International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

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ARTICLE TITLE	THE ROLE OF MACROPHAGES IN THE RETENTION AND TRANSFORMATION OF PIGMENT IN THE SKIN – THE IMMUNOLOGY OF TATTOOS
DOI	https://doi.org/10.31435/ijitss.3(47).2025.4072
RECEIVED	30 July 2025
ACCEPTED	16 September 2025
PUBLISHED	30 September 2025
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THE ROLE OF MACROPHAGES IN THE RETENTION AND TRANSFORMATION OF PIGMENT IN THE SKIN – THE IMMUNOLOGY OF TATTOOS

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ABSTRACT

Tattooing involves intradermal deposition of pigment that elicits a long-lasting immune response. Dermal macrophages play a key role in maintaining pigment by capturing pigment particles and retaining them inside their phagolysosomes. The aim of this paper is to analyze the mechanisms of phagocytosis of tattoo pigment by dermal macrophages, their impact on tattoo persistence, and to assess the significance of phenotypic differentiation (M1/M2) in the context of inflammation, laser therapy, and potential biomedical applications. We reviewed data from recent experimental studies, including 3D skin models, electron microscopy, flow cytometry, and TPE-FLIM imaging. We also considered the effect of pigment chemical composition on activation of immune cells. Dermal macrophages demonstrate high efficiency in phagocytosis and long-term storage of pigment. The observed "capture–release–recapture" mechanism ensures pigment stability despite natural cellular turnover. Pigment composition influences macrophage polarization (M1 or M2), which may determine chronic inflammation versus regeneration. Understanding macrophage–pigment dynamics provides new insights into tattoo durability and opens opportunities to improve the effectiveness of laser removal. Advances in imaging and the use of biosensor cells point to potential future applications of tattoos in diagnostic and regenerative medicine.

KEYWORDS

Dermal Macrophages, Pigment Phagocytosis, Tattoo Immunobiology, M1/M2 Phenotype, Pigment Persistence

CITATION

Amelia Kosowska, Michalina Kosowska, Marlena Radzka, Izabela Radzka, Justyna Jankowska, Jonatan Rataj, Kamil Harenza, Karolina Sara Ollik, Magdalena Barbara Kukulska, Michał Kowalczyk. (2025) The Role of Macrophages in the Retention and Transformation of Pigment in the Skin – the Immunology of Tattoos. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.4072

Introduction and Aim

Tattoos, as a form of cultural expression and communication, have roots dating back thousands of years. The oldest confirmed traces of tattooing were found on the mummy Ötzi (ca. 3370–3100 BCE) and across numerous cultures of Europe, Siberia, China, and the Andean region of South America (Deter-Wolf, A et. Al., 2016). In ancient Egypt, women's tattoos carried diverse meanings related to fertility, protection, and aesthetics (Fisher, J. A. 2002). In Austroasiatic and Polynesian societies, tattoos signified status, bravery, and tribal belonging—such as the Moko tradition among the Māori and the Peʻa in Samoa (Krutak, L. F. 2012). In Western culture, tattoos were often associated with penal markings—used in ancient Greece and Rome to mark enslaved people or criminals (Caplan, J. (Ed.). 2000). During the Middle Ages, under Christian influence, tattoos—especially as forms of body modification—were condemned and marginalized (Fisher, J. A. 2002). In the modern era, with expeditions to Polynesia and encounters with Indigenous cultures, tattoos entered European and American culture via sailors and explorers, popularized by the Tahitian word "tatau," from which the word "tattoo" derives (Vail, D. A., et al., 2009). In nineteenth-century Britain, tattoos became common among sailors and prisoners but—paradoxically—also gained popularity among elites and aristocracy as a fashion element (Alker, Z.,2022). At the same time, cultural studies framed tattoos as expressions of individual identity, personal memory, and resistance to social norms—interpreted as both subversion and authentic identity transformation (DeMello, M. 2000), Pitts, V. 2003). Today, tattoos serve aesthetic, expressive, and often symbolic or spiritual functions, widely practiced within popular culture and everyday life across many social groups (Atkinson, M. 2003). They also remain an area of research for anthropologists, sociologists, and psychologists exploring the meanings of body tattooing.

