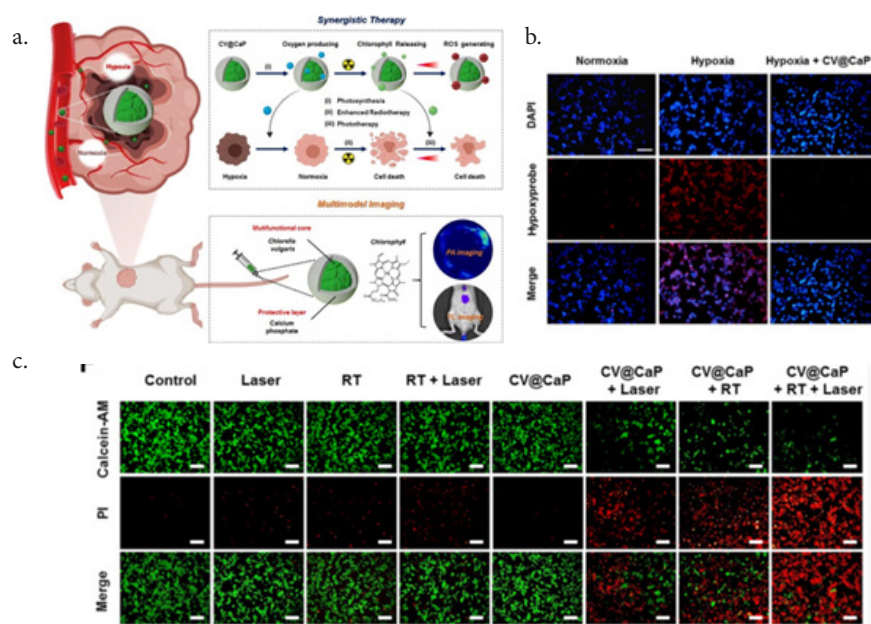


Figure 2: (a) Schematic illustration of biomimeticized *Chlorella vulgaris* (CV@CaP) as a photosynthetic therapeutic platform that alleviates tumor hypoxia through in situ oxygen generation, thereby enhancing radiotherapy and synergistic photo-induced cancer treatment. (b) Alleviation of hypoxia in 4T1 tumor cells. (c) Fluorescence images of live/dead staining of 4T1 cells in different treated groups. The cells were co-stained with Calcein-AM (green, living cells) and PI (red, dead cells), reproduced with permission [75].

Table 2: Major Phycocyanin pigments purified from *Spirulina* alga showing anti-proliferative effect against breast cancer cell lines:

Components	Anti-tumor mechanisms	References
C-Phycocyanin	Induces pathogenic alterations and DNA fragmentation; upregulates Fas and ICAM expression; downregulates anti-apoptotic proteins	76
Selenium Phycocyanin	Anti-proliferative agent on human melanoma A375 cells and human breast adenocarcinoma MCF-7 cells	77
c-phycocyanin	Enhancement of anti-tumor effect of NK cells	65
Allophycocyanin	Enhancement of anti-tumor effect of NK cells	78
Phycocyanin	Arrest of cancer cell cycle progression	78

8. Summary:

This review explores the integration of synthetic biology and nanotechnology to enhance the therapeutic potential of microalgae for cancer treatment. Although microalgae possess many advantages such as biocompatibility, photosynthetic oxygen generation, and the production of bioactive metabolites, their clinical application is limited by poor tumor targeting, low therapeutic activity, and delivery challenges. Although there have been

significant advances in engineering therapeutic microalgae, many challenges remain before widespread clinical application can be realised. Concerns about biosafety, including environmental discharge, horizontal gene transfer, and possible off-target impacts of genetic alterations, greatly highlight the need for thorough assessment and regulatory supervision. Additionally, limited in vivo research, scalability problems, and manufacturing uniformity impede clinical translation. Furthermore, the special adaptability of microalgae has intriguing prospects for customized cancer treatment, whereby genetically modified microalgae might be customized to deliver immune-active molecules or patient-specific therapeutic compounds with the use of synthetic biology. Additionally, combining synthetic biology, artificial intelligence, and nanotechnology could accelerate the development of programmable algal systems with improved targeting efficiency, controlled therapeutic release, and real-time monitoring capabilities. However, these developments might result in the development of microalgal systems that could function as multipurpose platforms for customized medicine and next-generation precision oncology.

9. Acknowledgement:

Authors acknowledge the funding support from the Council of Scientific and Industrial Research (CSIR), India (37WS(0002)/2023-24/EMR-II/ASPIRE).

10. References:

1. Victoir B, Croix C, Gouilleux F, Prié G. Targeted therapeutic strategies for the treatment of cancer. *Cancers*. 2024;16(2):461.
2. El-Sheekh MM, AlKafaas SS, Rady HA, Abdelmoaty BE, Bedair HM, Ahmed AA, et al. How synthesis of algal nanoparticles affects cancer therapy?—A complete review of the literature. *Int J Nanomed*. 2023;18:6601-6638.
3. Montané X, Bajek A, Roszkowski K, Montornés JM, Giamberini M, Roszkowski S, et al. Encapsulation for cancer therapy. *Molecules*. 2020;25(7):1605.
4. Silva M, Geada P, Pereira RN, Teixeira JA. Microalgae Biomass—A Source of Sustainable Dietary Bioactive Compounds towards Improved Health and Well-Being. *Food Chem Adv*. 2025;6:100926. doi:10.1016/j.focha.2025.100926.
5. Asimakis E, Shehata AA, Eisenreich W, Acheuk F, Lasram S, Basiouni S, et al. Algae and their metabolites as potential bio-pesticides. *Microorganisms*. 2022;10(2):307.
6. Abd El-Hack ME, Abdelnour S, Alagawany M, Abdo M, Sakr MA, Khafaga AF, et al. Microalgae in Modern Cancer Therapy: Current Knowledge. *Biomed Pharmacother*. 2019;111:42-50. doi:10.1016/j.biopha.2018.12.069.

7. Al Monla R, Dassouki Z, Sari-Chmaysssem N, Mawlawi H, Gali-Muhtasib H. Fucoidan and alginate from the brown algae *Colpomenia sinuosa* and their combination with vitamin C trigger apoptosis in colon cancer. *Molecules*. 2022;27(2):358.
8. Karimi S, Shaygannejad V, Mohammadalipour A, Feizi A, Hooshmand S, Kafeshani M. Effects of *spirulina* (Arthrospira) *platensis* supplementation on inflammation, physical and mental quality of life, and anthropometric measures in patients with relapsing-remitting multiple sclerosis (RRMS): a triple-blinded, randomized, placebo-controlled trial. *Nutr J*. 2025;24(1):132.
9. Wang P, Liu C, Zheng L. Unlocking the Potential of Microalgae-Derived Therapeutic Carriers: Characteristics, Types, and Nanomedical Applications. *Mater Today Bio*. 2025;33:102037. doi:10.1016/j.mtbio.2025.102037.
10. Pereira L, Ismail G, Abomohra A. Editorial: Algal biotechnology: Current trends and nanotechnology prospective. *Front Mar Sci*. 2023;10:1181665. doi:10.3389/fmars.2023.1181665.
11. Dhokane D, Shaikh A, Yadav A, Giri N, Bandyopadhyay A, Dasgupta S, et al. CRISPR-based bioengineering in microalgae for production of industrially important biomolecules. *Front Bioeng Biotechnol*. 2023;11:1267826. doi:10.3389/fbioe.2023.1267826.
12. Yao Y, Zhou Y, Liu L, Xu Y, Chen Q, Wang Y, et al. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance. *Front Mol Biosci*. 2020;7:193. doi:10.3389/fmolb.2020.00193.
13. Chen S, Li M, Zhang Y, Dong Y, Wu J, Li L, et al. Photoactivatable immunostimulatory nanoengineered microalgae for boosting cascade-activated antitumor immunity. *Sci Adv*. 2025;11(41):eadw4212. doi:10.1126/sciadv.adw4212.
14. Cinar O, Kimiz-Gebologlu I, Kurt S, Oncel SS. Microalgae-Derived Biomolecule and Nanoparticle Conjugates: Emerging Therapeutic Platforms for Cancer Treatment. *OpenNano*. 2026;28:100291. doi:10.1016/j.onano.2026.100291.
15. Wang R, Wang Z, Zhang M, Zhong D, Zhou M. Application of Photosensitive Microalgae in Targeted Tumor Therapy. *Adv Drug Deliv Rev*. 2025;219:115519. doi:10.1016/j.addr.2025.115519.
16. Carmichael WW. Cyanobacteria secondary metabolites—the cyanotoxins. *J Appl Bacteriol*. 1992;72(6):445-459.
17. Davidson BS. New Dimensions in Natural Products Research: Cultured Marine Microorganisms. *Curr Opin Biotechnol*. 1995;6(3):284-291. doi:10.1016/0958-1669(95)80049-2.