A tattoo is the artificial introduction of pigment into the dermis, triggering an immune response and leading to the long-term presence of pigment within the skin. Cutaneous macrophages are central to this process and influence both pigment longevity and the immune response to tattooing.

Skin macrophages (both ontogenically resident and monocyte-derived) phagocytose pigment particles but are biologically unable to degrade them completely—the pigment remains intracellular across many

cellular life cycles. When a macrophage dies, it releases pigment that is captured by other macrophages, resulting in a "capture–release–recapture" mechanism that underlies tattoo stability despite cellular turnover. (Barańska et al., 2018) showed in a mouse model that pigment resides almost exclusively in dermal macrophages—fibroblasts contain pigment far less frequently, and even substantial fibroblast pigment accumulation does not impact overall tattoo stability. In a study by (Lin et al., 2023), the authors analyzed the effect of tattoo ink on human monocytes and macrophages. They found that monocytes internalize pigment efficiently but exhibit reduced viability, whereas macrophages are most effective at pigment uptake, show no pigment-related toxicity, and do not secrete elevated inflammatory mediators. Sleth's histologic work (Sleth, J. C., 2017) corroborates pigment presence in macrophages and fibroblasts, emphasizing the greater contribution of macrophages to pigment fixation and their role in inflammation following skin puncture during tattooing.

This paper presents the role of skin macrophages in tattoo persistence and immunobiology, with particular emphasis on pigment phagocytosis mechanisms, pigment retention in the dermis, and the impact of macrophage phenotypic polarization (M1/M2) on the inflammatory response. We also analyze current data on interactions between pigments and immune cells and discuss clinical implications for more effective laser tattoo removal. Emerging directions include cell-engineering approaches and biosensing technologies in diagnostics and regenerative medicine using tattoo-like structures.

Structure of the Epidermis and Dermis

The skin, the body's largest organ, consists of three main layers: the epidermis, the dermis, and the hypodermis. For tattoo immunology, the epidermis and dermis—especially the papillary dermis where pigment is deposited—are most relevant.

The epidermis is composed mainly of keratinocytes (~90%), forming a mechanical and chemical barrier. Within the spinous and granular layers reside Langerhans cells—members of the dendritic cell family—serving as antigen-presenting cells (APCs) that initiate cell-mediated immune responses. Because the epidermis lacks blood vessels, nutrition occurs via diffusion from underlying layers. As resident APCs, Langerhans cells constitute the first line of cutaneous immune defense and can migrate to lymph nodes to present antigens to T cells (Kaplan, D. H. 2017). The dermis is divided into a superficial papillary layer, rich in capillaries and immune cells, and a deeper reticular layer composed of type I collagen and elastin fibers with a sparser immune cell network.

Within the dermis are dermal macrophages—the principal participants in the immune response to tattoo pigment. They possess a phenotype distinct from monocytes and are present under physiologic conditions. They do not migrate to lymph nodes but retain pigment locally, explaining the long-term persistence of tattoos. Other dermal cells include mast cells, fibroblasts, dermal dendritic cells (distinct from Langerhans cells), among others (Tamoutounour, S. et al., 2013, Rittig, S. M. et al., 2017). Table 1 presents a comparison of the characteristics of the epidermis and dermis.

Table 1. Differences between Langerhans cells and dermal macrophages

Feature	Langerhans cells (epidermis)	Dermal macrophages (dermis)
Location	Spinous layer of the epidermis	Papillary and reticular dermis
Origin	Bone marrow (hematopoietic)	Embryonic (yolk sac)
Migratory capacity	Yes (to lymph nodes)	No (persist locally)
Function	Antigen presentation	Pigment phagocytosis, local homeostasis
Surface markers	CD207 (Langerin), MHC-II	CD64, F4/80, MerTK

Significance in the Context of Tattooing

During tattooing, pigment is introduced into the papillary dermis—the niche of resident dermal macrophages. These cells first capture pigment particles (Tab. 2 and 3). Importantly, they do not leave the tattoo site, enabling local pigment retention rather than clearance via the lymphatic system.

Table 2. Pigment uptake capacity by different cell types (Lin et al. 2023)

Cell type	% uptake at 24 h	Cytokines induced	Properties after exposure
Macrophages	~80%	no increase	no cytotoxicity
Monocytes	~85%	slight increase	reduced viability
Lymphocytes	transient uptake	no increase	no toxicity

Table 3. Effects of metallic pigments on macrophage function (Devčić et al. 2022)

Pigment	TNFα↑	IL-6↑	MCP-1↓	CD11b↓
PV14	YES	not noticeable	YES	YES
PB28	YES (sustained)	YES	YES	YES
PW4	YES	short-lived	no change	no change

Macrophages—Key Participants in the Immune Response to Tattoo Pigment

Macrophages exhibit high plasticity and can polarize in response to environmental cues. Classically activated M1 macrophages (induced by LPS and IFN-γ) produce pro-inflammatory cytokines (IL-6, TNF-α, IL-12) and reactive species (ROS, NO), fostering a microbicidal state. Alternatively activated M2 macrophages (driven by IL-4/IL-13) secrete IL-10 and TGF-β and participate in tissue repair and resolution of inflammation. Intermediate or hybrid states form a continuum between M1 and M2 depending on local immunologic signals (Barańska, A et al. 2018, 17]. According to (Devčić et al. 2016), cobalt- and zinc-containing pigments raise IL-6 and TNF-α, reduce MCP-1 and CD11b expression, and promote remodeling toward an M1-dominant phenotype during chronic exposure. An increased M1 fraction supports persistent inflammation, whereas M2 predominance may favor pigment retention and scarring.

Figure 1. Differences in typical immunologic marker expression between M1 and M2 macrophages. M1 cells show higher expression of pro-inflammatory cytokines (TNF-α, IL-6) and the co-stimulatory molecule CD86. M2 cells exhibit higher anti-inflammatory markers (IL-10, TGF-β) and CD206 expression.

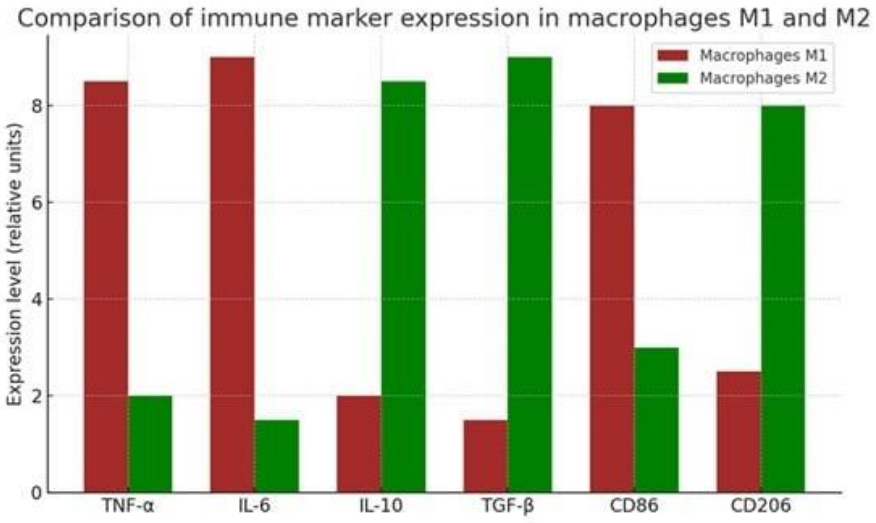

Fig. 1. *Expression of typical immune markers in M1 and M2 macrophages*

Figure 2. Contribution of specific cell types to phagocytosis of tattoo pigment. Dermal macrophages are the primary cells that engulf and store pigment particles. Pigment is sequestered into phagosomes and remains for extended periods. Newly recruited macrophages capture pigment from dying cells ("capture–release–recapture"), ensuring tattoo persistence. Dermal fibroblasts can phagocytose pigment but generally contain fewer particles compared with macrophages. Mast cells and other cells (including keratinocytes and epidermal dendritic cells) may contain pigment particularly during early healing and at remote skin locations (Strandt, H. et al., 2021, Kröger, M. et al. 2023).