18. Carte BK. Biomedical potential of marine natural products. *BioScience*. 1996;46(4):271-286.
19. Sharma R, Mondal AS, Trivedi N. Anticancer potential of algae-derived metabolites: recent updates and breakthroughs. *Future J Pharm Sci*. 2023;9(1):44. doi:10.1186/s43094-023-00497-z.
20. Han D, Zhang X, Ma Y, Yang X, Li Z. The Development of Live Microorganism-Based Oxygen Shuttles for Enhanced Hypoxic Tumor Therapy. *Mater Today Bio*. 2023;18:100517. doi:10.1016/j.mtbio.2022.100517.
21. Chen HY, Chiang YF, Huang CY, Shieh TM, Kao C, Chang FK, et al. *Spirulina* phycocyanin extract and its active components suppress epithelial-mesenchymal transition process in endometrial cancer via targeting TGF-beta1/SMAD4 signaling pathway. *Biomed Pharmacother*. 2022;152:113219. doi:10.1016/j.biopha.2022.113219.
22. Hyrslova I, Krausova G, Mrvikova I, Stankova B, Branyik T, Malinska H, et al. Functional properties of *Dunaliella salina* and its positive effect on probiotics. *Mar Drugs*. 2022;20(12):781. doi:10.3390/md20120781.
23. Frazzini S, Rossi L. Anticancer properties of macroalgae: a comprehensive review. *Mar Drugs*. 2025;23(2):70. doi:10.3390/md23020070.
24. Sanniyasi E, Gopal RK, Damodharan R, Arumugam A, Sampath Kumar M, Senthilkumar N, et al. In vitro anticancer potential of laminarin and fucoidan from Brown seaweeds. *Sci Rep*. 2023;13(1):14452. doi:10.1038/s41598-023-41221-y.
25. Khongthong S, Theapparat Y, Roekngam N, Tantisuwanno C, Otto M, Piewngam P. Characterization and Immunomodulatory Activity of Sulfated Galactan from the Red Seaweed *Gracilaria fisheri*. *Int J Biol Macromol*. 2021;189:705-714. doi:10.1016/j.ijbiomac.2021.08.182.
26. Pradhan B, Bhuyan PP, Ki JS. Immunomodulatory, antioxidant, anticancer, and pharmacokinetic activity of Ulvan, a seaweed-derived sulfated polysaccharide: An updated comprehensive review. *Mar Drugs*. 2021;21(5):300. doi:10.3390/md21050300.
27. Huang H, Lang Y, Wang S, Zhou M. Microalgae-based drug delivery systems in biomedical applications. *Eng Regen*. 2024;5(3):361-374. doi:10.1016/j.engreg.2024.01.002.
28. Cadar E, Popescu A, Dragan AML, Pesterau AM, Pascale C, Anuta V, et al. Bioactive compounds of marine algae and their potential health and nutraceutical applications: a review. *Mar Drugs*. 2025;23(4):152. doi:10.3390/md23040152.

29. Liu J, Luthuli S, Wu Q, Wu M, Choi J, Tong H. Pharmaceutical and Nutraceutical Potential Applications of *Sargassum fulvellum*. *BioMed Res Int*. 2020;2020:2417410. doi:10.1155/2020/2417410.
30. Nazarudin MF, Isha A, Mastuki SN, Ain NM, Mohd Ikhsan NF, Abidin AZ, et al. Chemical Composition and Evaluation of the α -Glucosidase Inhibitory and Cytotoxic Properties of Marine Algae *Ulva intestinalis*, *Halimeda macroloba*, and *Sargassum ilicifolium*. *Evidence-Based Complementary Altern Med*. 2020;2020:2753945. doi:10.1155/2020/2753945.
31. De Almeida CLF, Falcão HDS, Lima GRDM, Montenegro CDA, Lira NS, de Athayde-Filho PF, et al. Bioactivities from marine algae of the genus *Gracilaria*. *Int J Mol Sci*. 2011;12(7):4550-4573. doi:10.3390/ijms12074550.
32. Aziz E, Batool R, Khan MU, Rauf A, Akhtar W, Heydari M, et al. An Overview on Red Algae Bioactive Compounds and Their Pharmaceutical Applications. *J Complement Integr Med*. 2020;17(4):20190203. doi:10.1515/jcim-2019-0203.
33. Bouafir Y, Bouhenna MM, Nebbak A, Belfarhi L, Aouzal B, Boufahja F, et al. Algal Bioactive Compounds: A Review on Their Characteristics and Medicinal Properties. *Fitoterapia*. 2025;183:106591. doi:10.1016/j.fitote.2025.106591.
34. Matin M, Koszarska M, Atanasov AG, Król-Szmajda K, Jóźwik A, Stelmasiak A, et al. Bioactive potential of algae and algae-derived compounds: focus on anti-inflammatory, antimicrobial, and antioxidant effects. *Molecules*. 2024;29(19):4695. doi:10.3390/molecules29194695.
35. Wang T, Shi W, Mao Z, Xie W, Wan G. Neuroprotective Mechanisms of Red Algae-Derived Bioactive Compounds in Alzheimer's Disease: An Overview of Novel Insights. *Mar Drugs*. 2025;23(7):274. doi:10.3390/md23070274.
36. Ślusarczyk J, Adamska E, Czerwik-Marcinkowska J. Fungi and Algae as Sources of Medicinal and Other Biologically Active Compounds: A Review. *Herba Pol*. 2021;67(4):47-58. doi:10.2478/hepo-2021-0023.
37. Khandwal D, Patel S, Pandey AK, Mishra A. A comprehensive, analytical narrative review of polysaccharides from the red seaweed *Gracilaria*: pharmaceutical applications and mechanistic insights for human health. *Nutrients*. 2025;17(5):744. doi:10.3390/nu17050744.
38. Xu L, Zhu Z, Sun DW. Bioinspired nanomodification strategies: moving from chemical-based agrosystems to sustainable agriculture. *ACS Nano*. 2021;15(8):12655-12686. doi:10.1021/acsnano.1c03927.
39. Wahid MH, Eroglu E, Chen X, Smith SM, Raston CL. Functional

- Multi-Layer Graphene–Algae Hybrid Material Formed Using Vortex Fluidics. *Green Chem.* 2013;15(3):650-655. doi:10.1039/c2gc36892g.
40. He T, Liu Y, Yang Z, Zhai S, Wu Y, Shi X, et al. Recent advances in microalgae robots for biomedical applications. *ACS Biomater Sci Eng.* 2025;11(7):3875-3892. doi:10.1021/acsbiomaterials.4c01726.
 41. Roy S, Chakraborty T, Malakar C. Microalgal Nanocarrier Drug Delivery in Cancer Therapy. *Int J Pharm Sci Rev Res.* 2023;81(1):162-171. doi:10.47583/ijpsrr.2023.v81i01.029.
 42. Sun X, Zhang M, Liu J, Hui G, Chen X, Feng C. The art of exploring diatom biosilica biomaterials: from biofabrication perspective. *Adv Sci.* 2024;11(6):2304695. doi:10.1002/adv.202304695.
 43. Zhong D, Zhang D, Xie T, Zhou M. Biodegradable Microalgae-Based Carriers for Targeted Delivery and Imaging-Guided Therapy toward Lung Metastasis of Breast Cancer. *Small.* 2020;16(20):2000819. doi:10.1002/sml.202000819.
 44. Zhang X, Zhang X, Liu S, Zhang W, Dai L, Lan X, et al. Achieving Deep Intratumoral Penetration and Multimodal Combined Therapy for Tumor through Algal Photosynthesis. *J Nanobiotechnol.* 2024;22(1):227. doi:10.1186/s12951-024-02476-7.
 45. Gao C, Kwong CH, Wang Q, Kam H, Xie B, Lee SMY, et al. Conjugation of macrophage-mimetic microalgae and liposome for antitumor sonodynamic immunotherapy via hypoxia alleviation and autophagy inhibition. *ACS Nano.* 2023;17(4):4034-4049. doi:10.1021/acsnano.3c00424.
 46. Cui H, Su Y, Wei W, Xu F, Gao J, Zhang W. How Microalgae Is Effective in Oxygen Deficiency Aggravated Diseases? A Comprehensive Review of Literature. *Int J Nanomed.* 2022;17:3101-3122. doi:10.2147/IJN.S368763.
 47. El Shehawy AS, Elsayed A, Ali EM. Biogenic synthesis of iron nanoparticles using *Laurencia papillosa*: characterization, optimization, and dual applications in heavy metal removal and potential cancer treatment. *Sci Rep.* 2026;16(1):7191. doi:10.1038/s41598-026-07191-w.
 48. El Shehawy AS, Elsayed A, Ali EM. Biogenic synthesis of iron nanoparticles using *Laurencia papillosa*: characterization, optimization, and dual applications in heavy metal removal and potential cancer treatment. *Sci Rep.* 2026;16(1):7191. doi:10.1038/s41598-026-07191-w.
 49. Antonacci A, Masi A, Vedi V, Colella S, Musella F, Fiorentino G, et al. CRISPR-Cas technology turns *Chlamydomonas reinhardtii* into a flagship for algal biotechnology. *Mar Drugs.* 2025;24(1):1. doi:10.3390/md24010001.