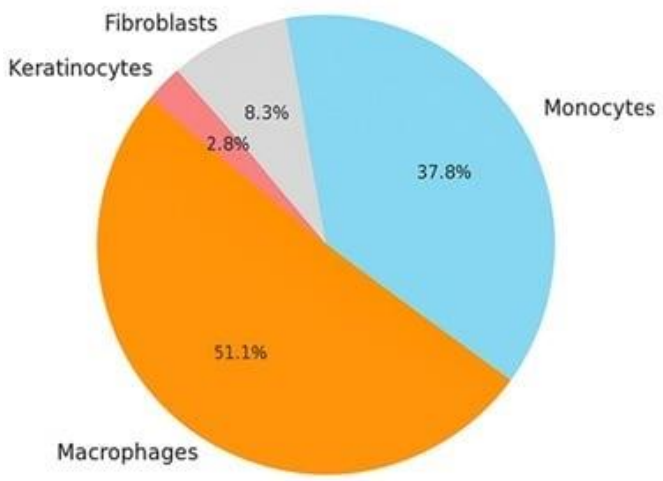

Fig. 2. *The role of different cell types in the phagocytosis of tattoo pigment*

Phagocytosis of Pigment and Its Role in Retention

(Barańska et al. 2018) demonstrated that resident dermal $CD64^+$ macrophages are uniquely capable of long-term capture of tattoo pigment. Pigment remains within cellular processes and lysosomes; cell death does not clear it because subsequent macrophages re-capture the particles—i.e., a release–recapture mechanism. (Lin et al., 2024) compared macrophages, monocytes, and other immune cells using 3D skin models and cytometry, finding macrophages most efficient at pigment internalization without increased inflammatory markers or loss of viability, whereas monocytes internalized pigment rapidly but exhibited significant cytotoxicity and reduced survival. These observations support the concept that dermal macrophages stabilize and retain pigment locally over the long term.

Clinical and Therapeutic Implications

Understanding the role of dermal macrophages is essential for optimizing laser-based tattoo removal. Following Q-switched (QS) laser exposure, tattoo pigment particles undergo photothermal and photoacoustic fragmentation into smaller particles. These are subsequently phagocytosed predominantly by dermal macrophages, fibroblasts, and mast cells, enabling lymphatic clearance and gradual elimination (Barua, S. 2015, Bäumler, et al., 2017]. In animal models, 1064-nm laser treatment increases local accumulation of $CD68^+$ macrophages within the tattoo area, peaking around day 3 post-procedure (Du, X. J.,et al., 2022). Experimental data suggest that stimulating macrophage activity with macrophage colony-stimulating factor (M-CSF) may accelerate pigment clearance after laser treatment (Malca, N., et al.,2017) an immunomodulatory strategy that could complement standard care.

Research Perspectives on Tattoo Immunobiology

Modern imaging techniques such as two-photon excited fluorescence lifetime imaging (TPE-FLIM) allow in vivo localization of tattoo pigments in the epidermis and dermis—even in tattoos several years old (Kröger, M., et al 2023). Scanning electron microscopy (SEM) and flow cytometry have also been used to analyze ink particles and their phagocytosis by macrophages and monocytes within human 3D skin models (Lin, C et al., 2024). These methods enable both visualization and quantitative assessment of pigment retention and movement. Engineered cellular systems can produce pigment as a biological reporter; for example, cells

with calcium-responsive control of tyrosinase expression can synthesize melanin, creating a visible melanotic "tattoo" to detect hypercalcemia (Tastanova, A., et al., 2018 In addition, bacterial biosensor microgels introduced into the skin as tattoos can monitor interstitial fluid and respond to biochemical cues via genetic logic circuits (Allen, M. E., et al., 2024, He, et al., 2021). These innovations align with broader trends in bioinks and 3D bioprinting for regenerative medicine, including diagnostic, therapeutic, and monitoring applications using bioinks and structures containing living cells (Debnath, S., et al., 2025, Burns, N., et al., 2025, Byrne, et al., 2024)

Summary

A tattoo is a long-lasting skin modification whose persistence relies on immunologic retention of pigment by dermal macrophages. Through a "capture–release–recapture" mechanism, these cells not only engulf pigment but also maintain it within the skin for the host's lifetime. Macrophages are more effective than monocytes or fibroblasts at pigment phagocytosis without exhibiting toxicity or excessive inflammation (Lin, C.et al., 2024 Barańska, A et. Al., 2018). Importantly, macrophage polarization into M1 and M2 phenotypes shapes the local immune microenvironment, with implications for tattoo stability and removal. Modern imaging techniques—such as TPE-FLIM and flow cytometry—have enabled detailed analysis of pigment localization in skin cells. Parallel advances in biosensors and bioinks suggest potential applications of pigment-producing cells in diagnostics and personalized medicine. Therapeutically, augmenting macrophage recruitment and function may enhance the outcomes of laser tattoo removal.

Authors' Contribution

Amelia Kosowska: Conceptualization, writing-rough preparation, investigation,
Michalina Kosowska:,: Conceptualization, supervision
Marlena Radzka: Formal analysis, supervision
Izabela Radzka: Visualization, data curation
Justyna Jankowska: Conceptualization, data curation
Jonatan Rataj: Methodology, project administration
Kamil Harenza: Conceptualization, methodology, supervision
Karolina Sara Ollik: Resources, writing-rough preparation
Magdalena Barbara Kukulska: project administration, data curation
Michał Kowalczyk: methodology, supervision

All authors have read and agreed to the published version of the manuscript.

Acknowledgments - No acknowledgments.
Ethical approval - Not applicable.
Informed consent - Not applicable.
Funding - This study has not received any external funding.
Conflict of interest - The authors declare that there is no conflict of interests.
Data and materials availability - All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES

1. Deter-Wolf, A., Robitaille, B., Krutak, L., & Galliot, S. (2016). The world's oldest tattoos. Journal of Archaeological Science: Reports, 5, 19–24.
2. Fisher, J. A. (2002). Tattooing the body, marking culture. Body & Society, 8(4), 91–107. https://doi.org/10.1177/1357034X02008004005
3. Krutak, L. F. (2012). Spiritual skin: magical tattoos and scarification: Wisdom, healing, shamanic power, protection. Ed. Reuss.
4. Caplan, J. (Ed.). (2000). Written on the body: The tattoo in European and American history. Princeton University Press.
5. Vail, D. A., Sanders, C. (2009). Customizing the Body: The Art and Culture of Tattooing. Temple University Press.
6. Alker, Z., Shoemaker, R. Convicts and the Cultural Significance of Tattooing in Nineteenth-Century Britain. Journal of British Studies 2022;61(4):835–862. https://doi.10.1017/jbr.2022.117