50. Chen S, Zhu H, Radican E, Wang R, Wang X, Xiao Z, et al. Engineering approaches for sustainable protein production in microalgae: a comprehensive review. *Compr Rev Food Sci Food Saf*. 2025;24(6):e70308. doi:10.1111/1541-4337.70308.
51. Wang Y, Xue P, Cao M, Yu T, Lane ST, Zhao H. Directed evolution: methodologies and applications. *Chem Rev*. 2021;121(20):12384-12444. doi:10.1021/acs.chemrev.1c00260.
52. Liang Y, Yu H. Genetic Toolkits for Engineering *Rhodococcus* Species with Versatile Applications. *Biotech Advances*. 2021;49:107748. doi:10.1016/j.biotechadv.2021.107748.
53. Webster LJ, Villa-Gomez D, Brown R, Clarke W, Schenk PM. A Synthetic Biology Approach for the Treatment of Pollutants with Microalgae. *Front Bioeng Biotechnol*. 2024;12:1379301. doi:10.3389/fbioe.2024.1379301.
54. Baek K, Kim DH, Jeong J, Sim SJ, Melis A, Kim JS, et al. DNA-free two-gene knockout in *Chlamydomonas reinhardtii* via CRISPR-Cas9 ribonucleoproteins. *Sci Rep*. 2016;6(1):30620. doi:10.1038/srep30620.
55. Le Anh P, Oanh D, Doan L, Nguyen T, Nguyen N, Pham T, et al. Growth and Lipid Accumulation in Isolated Microalgae Strains from Vietnamese Waterbodies for Biodiesel Production. *Chiang Mai J Sci*. 2025;52:1-15. doi:10.12982/CMJS.2025.076.
56. Kselíková V, Singh A, Bialevich V, Čížková M, Bišová K. Improving Microalgae for Biotechnology — From Genetics to Synthetic Biology – Moving Forward but Not There Yet. *Biotech Advances*. 2022;58:107885. doi:10.1016/j.biotechadv.2021.107885.
57. Jagadevan S, Banerjee A, Banerjee C, Guria C, Tiwari R, Baweja M, et al. Recent Developments in Synthetic Biology and Metabolic Engineering in Microalgae towards Biofuel Production. *Biotechnol Biofuels*. 2018;11(1):185. doi:10.1186/s13068-018-1181-1.
58. Baek K, Kim DH, Jeong J, Sim SJ, Melis A, Kim JS, et al. DNA-free two-gene knockout in *Chlamydomonas reinhardtii* via CRISPR-Cas9 ribonucleoproteins. *Sci Rep*. 2016;6(1):30620. doi:10.1038/srep30620.
59. Shitanaka T, Wang Y, Do S, Yuson J, Khanal SK, Zienkiewicz K, et al. Synthetic Biology and Metabolic Engineering of Microalgae for Sustainable Lipid and Terpenoid Production: An Updated Perspective. *Plant Biotechnol J*. 2026;24(3):1359-1376. doi:10.1111/pbi.70405.
60. Fu S, Ma K, Song X, Sun T, Chen L, Zhang W. Synthetic biology strategies and tools to modulate photosynthesis in microbes. *Int J Mol Sci*. 2025;26(7):3116. doi:10.3390/ijms26073116.

61. Fu S, Ma K, Song X, Sun T, Chen L, Zhang W. Synthetic biology strategies and tools to modulate photosynthesis in microbes. *Int J Mol Sci.* 2025;26(7):3116. doi:10.3390/ijms26073116.
62. Carneiro DC, Rocha VPC, Damasceno PKF, Barbosa JDV, Soares MBP. Therapeutic Applications of Synthetic Gene/Genetic Circuits: A Patent Review. *Front Bioeng Biotechnol.* 2024;12:1425529. doi:10.3389/fbioe.2024.1425529.
63. Mittal D, Thakur R, Singh S, Chauhan A, Devi R. Microalgae-derived bioactive compounds-A natural ally in cancer immunotherapy. *Appl Biol Chem J.* 2025;6(2):62002.
64. Garlapati VK, Sharma S, Sharma D, Kumar SPJJ, Jacob S, Kuila A, et al. Sustainable Production of Microalgal Nanoparticles through Green Synthesis towards Cancer Treatment. *Front Bioeng Biotechnol.* 2025;13:1621876. doi:10.3389/fbioe.2025.1621876.
65. Fayyad RJ, Mohammed Ali AN, Hamdan NT. The Specific Anti-Cancerous Mechanisms Suggesting Spirulina Alga as a Promising Breast Cancer Fighter. *Res J Pharm Technol.* 2021;14(10):5599-5602. doi:10.52711/0974-360X.2021.00974.
66. Hannan MA, Dash R, Haque MN, Mohibullah M, Sohag AAM, Rahman MA, et al. Neuroprotective Potentials of Marine Algae and Their Bioactive Metabolites: Pharmacological Insights and Therapeutic Advances. *Mar Drugs.* 2020;18(7):347. doi:10.3390/md18070347.
67. Mani A, Narayanan M, Rajinikanth V. Neurodegenerative Marine Algae Bioactive Compounds: A Viable Cure to Treat Amyotrophic Lateral Sclerosis (ALS): A Review. *Depicting Med J.* 2024;7(3):201-217. doi:10.18502/dmj.v7i3.17735.
68. Zhang R, Zhang X, Tang Y, Mao J. Composition, Isolation, Purification and Biological Activities of *Sargassum Fusiforme* Polysaccharides: A Review. *Carbohydr Polym.* 2020;228:115381. doi:10.1016/j.carbpol.2019.115381.
69. Che Y, Song X, Zhang L. Engineering Microalgae-Based Biohybrid Robots for Biomedical Applications. *Cell Biomater.* 2025;1(8):100103. doi:10.1016/j.celbio.2025.100103.
70. Zhang C, Liu S, Cao Y, Zhang W, He Y, Tu W, et al. *Chlorella*-Based Bioactive Oxygen Generator for Sustained Tumor Hypoxia Alleviation and Combined-Modality Tumor Therapy. *J Colloid Interface Sci.* 2026;702:138999. doi:10.1016/j.jcis.2025.138999.
71. Majernik M, Jendželovský R, Vargova J, Jendželovská Z, Fedoročko P. Multifunctional nanoplatforms as a novel effective approach in photodynamic therapy and chemotherapy, to overcome multidrug resistance in cancer. *Pharmaceutics.* 2022;14(5):1075. doi:10.3390/pharmaceutics14051075.

72. Jiang S, Hao B, Song X, Jiang Y, Guo J, Wang Y, et al. Living Microalgae-Based Magnetic Microrobots for Calcium Overload and Photodynamic Synergetic Cancer Therapy. *Adv Healthc Mater.* 2025;14(11):2403866. doi:10.1002/adhm.202403866.
73. Wang Z, Wang C, Ji Y, Yang M, Li C, Li M, et al. Magnetically Driven Bionic Nanorobots Enhance Chemotherapeutic Efficacy and the Tumor Immune Response via Precise Targeting. *The Innovation.* 2025;6(2):100777. doi:10.1016/j.xinn.2024.100777.
74. Zhang L, Zhang X, Ran H, Chen Z, Ye Y, Jiang J, et al. A NIR-Driven Green Affording-Oxygen Microrobot for Targeted Photodynamic Therapy of Tumors. *Nanoscale.* 2024;16(2):635-644. doi:10.1039/d3nr03801g.
75. Zhong D, Li W, Hua S, Qi Y, Xie T, Qiao Y, et al. Calcium Phosphate Engineered Photosynthetic Microalgae to Combat Hypoxic-Tumor by in-Situ Modulating Hypoxia and Cascade Radio-Phototherapy. *Theranostics.* 2021;11(8):3580-3594. doi:10.7150/thno.55441.
76. Medina RA, Goeger DE, Hills P, Mooberry SL, Huang N, Romero LI, et al. Coibamide A, a Potent Antiproliferative Cyclic Depsipeptide from the Panamanian Marine Cyanobacterium *Leptolyngbya* Sp. *J Am Chem Soc.* 2008;130(20):6324-6325. doi:10.1021/ja801383f.
77. Chen T, Wong YS. In Vitro Antioxidant and Antiproliferative Activities of Selenium-Containing Phycocyanin from Selenium-Enriched *Spirulina Platensis*. *J Agric Food Chem.* 2008;56(12):4352-4358. doi:10.1021/jf073399k.
78. Jiang L, Wang Y, Yin Q, Liu G, Liu H, Huang Y, et al. Phycocyanin: A Potential Drug for Cancer Treatment. *J Cancer.* 2017;8(17):3416-3429. doi:10.7150/jca.21058.



From Lab to Market: Bridging Academia-Industry Gaps in MedTech Innovation

Subhash N. N. *, Muraleedharan C. V.

*Department of Medical Device Engineering, Biomedical Technology Wing,
Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST),
Thiruvananthapuram- 695012, Kerala, India.*

Abstract

Translating laboratory findings into commercially viable products is a critical yet challenging endeavor within scientific and engineering domains, particularly in medical technology. While universities generate innovative and valuable discoveries, the transition from research to market is often hindered by structural, regulatory, and organizational barriers. Addressing these challenges requires strong, sustained collaborations that effectively bridge academia and industry. This paper presents practical recommendations for establishing and maintaining productive partnerships that can streamline the commercialization of laboratory research. Drawing on detailed case studies of cardiovascular devices, orthotics and prosthetics, and other life-saving healthcare solutions, it highlights strategies for fostering collaboration, aligning with industry development and sales cycles, and disseminating institutional best practices. Additionally, the paper incorporates industry perspectives on effective engagement with academic institutions. Overall, the findings demonstrate that well-coordinated academia–industry partnerships not only secure critical funding for research and development but also accelerate innovation timelines, ultimately delivering significant benefits to both businesses and public health.



Citation: Subhash NN, Muraleedharan CV.
From Lab to Market: Bridging Academia-
Industry Gaps in MedTech Innovation. *Opn.
Med. Sci. Technol. Health.* 2026; 4(1):
e26004.

Received: Feb 20, 2026

Accepted: May 14, 2026

Published: June 30, 2026

Keywords: lab-to-market transition, MedTech

Copyright: © 2026 Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the manuscript.

Funding: None Declared.

Competing interests: None declared.

***Corresponding Author Address:**

Subhash NN,
Department of Medical Device Engineering,
Biomedical Technology Wing,
Sree Chitra Tirunal Institute for Medical
Sciences and Technology (SCTIMST),
Trivandrum- 695012, Kerala, India.
Email: nnsbhash@gmail.com
ORCID ID: 0000-0003-3410-1515

1. Introduction

The fundamental nature of industry is driven by the principles of buying and selling, with a strong focus on efficiency and time-to-market. While industries are generally willing to provide financial support to academic institutions, delays in research processes are often a significant concern. Nevertheless, even when a project lies outside an institution's core expertise, engaging with it can enhance teaching quality, foster skill development, and promote meaningful knowledge exchange. It is essential to clearly define the intended depth of institute–industry collaboration—whether it involves limited engagement, such as consultancy, or deeper partnerships, such as co-development. Additionally, government policies increasingly encourage the effective utilization of institutional infrastructure and resources to support industry collaborations. In this context, two primary avenues for institute–industry engagement are outlined below.

Several structured models have been proposed in the literature to explain how academia and industry can collaborate effectively. The Triple Helix model, developed by Etzkowitz and Leydesdorff [1], conceptualizes innovation as emerging from dynamic interactions among universities, industry, and government. More operationally oriented frameworks, such as those reviewed by Ankrah and Al-Tabbaa [2], classify university-industry engagement mechanisms along a spectrum ranging from consultancy and contract research to joint ventures and academic spin-offs, emphasizing that the most suitable model depends on the strategic objectives of the participating organizations. Similarly, Perkmann and Walsh [3] distinguish between knowledge transfer activities, collaborative research, and commercialization pathways, highlighting that both the intensity and the form of engagement vary according to organizational context and institutional maturity. Collectively, these frameworks provide a comprehensive basis for understanding and structuring effective academia-industry partnerships.

Within this broader landscape, two collaborative pathways are particularly relevant to the academia-industry interface in medical technology. The first involves exploratory or “blue-sky” research, in which industry partners support long-term scientific investigations with potential future applications. The second pathway focuses on targeted co-development projects that address clearly defined industrial or clinical needs, often with explicit commercialization objectives. The case studies presented in this paper demonstrate how these collaborative approaches can be effectively implemented in practice, thereby facilitating successful transitions from laboratory research to market-ready solutions.

Blue-sky research enables exploratory investigations that are not necessarily directed toward immediate commercial outcomes. This mode of research fosters creativity, allowing scholarly teams to address high-risk and complex problems using novel and unconventional approaches. Such initiatives are often supported by large industry consortia seeking global visibility, and they typically permit unrestricted dissemination of research findings. For academic institutions, these opportunities contribute to the enhancement of advanced research infrastructure and the development of specialized expertise. In parallel, many companies prefer to outsource research and development activities while focusing their internal efforts on product engineering. Successful models of such collaborations are evident in countries such as Israel, the United States, the United Kingdom, and Japan.

By contrast, one-to-one research projects involve direct collaboration between an academic group and a single industrial partner. These engagements are usually governed by confidentiality agreements and provisions for sharing proprietary information. Industry collaborators provide targeted funding with the expectation of gaining a competitive advantage through the intellectual property generated. Unlike blue-sky research, the primary objective of such partnerships is the practical application of research toward product development rather than exploratory investigation.

2. Strategies for collaboration with industry

Between 2020 and 2025, several collaborative strategies were implemented to strengthen academia-industry engagement:

- Addressing immediate, industry-specific technical challenges through targeted problem-solving approaches
- Establishing medium- to long-term partnerships within well-defined domains of expertise
- Engaging in joint product development initiatives to accelerate innovation
- Facilitating the commercialization of laboratory-developed technologies through structured industry collaboration
- Undertaking projects aligned with corporate social responsibility (CSR) objectives
- Providing flexible research support while simultaneously enhancing institutional capacity and professional credibility

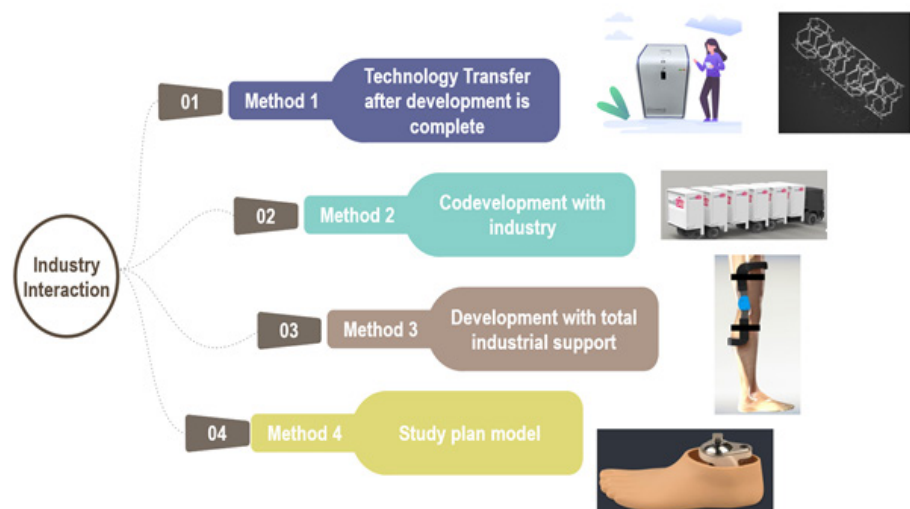


Figure 1. Industry interaction case studies at SCTIMST during 2020–2025

The following case studies illustrate the practical implementation of each collaboration strategy. Collectively, they present representative models of academia-industry engagement across various stages of medical technology development and commercialization.

Table 1. Mapping of collaboration strategies to case studies

Collaboration Strategy	Representative Case Study	Purpose of Engagement
Addressing immediate industry-specific technical challenges	FUPRO Grace Foot	Design verification and structural performance assessment using computational and experimental methods
Building medium- to long-term partnerships	VR for Rehabilitation	Long-term digital therapeutics development through institutional partnership
Participating in joint product development	OA Knee Brace	Co-development of orthotic products with industry funding and shared technical inputs
Commercializing laboratory-developed technologies	TiN-Coated Coronary Stent; UV-C Disinfection Devices	Translation of institute-developed technologies into commercial products through licensing and industrial scale-up
Projects aligned with societal or CSR objectives	Four-Zone MediCAB	Rapid development of healthcare infrastructure solutions during the COVID-19 crisis
Flexible research support and institutional capacity building	Multiple case studies	Strengthening translational research capability while supporting industry innovation

Case Study 1: TiN-Coated Coronary Stent System

This case study illustrates how a research institute and a private company collaborated to translate a laboratory-developed medical technology into a viable product pathway. Coronary stents, typically fabricated from metal alloys, are deployed into occluded arteries using balloon catheters to restore blood flow. While bare-metal stents help mitigate early complications such as elastic recoil, they do not prevent neointimal tissue proliferation, which can lead to in-stent restenosis. Drug-eluting stents have demonstrated improved outcomes in reducing restenosis and the need for repeat interventions; however, they are associated with an increased risk of late stent thrombosis.