7. DeMello, M. (2000). Bodies of inscription: A cultural history of the modern tattoo community. Duke University Press.
8. Pitts, V. (2003). In the flesh: The cultural politics of body modification. Springer.
9. Atkinson, M. (2003). Tattooed: The sociogenesis of a body art. University of Toronto Press.
10. Barańska, A., Shawket, A., Jouve, M., Baratin, M., Malosse, C., Voluzan, O., ... & Malissen, B. (2018). Unveiling skin macrophage dynamics explains both tattoo persistence and strenuous removal. Journal of Experimental Medicine, 215(4), 1115–1133. https://doi.10.1084/jem.20171005
11. Lin, C., Marquardt, Y., Rütten, S. et al. Macrophage-like rapid uptake and toxicity of tattoo ink in human monocytes. Immunology. 2023;171(3):388–401. https://doi.10.1111/imm.13714
12. Sleth, J. C. Epidural anaesthesia and lumbar tattoo. Histology of tattoo: The missing link? Ann Fr Anesth Reanim. 2007;26(3):266–267. https://doi.10.1016/j.annfar.2006.11.007
13. Kaplan, D. H. Langerhans cells: not your average dendritic cell. Trends Immunol. 2017;38(11):798–808. https://doi.10.1016/j.it.2017.07.006
14. Tamoutounour, S. et al. Origins and functional specialization of macrophages and of conventional and monocyte-derived dendritic cells in mouse skin. Immunity. 2013;39(5):925–938. https://doi.10.1016/j.immuni.2013.10.004
15. Rittig, S. M. et al. Skin immunology: macrophages in the dermis originate from yolk sac progenitors and maintain themselves through local proliferation. Pflügers Archiv – European Journal of Physiology. 2017;469(3–4):527–536. https://doi.10.1007/s00424-017-1986-1
16. Devčić, J., Dussol, B., Collin-Faure, V. et al. Immediate and sustained effects of cobalt- and zinc-containing pigments on macrophages. Front Immunol. 2022;13:865239. doi:10.3389/fimmu.2022.865239
17. Lin, C., Marquardt, Y., Rütten, S. et al. Macrophage-like rapid uptake and toxicity of tattoo ink in human monocytes. Immunology. 2024;171(3):388–401. https://doi.10.1111/imm.13714
18. Strandt, H., Voluzan, O., Niedermair, T., Ritter, U., Thalhamer, J., Malissen, B., Stoecklinger, A., Henri. Macrophages and Fibroblasts Differentially Contribute to Tattoo Stability. Dermatology. 2021;237(2):296–302. https://doi.10.1159/000506540
19. Kröger, M., Schleusener, J., Lademann, J., Meinke, M. C., Jung, S., Darvin, M. E. Tattoo pigments are localized intracellularly in the epidermis and dermis of fresh and old tattoos: In vivo study using two-photon excited fluorescence lifetime imaging. Dermatology. 2023;239(3):478–493. https://doi.10.1159/000529577
20. Barua, S. Laser-tissue interaction in tattoo removal by Q-switched lasers. J Cutan Aesthet Surg. 2015;8(1):5–8. https://doi.10.4103/0974-2077.155063
21. Bäumler, W. Laser Treatment of Tattoos: Basic Principles. Curr Probl Dermatol. 2017;52:94–104. https://doi.10.1159/000450809
22. Du, X. J., Zhou, H. M., Wang, Z., Liu, J., Wang, J. F., Li, D., Wu, T. T., Chen, B., Zeng, W. H. Comparative study of 1064 nm nanosecond, 1064 nm picosecond, 755 nm, and 595 nm lasers for tattoo removal: An essential role by macrophage. Lasers Surg Med. 2022;54(5):737–746. https://doi.10.1002/lsm.23535
23. Malca, N., Boulart, L., Noël, W., de Runz, A., Chaouat, M., Mimoun, M., Boccara, D. The adjuvant use of macrophage colony-stimulating factor in tattoo removal using laser surgery. Ann Chir Plast Esthet. 2017;62(2):e15–e21. https://doi.10.1016/j.anplas.2016.09.005
24. Tastanova, A., Folcher, M., Müller, M., Camenisch, G., Ponti, A., Horn, T., ... & Fussenegger, M. (2018). Synthetic biology-based cellular biomedical tattoo for detection of hypercalcemia associated with cancer. Science Translational Medicine, 10(437). https://doi.10.1126/scitranslmed.aap856
25. Allen, M. E., Kamilova, E., Monck, C., Ceroni, F., Hu, Y., Yetisen, A. K., Elani, Y. Engineered bacteria as living biosensors in dermal tattoos. Adv Sci (Weinh). 2024;11(30):e2309509. https://doi.10.1002/advs.202309509
26. He, R., Liu, H., Fang, T., Niu, Y., Zhang, H., Han, F., Gao, B., Li, F., Xu, F. A colorimetric dermal tattoo biosensor fabricated by microneedle patch for multiplexed detection of health-related biomarkers. Adv Sci (Weinh). 2021;8(24):e2103030. https://doi.10.1002/advs.202103030
27. Debnath, S., Agrawal, A., Jain, N., Chatterjee, K., & Player, D. J. (2025). Collagen as a bio-ink for 3D printing: A critical review. Journal of Materials Chemistry B, 13, 1890–1919. https://doi.org/10.1039/D4TB01060D
28. Burns, N., Rajesh, A., Manjula-Basavanna, A., & Duraj-Thatte, A. (2025). 3D extrusion bioprinting of microbial inks for biomedical applications. Advanced Drug Delivery Reviews, 217, 115505. https://doi.org/10.1016/j.addr.2024.115505
29. Byrne, R., Carrico, A., Lettieri, M., Rajan, A. K., Forster, R. J., & Cumba, L. R. (2024). Bioinks and biofabrication techniques for biosensors development: A review. Materials Today Bio, 28, 101185. https://doi.org/10.1016/j.mtbio.2024.101185