Titanium nitride (TiN)-coated coronary stents have emerged as a promising alternative to address these limitations. Studies indicate that TiN coatings can reduce both restenosis and late thrombosis, while also minimizing the release of nickel ions following implantation, thereby improving biocompatibility. These findings suggest that TiN-coated stents represent a clinically relevant

and commercially viable solution [4]. In 2024, the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) entered into a collaborative agreement with Invasive Technologies Pvt. Ltd. to support the scale-up and commercialization of this technology. The projected development timeline of 3–5 years encompasses preclinical evaluation, clinical trials, and regulatory approval processes.

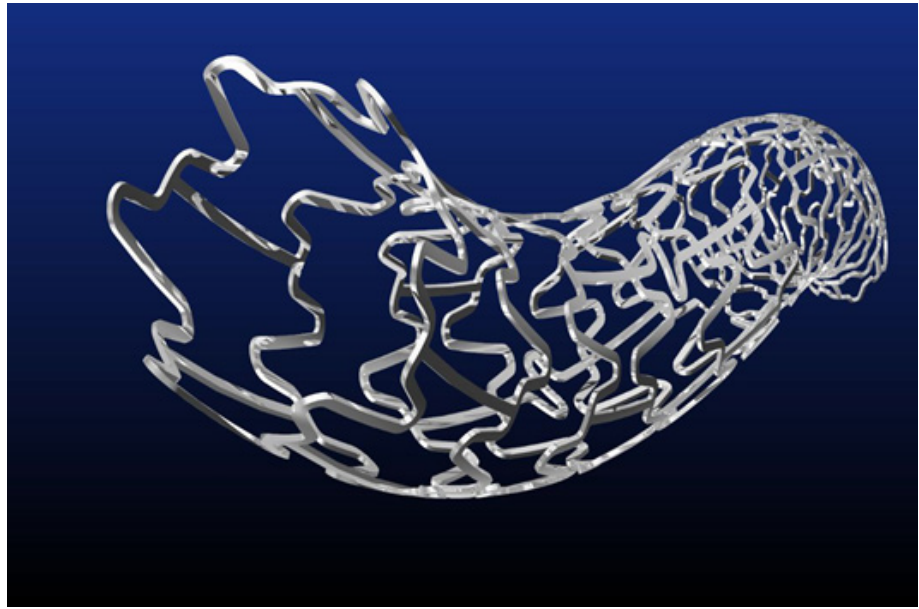


Figure 2. Coronary stent

Case Study 2: UV-C Disinfection Devices

This case study exemplifies how the institute commercialized a medical prototype developed internally as a result of technology-transfer process. Used face masks constitute biomedical waste that must be disposed of promptly and safely to prevent further spread of infection. The project therefore aimed to develop a scientifically validated UV-C–based disinfection solution that could be deployed rapidly under lockdown conditions. The project hence aimed at coming up with a scientifically proven solution of converting a disinfectant into a quick, locally available lockdown procedure during the COVID-19 lockdown in India.

The product got registered with the Central Drugs Standard Control Organization as a non-notified medical device after passing the safety and efficacy tests in accordance with the requirements of ICMR in innovative solutions to the COVID-19 epidemic. VST Mobility Pvt. Ltd. had recently signed a licensing deal and begun production (Bin19, and UVspot) to supply the much-needed demand on national scale [5].

The concept to market-ready product transition process was performed in eight weeks, which included the development of proof-of-concept, safety and efficacy, technology transfer through an expression of interest, regulatory approval and fast procurement and scale through nationwide lockdown constraints. This was greatly helped by the fact that SCTIMST possessed the ICMR-approved evaluation authority which greatly aided in the validation and deployment processes.



Figure 3. UV Spot manufactured by M/s VST Mobility Pvt. Ltd.

Case Study 3: FUPRO Grace Foot

This case represents a collaborative research project in which systematic engagement between academia and industry was established through a structured study-plan approach. The study explored whether trans-tibial prosthetic foot designs could be effectively evaluated using in silico methods prior to physical prototyping and in vitro validation. The central objective was to reduce the time and cost associated with traditional iterative development cycles.

The structural performance of the FUPRO Grace Foot was assessed through modal analysis, evaluation under forefoot and heel loading conditions, and finite element modelling to simulate system behavior. These computational predictions were subsequently validated through in vitro testing in accordance with ISO 22675 [6] and ISO 10328 [7] standards. The strong agreement between computational and experimental results demonstrates that analysis-driven design approaches, supported by in silico modelling, can reliably contribute to the development of safe and effective prosthetic devices.

Experimental outcomes further confirmed that the device successfully withstood cyclic endurance testing, establishing its structural integrity [8]. This academia-industry partnership facilitated the translation of prosthetics research into a practical assistive technology with tangible societal impact. The innovation has gained national recognition, including its feature on Shark Tank India, underscoring both its technological relevance and its contribution to contemporary healthcare solutions.



Figure 4. Structural testing of prosthetic foot

Case Study 4: Four-Zone MediCAB

This case study exemplifies a focused collaborative research and development project undertaken with a private industry partner, M/s Modulus Housing (Forbes 30 Under 30 India, 2026), during the COVID-19 crisis. The unprecedented surge in patient numbers placed immense strain on India's healthcare infrastructure, creating an urgent need for rapidly deployable and modular medical facilities - requirements that conventional construction methods were unable to meet within the necessary timelines.

The project centered on the design and development of cost-effective, quickly deployable field units that could be assembled using domestically available materials, even under lockdown conditions. A key innovation was the implementation of a four-zone system that effectively segregated healthcare workers, suspected cases, confirmed patients, and critical care units, thereby minimizing the risk of cross-infection.

This approach not only addressed the immediate demands of the pandemic but also demonstrated the potential for scalable micro-hospital networks as a long-term healthcare solution [9].

Case Study 5: OA Knee Brace

The project was fully funded by a private-sector co-development partner, TYNOR Orthotics Pvt. Ltd., through a structured collaboration model initiated in October 2020. This partnership generated valuable practical insights that informed the company's internal research and development strategies, enabled comparative evaluation against predicate knee-brace products, and supported the strategic advancement of its knee-brace product portfolio.

The collaboration also strengthened the institution's capacity to develop orthotic innovations. These outcomes underscore the critical role of publicly funded research institutions as catalysts for industrial refinement and the translational development of commercially viable healthcare products.

Case Study 6: VR for Rehabilitation

This project represents a successful collaboration between the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) and Skillver Training Solutions Pvt. Ltd., formalized through a Memorandum of Understanding in 2024. The partnership led to the development of a Software as a Medical Device (SaMD) in the form of a virtual reality-based platform designed to improve upper-limb mobility in patients with mild to moderate post-stroke impairments.

The initiative was fully funded by the industry partner and progressed from proof-of-concept to the development of nineteen interactive, game-based therapeutic modules. It also achieved regulatory advancement through the acquisition of a CDSCO MD-13 test license. This collaboration demonstrates the effectiveness of integrated technical, clinical, and regulatory teamwork.

The summary of key learnings from the interaction are shown in Table 2.

Table 2: Learnings from the Interaction

Bigger Industries	Smaller Industries and Start-ups
• Better traction • Structured decision-making • Professional liaising • High expectations associated with national institutes • Expect support in government approvals and inter-departmental coordination • Strong emphasis on time efficiency	• Lower administrative burden • Faster decision-making • Need for extensive technical, regulatory, and procedural support • Value close hand-holding and reduced red tape • Strong societal impact orientation

3. Conclusion

The journey from laboratory discovery to commercially viable medical products is rarely linear; it is shaped by the individuals involved, the contextual environment, the urgency of the problem, and the quality of early-stage decisions. An analysis of the presented case studies reveals a consistent pattern: success in lab-to-market transitions depends not only on technological excellence but also on the deliberate alignment of innovations with real clinical needs and practical delivery pathways.

Customer discovery emerges as both an intellectually rigorous and empathetic process. The development of TiN-coated coronary stents, for instance, was driven by the persistent clinical challenges of restenosis and late thrombosis. Similarly, UVC disinfection devices were conceived in response to urgent needs during the COVID-19 lockdown, where rapid deployment and safety were paramount. In projects such as the FUPRO Grace Foot and osteoarthritis knee brace, close engagement with patients, clinicians, and rehabilitation specialists ensured that technical optimization translated into real-world usability. These examples demonstrate that customer discovery is a continuous, iterative process that informs and refines technical decision-making.

Equally critical is the integration of business-model thinking into research and development. Tools such as the Business Model Canvas enabled the rapid translation of ideas into deployable solutions by aligning regulatory pathways, manufacturing strategies, and distribution channels. Initiatives such as the Four-Zone MediCAB highlight how design innovation must be closely integrated with operational realities, particularly during crisis situations. In contrast, long-term projects such as TiN-coated stents and virtual reality-based rehabilitation systems emphasize sustained strategies focused on regulatory rigor, scalability, and market readiness.

A key insight from these case studies is that embedding customer discovery and business-model frameworks within the R&D process does not dilute scientific rigor; rather, it enhances it. Early clarity on end users, value propositions, and translational pathways reduces uncertainty and accelerates impact. This integrated approach supports both agile startup collaborations and structured industry partnerships while maintaining a consistent translational philosophy.

4. Future perspectives

Looking ahead, the successful translation of medical technologies will increasingly depend on strengthening integrated innovation ecosystems that seamlessly connect academia, industry, healthcare providers, and regulatory bodies. Expanding early-stage customer discovery frameworks and embedding translational thinking into academic research training can further enhance the efficiency of lab-to-market pathways.

There is also a growing need to develop adaptive regulatory strategies and agile manufacturing models that can respond effectively to both routine healthcare demands and emergency situations. Digital health technologies, including Software as a Medical Device (SaMD), artificial intelligence, and virtual reality-based therapeutics, are expected to play a transformative role in shaping future MedTech innovation.

Furthermore, fostering long-term, trust-based partnerships between academic institutions and industry - supported by clear intellectual property frameworks and shared strategic goals - will be critical for sustaining innovation. Investment in translational infrastructure, interdisciplinary skill development, and global collaborative networks will further accelerate the commercialization of impactful healthcare solutions.

Ultimately, the convergence of scientific excellence, human-centered design, and strategic business thinking will define the next generation of successful lab-to-market transitions, ensuring that innovations reach patients efficiently and equitably across diverse healthcare settings.

5. References

1. Etzkowitz H, Leydesdorff L. The dynamics of innovation: from National Systems and “Mode 2” to a Triple Helix of university-industry-government relations. *Research Policy*. 2000;29(2):109-123.
2. Ankrah S, AL-Tabbaa O. Universities-industry collaboration: A systematic review. *Scandinavian Journal of Management*. 2015;31(3):387-408.
3. Perkmann M, Walsh K. University-industry relationships and open innovation: Towards a research agenda. *International Journal of Management Reviews*. 2007;9(4):259-280.

4. Subhash NN, Rajeev A, Sujesh S, Harikrishnan S, Muraleedharan CV. Application of optical NDE in design verification to assess the elastic recoil and foreshortening of coronary stents. *Journal of Non-Destructive Testing and Evaluation*. 2024;21(3):35–39.
5. Neelakandan SN, Sukesan A, Jerard J, Uthaman VP, Vasudevan VD, Sarojini Amma PKSP, Nandkumar MA, Vayalappil MC. Chitra Ultraviolet-C-Based Facemask Disposal Bin. *Transactions of the Indian National Academy of Engineering*. 2020;5(2):305–313.
6. International Organization for Standardization. Prosthetics—Testing of ankle-foot devices and foot units—Requirements and test methods. Geneva: ISO; 2016. Standard No. ISO 22675:2016.
7. International Organization for Standardization. Prosthetics—Structural testing of lower-limb prostheses—Requirements and test methods. Geneva: ISO; 2016. Standard No. ISO 10328:2016.
8. Subhash NN, Mehra N, Choudhary A, Baby CJ, Aravind AU, Benny P, Muraleedharan CV. Structural performance assessment of FUPRO Grace foot. *Trends in Biomaterials and Artificial Organs*. 2022;36(2):94–101.
9. Subhash NN, Muraleedharan CV, Shreeram R. Four-zone deployable MediCAB for COVID-19 management. Paper presented at: 5th World Congress on Disaster Management (WCDM);2021 Nov 25; New Delhi, India.



Post Neurosurgical Meningitis-

A Perspective on Laboratory Guided Management

Dr. Kavita Raja^{1*}

¹*Professor (Sr. Grade) and Head, Department of Microbiology,
Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Thiruvananthapuram Kerala, India – 695 011.*

Abstract

Meningitis following neurosurgical procedures is termed Post-neurosurgical meningitis. The disease poses specific challenges in diagnosis, classification for surveillance purposes and optimum management in the face of immune compromise and cerebrospinal fluid (CSF) levels of antimicrobials. Diagnosis involves culture of the CSF and correlation of the culture result with biochemical parameters. Antimicrobials used in the management have to be selected from the culture and sensitivity result. Administration has to be carefully modulated based on the pharmacokinetics and dynamics of each antibiotic.

Introduction

Post Neurosurgical Meningitis (PNM) is a complication of neurosurgical procedures and differs from community acquired meningitis in terms of risk factors, manifestation, aetiological agents and management. It is classified as an organ space infection under Surgical Site infections (SSI). The Microbiology and Biochemistry laboratories have a great role to play in the expert management of the disease. The disease poses specific challenges in diagnosis, classification for surveillance purposes and optimum management in the face of immune compromise and CSF levels of antimicrobials. This perspective will discuss these aspects and correct utilisation of laboratory results in the management for a better outcome.

Diagnosis

There are a few challenges in the diagnosis of meningitis after surgery. The patient is generally non responsive or disoriented after the surgery and will not complain of headache or neck stiffness. Fever as a sign may or may not occur. Non-infectious meningitis may occur as a result of sub-arachnoid haemorrhage, tumours that cause meningitis and due to blood products released during the surgical procedure [1-4]. Hence these have to be differentiated based on laboratory findings.

The incidence of Post neurosurgical meningitis reported in literature are:

Craniotomy: 0.3%-8.6%, Drainage devices: EVD: 0 – 22%, Internal (VP shunt): 4 – 17%, Lumbar: 0.8 – 7% [1,3].



Citation: Raja K. Post Neurosurgical Meningitis: A Perspective on Laboratory Guided Management. *Opn. Med. Sci. Technol. Health.* 2026; 4(1): e26005.

Received: Mar 2, 2026

Accepted: May 20, 2026

Published: June 30, 2026

Keywords: Meningitis, Cerebrospinal fluid, Antibiotic, Management

Copyright: © 2026 Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the manuscript.

Funding: None Declared.

Competing interests: None declared.

***Corresponding Author Address:**

Dr. Kavita Raja,
Professor (Sr Grade) and Head,
Department of Microbiology,
Sree Chitra Tirunal Institute for Medical
Sciences and Technology,
Thiruvananthapuram 695011, Kerala, India
Email ID: kavita_raja@sctimst.ac.in
ORCID ID: 0000-0003-1914-5034

Meningitis is an inflammation of the meninges, caused by infective agents, most commonly bacteria and rarely by fungi, leading to depletion of the glucose that is metabolised by bacteria to produce proteins that are by-products leading to an increase in CSF protein levels. When meningitis occurs within one month after a neurosurgical procedure that involves Craniotomy or craniectomy or insertion of a drainage device, or within one year after insertion of an implant in the brain, it is called an organ space infection, under Surgical Site Infections (SSI). A variety of risk factors for PNM are described in literature. A study from Taiwan (2016) [5], had 22 (1.4%) cases of meningitis from 4392 craniotomies. Significant risk factors were

1. Emergency procedure/Redo surgery
2. CSF leakage
3. EVD in situ > 72 hrs
4. Surgery duration > 4.5 hrs

A study from NIMHANS (2010), India had 415 cases (2.3%) of meningitis out of 18092 cases, with 7.7% among those with an existing pyogenic infection. They too found a slight increase in those with shunts in situ [6].

A study from Greece (2015) with 16 cases (4.8%) of meningitis out of 334 craniotomies. Risk factors were perioperative steroid use, CSF leak and external ventricular drainage in situ [7].

The biochemical analysis of CSF and the cell counts play a less significant role in the accurate diagnosis of PNM and interpretation is difficult unless, simultaneous culture of the pathogen is carried out. PNM, as opposed to community acquired meningitis, does not align to the concept of typical changes in the CSF. One review discusses the ratio between CSF Glucose and blood glucose levels. A ratio of CSF:blood glucose < 0.4, they conclude is indicative of meningitis along with a CSF Lactate > 4mmol/L. However, they also suggest incorporating Nucleic Acid Amplification (NAA) before stopping empirical antibiotics [1]. Other studies also remark on the futility of depending on CSF levels of Glucose, protein and leukocyte numbers in the diagnosis of PNM [2]. In addition to the CSF cell count and the CSF levels of glucose and protein, new parameters like CSF levels of Lactate, Procalcitonin and Interleukins have the potential to make diagnosis and monitoring more accurate as seen below:

Biomarker Levels suggesting CNS infection, in literature

- Procalcitonin (PCT) - CSF PCT $\geq$ 0.12 ng/ml (Sensitivity-85.7%, Specificity-51.6%) [4,8]
- Lactate (Lac) - CSF Lac $\geq$ 4.95 mmol/L (Sensitivity- 86%, Specificity-100%) [9]
- IL-1 Beta - CSF IL-1 $\geq$ 0.27 pg/ml

Microbiological analysis

Culture is the mainstay of diagnosis. The primary sample is cerebrospinal Fluid (CSF). CSF can be obtained by several methods- Lumbar puncture, ventricular tap, through ventricular drainage tubes and rhinorrhoea fluid. Of these the first two are the samples that are basically sterile fluids and any growth from these samples indicates infection of the meninges. Drainage tubes carry colonisers and these have to be differentiated from actual infection. Rhinorrhoea fluid is not an appropriate specimen due to the presence of nasal flora.

Microscopy: The Gram stain reveals presence of pus cells and bacteria. Pus cells indicate active inflammation of the meninges due to infection. Gram positive or Gram-negative bacteria in the presence of pus cells indicate meningitis of infectious aetiology.

Culture: After 24-48 hrs of incubation on Blood Agar and MacConkey agar, isolated colonies are put up for identification and antibiotic sensitivity testing. For common organisms like *Klebsiella pneumonia*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, the diagnosis is quite straightforward. However, for gram positives like *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Corynebacterium* species and others, a clinical correlation is essential for reporting them as the causative agent. *Staphylococcus aureus* meningitis (SAM) most often follows neurosurgical procedures (79%), VP shunts and EVDs and median time for infection to manifest was 11 days in a study from Spain in 2019 [7]. There was no significant difference in the rate of postoperative meningitis based on MRSA/MSSA colonization status (3.9% for colonized patients vs. 2.5% for noncolonized patients, $P = 0.79$) after endoscopic surgery [10,11]. Gram negatives that are rare like *Elizabethkingia meningosepticum*, *Stenotrophomonas maltophilia* and others have to be carefully correlated and confirmed with repeat samples. Fungal meningitis is extremely rare postoperatively.

A review of literature revealed that there is a wide variety of bacteria that cause PNM, pointing to the fact that causative organisms are diverse maybe due to the prevailing circumstances at each healthcare facility (Figure 1).

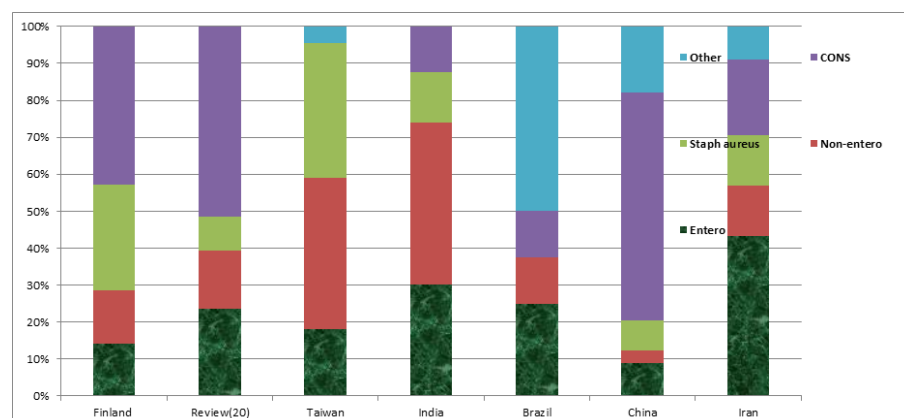


Fig 1. Distribution of pathogens in literature

On isolation of the pathogen, treatment is guided by the sensitivity tests, which have to include the Minimal inhibitory concentration of each antibiotic reported. In Table 1, it is seen how the pharmacodynamics and pharmacokinetics work in the management of meningitis.

Susceptibility testing: Pure culture of the isolated organism is subjected to susceptibility testing. This may be by two methods: Agar Disc diffusion and Micro-broth dilution. Disc diffusion includes Epsilon test (E-test), which ascertains the MIC. Microbroth dilution can be done either manually or by automated methods using VITEK2 (bioMerieux). Generally, a standard set of antibiotics are tested, following the guidelines of the clinical Laboratory Standards Institute (CLSI).

In case of post-op meningitis, it can be seen from the figure 1 that the primary causes of meningitis in the community, do not have any relevance in this context. To tackle the wide variety of organisms, a clear idea about the susceptibility patterns and the antimicrobials that can be used effectively in the cerebrospinal fluid, is needed. Table 1 shows the antimicrobials and their pharmacodynamics [12].

Table 1. Pharmacodynamics of antibiotics in Meningitis

Antibiotic	MIC	Dose	Interval	CSF Levels
Penicillin	0.06 mg/L	2.4 g	4th hrly	2 mg/L
Ampicillin	0.06 mg/L	2 g	4th hrly	2 mg/L
Ceftriaxone	1 mg/L	3 g	12th hrly	2-42 mg/L
Chloramphenicol	0.5 mg/L	750 mg	6th hrly	6 mg/L
Fosfomycin	32 mg/L	4 g	24 hrs	70 mg/L
Meropenem	0.125 mg/L	2 g	8th hrly	1 mg/L
Vancomycin	0.5 mg/L	1 g	12th hrly / continuous	2-4 mg/L
Linezolid	0.5 mg/L	600 mg	12th hrly	6.1-10.8 mg/L
Co-trimoxazole	2-38 mg/L	800 mg+160 mg	12th hrly	30-40 mg/L

Aminoglycosides, Tigecycline, Teicoplanin, Cefoperazone, Colistin, Polymyxin B, Clindamycin, Piperacillin-Tazobactam, 1st and 2nd Gen Cephalosporins do not cross the blood brain barrier and hence cannot be used in meningitis. However, Amikacin and Colistin can be administered intrathecally.

In conclusion, the following have to be kept in mind while managing a case of PNM;

1. Risk Factors

- a. Emergency procedure/Repeat surgery
- b. CSF leakage
- c. EVD in situ > 72 hrs
- d. Surgery duration > 4.5 hrs

- e. Peri-operative steroids
 - f. Existing pyogenic infection
2. Laboratory guidance for Antibiotic choice is essential. Intrathecal approach and right knowledge of PK-PD.
 3. Surgical antimicrobial prophylaxis (SAP) should be only for 48hrs. For existing infection add the antibiotic as SAP.

References

1. Hussein K, Bitterman R, Shofty B, Paul M, Neuberger A. Management of post-neurosurgical meningitis: narrative review. *Clin Microbiol Infect.* 2017;23(9):621-628.
2. Bao MY, Xie HT, Gao P, Mao X, Li ZY, Wang WH, Sopheak S, Cheng HW, Ye L, Zhang X. Current diagnosis and potential obstacles for post-neurosurgical bacterial meningitis. *Eur Rev Med Pharmacol Sci.* 2022;26(17):6351-6360.
3. Cherian A, Baheti NN, Easwar HV, Nair DS, Iype T. Recurrent meningitis due to epidermoid. *J Pediatr Neurosci.* 2012;7(1):47-8.
4. Forgacs P, Geyer CA, Freidberg SR. Characterization of Chemical Meningitis after Neurological Surgery. *Clinical Infectious Diseases.* 2001;32(2):179-185.
5. Chen CH, Chang CY, Lin LJ, Chen WL, Chang YJ, Wang SH, Cheng CY, Yen HC. Risk factors associated with postcraniotomy meningitis: A retrospective study. *Medicine (Baltimore).* 2016;95(31):e4329.
6. Srinivas D, Veena Kumari HB, Somanna S, Bhagavatula I, Anandappa CB. The incidence of postoperative meningitis in neurosurgery: an institutional experience. *Neurol India.* 2011;59(2):195-8.
7. Kourbeti IS, Vakis AF, Ziakas P, Karabetsos D, Potolidis E, Christou S, Samonis G. Infections in patients undergoing craniotomy: risk factors associated with post-craniotomy meningitis. *J Neurosurg.* 2015;122(5):1113-9.
8. Tian R, Hao S, Hou Z, Gao Z, Liu B. The characteristics of post-neurosurgical bacterial meningitis in elective neurosurgery in 2012: A single institute study. *Clin Neurol Neurosurg.* 2015;139:41-5.
9. Wang Q, Wang Y, Yang Y, Kong Y, Peng Y. The value of elevated cerebrospinal fluid lactate concentrations in post-neurosurgical bacterial meningitis. *BMC Neurol.* 2023;23(1):377.
10. Pintado V, Pazos R, Jiménez-Mejías ME, Rodríguez-Guardado A, Díaz-Pollán B, Cabellos C, García-Lechuz JM, Lora-Tamayo J, Domingo P, Muñoz E, Domingo D, González-Romo F, Lepe-Jiménez JA, Rodríguez-Lucas C, Gil A, Pelegrín I, Chaves F, Pomar V, Ramos A, Alarcón T, Pérez-Cecilia E. *Staphylococcus aureus* meningitis in adults: A comparative cohort study of infections caused by meticillin-resistant and meticillin-susceptible strains. *J Hosp Infect.* 2019;102(1):108-115.

11. Orillac C, Patel A, Dastagirzada Y, Benjamin C, Lieberman S, Lebowitz R, Golfinos JG, Pacione D. Comparing Rates of Postoperative Meningitis After Endoscopic Endonasal Procedures Based on Methicillin-Resistant *Staphylococcus aureus*/Methicillin-Sensitive *Staphylococcus aureus* Colonization and Antibiotic Prophylaxis. *World Neurosurg.* 2022;167:e858-e864.
12. Nau R, Blei C, Eiffert H. Intrathecal Antibacterial and Antifungal Therapies. *Clin Microbiol Rev.* 2020;33(3):e00190-19.

ADVERTISING FEATURE

SCTIMST: Your Trusted Partner for Testing and Biological Evaluation of Medical Devices & Biomaterials

Meeting stringent regulatory requirements is a critical milestone for medical device manufacturers today. As global and domestic standards evolve, ensuring the safety, quality, and biological compatibility of biomaterials is paramount. The Biomedical Technology Wing (BMT) of the Sree Chitra Tirunal Institute for Medical Sciences & Technology (SCTIMST) has established itself as a national pioneer, offering comprehensive, accredited testing services to both academia and the medical device industry.

Medical device manufacturers across the country extensively utilize the testing services of the Institute. This rigorous testing framework has successfully enabled companies to secure vital regulatory approvals from prestigious bodies, including the Central Drugs Standard Control Organization (CDSCO), the US Food and Drug Administration (USFDA), and European Union (EU) CE Mark certification.

To ensure global compliance, the Quality Management System (QMS) for SCTIMST's testing services strictly conforms to the international standard ISO/IEC 17025 ("General requirements for the competence of testing and calibration laboratories").

Physicochemical Characterisation

- Imaging: SEM, TEM, Stereo microscopy, Fluorescence microscopy, Confocal Microscopy, Micro CT, Atomic Force microscopy, Live Animal Imaging
- Spectroscopy: FTIR, X-ray Diffraction Spectroscopy, UV-Vis, Micro Raman Spectroscopy
- Chromatography: HPLC, GC, Gel Permeation Chromatography
- Particle Analysis: DLS, Zeta potential tracking
- Elemental & Chemical Analysis: Trace element analysis (ICP-OES), Residual EO Analysis
- Surface Testing: Profilometry (line/surface scanning), along with targeted tests for PPE and fabrics
- Thermal analysis: DSC, TGA, DTA
- Microhardness Testing - Microscopic indentation test method
- Mechanical Testing - Tensile, Compressive, shear, 3-point bending, DMA
- Impact Testing: IZOD & CHARPY protocols

Biocompatibility Testing

Approximately twenty biological and biocompatibility tests are fully accredited by Le Comité Français d'Accréditation (COFRAC), France.

- In vitro Cytotoxicity: Direct & indirect contact, Test on extract (ISO 10993-5) & MTT assay
- Toxicity: Acute Systemic Toxicity (ISO 10993-10)
- Irritation: Intracutaneous, Animal Skin, Penile, Vaginal testing (ISO 10993-23)

- Sensitization: Maximization & Closed Patch (ISO 10993-10)
- Blood & Pyrogen Compatibility: Hemolytic property evaluation (ASTM 756), Pyrogen testing
- Implantation Studies: Subcutaneous, Muscle, & Bone evaluations (ISO 10993-6)
- Genotoxicity: Full standard testing (ISO 10993-3)
- Hemocompatibility: Comprehensive in vitro assessments (ISO 10993-4)
- Histopathology: Gross and histopathological evaluation (ISO 10993-6), Gross and histopathological evaluation- soft and hard tissue, necropsy, grossing & tissue sampling, tissue processing, block making, microtomy, HE staining, special staining, qualitative microscopy, immunohistochemistry
- Microbiological Safety: Sterility Testing, Bioburden Analysis, Bacterial adhesion studies, Spore viability testing, Antimicrobial Studies, Genotoxicity, Air monitoring, Microbiological analysis of water

Accredited Calibration Services

Calibration services are accredited by the National Accreditation Board for Testing & Calibration Laboratories (NABL) across the following key industrial disciplines:

- Mechanical Calibration,
- Thermal Calibration
- Electro-Technical Calibration

Customized Study Mode Evaluations

For non-regular, highly specialized industry requirements, SCTIMST designs tailor-made evaluation programs. These studies are executed under the strict oversight and responsibility of a designated Study Director.

- Medical device functional safety and performance in large animal models
- Preclinical small animal evaluation to prove the efficacy of a medical device/biomaterial
- Acute and chronic toxicity studies
- In vivo genotoxicity studies
- Gross and histopathological evaluation
- Drug release studies
- Antimicrobial evaluations
- Studies on antimicrobial coatings
- Toxicokinetic studies
- Accelerated ageing studies
- Microscopy imaging and quantification
- Histomorphological analysis

- Blood bag evaluations
- In vitro cell adhesion studies
- Cytocompatibility evaluations
- In vitro osteogenesis evaluation of biomaterials
- Validation of ETO sterilisation systems
- Cellular uptake studies
- In vitro hepatotoxicity studies

Connect with Team CSC

All essential documentation including Test Request forms, procedural guidelines, sample submission protocols, service charges, and electronic payment modes can be accessed directly via the institute's dedicated web portal:

Web Link: www.sctimst.ac.in/tcs

Customer Service Cell Email: csc@sctimst.ac.in

Customer Service Cell Phone: 0471-2520307/2520309

For personalized assistance or technical inquiries regarding your specific medical device evaluation requirements at SCTIMST, you may directly reach out to Team CSC:

Ms. Asha Rani V. (Senior Technical Assistant) — Phone: 0471-2520307

Ms. Sandhya C.G. (Scientist G) — Phone: 0471-2520309

Mr. Balram S. (Scientist G (Sr. Gr.) & SIC) — Phone: 0471-2520308

Call for Papers/Submission Deadlines

We invite submissions for our upcoming issue. We welcome reviews, perspectives and commentaries advancing the field of medical sciences, health and technology.

Submission deadline: September 30, 2026.

Acceptance notification: November 30, 2026.

Publication date: December 30, 2026.

Submission guidelines

Authors must review and check off each item below before uploading their submission package to omsth.sctimst.ac.in. Incomplete submissions will be returned immediately by the journal desk.

No.	Submission Requirement	Guidelines & Specifications	Yes
1.	Cover letter	Attached as a separate file, explicitly stating the significance to health care delivery from ideation to commercialization-Reviews, Opinions, Perspectives, Commentaries	
2.	Suggested referees	Five (5) potential reviewers included in the cover letter with their full names, institutional affiliations, and institutional email addresses (Referees must be subject experts with no close personal or professional connection to any author).	
3.	Co-author consent	Verified that all listed authors have read and approved the final version of the manuscript	
4.	Originality confirmation	Verified that this work is original, has not been published previously, and is not currently under evaluation by any other journal	
6.	File format	Main text document is saved and uploaded strictly as a .docx file	
7.	Typography	Entire document is formatted in Times New Roman, 12 pt, double-spaced	
8.	Page numbers	Inserted accurately at the bottom right corner of every page	
9.	Word count compliance	Reviews: More than 5000 words	
		Perspectives/Commentaries: Less than 3000 words	
10.	Title and running title	Concise, informative, and free of abbreviations, acronyms, or formulas	
11.	Author metadata	Full names, complete physical institutional addresses (including country), and active email addresses provided for every author	
12.	ORCID ID	Provide ORCID ID of all authors, but compulsorily for the corresponding author	
13.	Abstract	Completely unstructured, within 250 words, no reference citations and no abbreviations	
14.	Keywords	5 relevant keywords	
16.	AI usage declaration	Formal statement detailing the use of AI tools included	
17.	Conflict of interests	Clear disclosure statement included within the submission workflow	
18.	Funding and Acknowledgement	Positioned in a separate section right before the references, with all funding agencies named in full text	
19.	Referencing	Formatted precisely in Vancouver style, numbered sequentially, and containing up to 50-75 citations for review papers	
20.	Image files	All figures uploaded as separate individual files in .jpeg, .png, or .tiff formats	
21.	Image specifications	Checked against the PLOS ONE Image Guidelines for resolution and sizing	
22.	In-text citations	All tables, figures, and schemes are cited in numerical order within the text and match their respective captions and reflected in the text within square boxes	
23.	Graphical abstract	Provided and uploaded separately if required by the thematic call	
24.	Plagiarism	Authors must certify that the manuscript was screened and verified as plagiarism-free before submission to ensure complete originality	

JUNE 30, 2026

OPINIONS IN **Medical Sciences, Technology and Health**

VOLUME 4, ISSUE 1

