

Trach Rosolovska S.V., Mykolenko A.Z., Orel Y.M., Holovata T.K., Furdela M.Ya.
I.Ya. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine

CURRENT APPLICATIONS OF PROTEOMICS IN FORENSIC MEDICINE AND PATHOLOGICAL ANATOMY

e-mail: trachros@tdmu.edu.ua

The purpose of the study was to analyse current scientific data on the potential applications of proteomic technologies in forensic medicine and pathological anatomy, and to determine their diagnostic potential, key advantages, limitations and prospects for integration into practical approaches to the analysis of biological material. A narrative review of scientific publications was conducted using PubMed, Web of Science and Scopus databases devoted to the use of proteomic methods, in particular mass spectrometric proteomics, LC-MS/MS, MALDI imaging mass spectrometry and spatial proteomics. The potential applications of proteomic analysis in forensic medicine for the identification of biological fluids, the examination of degraded biological materials, the characterisation of human remains and the assessment of post-mortem changes have been analysed. In pathological anatomy, proteomics is regarded as a complementary tool to traditional morphological and immunohistochemical methods, enabling the identification of specific protein profiles, potential biomarkers and molecular features of pathological processes. Spatial proteomic technologies, which combine molecular information with the morphological structure of tissues, as well as the analysis of formalin-fixed paraffin-embedded specimens, offer particular promise. It has been established that proteomics has significant potential for the development of comprehensive molecular research in forensic medicine and pathological anatomy; however, its widespread implementation requires the standardisation of methodologies, the refinement of bioinformatic analysis, the accumulation of an evidence base and improved access to technologies. The integration of proteomic approaches with genomic, transcriptomic and information-analytical platforms could form the basis for a new paradigm in the study of biological systems and pathological processes.

Key words: proteomics, forensic medicine, pathological anatomy, mass spectrometry, biomarkers, molecular diagnostics.

Трач Росоловська С.В., Миколенко А.З., Орел Ю.М., Головата Т.К., Фурдела М.Я. СУЧАСНІ МОЖЛИВОСТІ ПРОТЕОМІКИ У СУДОВІЙ МЕДИЦИНІ ТА ПАТОЛОГІЧНІЙ АНАТОМІЇ

Метою дослідження було проведення аналізу сучасних наукових даних щодо можливостей застосування протеомних технологій у судовій медицині та патологічній анатомії, визначення їх діагностичного потенціалу, основних переваг, обмежень та перспектив інтеграції у практичні підходи дослідження біологічного матеріалу. Проведено наративний огляд наукових публікацій з використанням баз даних PubMed, Web of Science та Scopus, присвячених використанню протеомних методів, зокрема мас-спектрометричної протеоміки, LC-MS/MS, MALDI imaging mass spectrometry та просторової протеоміки. Проаналізовано можливості застосування протеомного аналізу в судово-медичній практиці для ідентифікації біологічних рідин, дослідження деградованих біологічних матеріалів, характеристики людських останків та оцінки посмертних змін. У патологічній анатомії протеоміка розглядається як додатковий інструмент до традиційних морфологічних та імуногістохімічних методів, що дозволяє виявляти специфічні білкові профілі, потенційні біомаркери та молекулярні особливості патологічних процесів. Особливу перспективу становлять просторові протеомні технології, які забезпечують поєднання молекулярної інформації з морфологічною структурою тканин, а також аналіз формалін-фіксованих парафінових зразків. Встановлено, що протеоміка має значний потенціал для розвитку комплексного молекулярного дослідження у судовій медицині та патологічній анатомії, однак її широке впровадження потребує стандартизації методик, удосконалення біоінформатичного аналізу, накопичення доказової бази та підвищення доступності технологій. Інтеграція протеомних підходів із геномними, транскриптомними та інформаційно-аналітичними платформами може стати основою формування нової парадигми дослідження біологічних систем і патологічних процесів.

Ключові слова: протеоміка, судова медицина, патологічна анатомія, мас-спектрометрія, біомаркери, молекулярна діагностика.

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The study of biological material in forensic medicine and pathological anatomy typically involves a combination of morphological, histological, molecular-genetic, and laboratory-analytical methods. Macroscopic examination, histological analysis, immunohistochemistry, toxicological methods, and DNA analysis remain fundamental tools for determining the nature of pathological processes, identifying biological specimens, and establishing the cause of death. At the same time, the increasing complexity of modern forensic tasks creates a need to expand the methodological framework through the use of highly sensitive molecular technologies [19, 28, 35].

In forensic medical practice, the examination of significantly degraded biological material poses a particular challenge, as standard methods may provide limited information. Fragmentation of human remains, prolonged exposure of biological specimens to environmental factors, thermal damage, and decomposition processes can lead to structural changes in nucleic acids and reduced effectiveness of standard molecular-genetic approaches. DNA degradation, particularly fragmentation and chemical modifications, is one of the factors that complicates the generation of comprehensive genetic profiles in complex forensic cases [7, 45].

The identification of new molecular markers has become particularly important in the context of current challenges associated with large-scale identification efforts, the examination of fragmented remains, and the analysis of biological samples that have been significantly affected by adverse factors. In Ukraine, these issues have acquired particular significance due to armed aggression, which has resulted in an increase in cases of mass fatalities, the need to identify unidentified individuals, and the conduct of comprehensive forensic medical investigations under challenging conditions.

At the same time, in pathological anatomy, there has been a shift from a predominantly morphological assessment of pathological changes towards integrated molecular analysis of tissues. Despite the high diagnostic value of histological and immunohistochemical examinations, certain pathological processes, particularly in oncology, are characterised by significant morphological similarity and require additional molecular characteristics to refine the diagnosis, predict the course of the disease and identify potential therapeutic targets [2, 33].

The development of forensic medicine and pathological anatomy requires the introduction of methods capable of providing additional information regarding the molecular composition of biological specimens, their origin, condition and the changes that occur during pathological or post-mortem transformations [6]. One of the promising areas of such development is proteomics, a branch of molecular analysis that enables the study of the proteome of biological systems and the changes therein as a function of physiological, pathological and environmentally induced processes [13, 31].

Proteomics is a branch of molecular biology that studies the complete set of proteins present in a given biological system under specific operating conditions. The concept of the 'proteome' encompasses not only the identification of protein molecules, but also the assessment of their quantitative ratios, structural variants, post-translational modifications and functional interactions [24]. Unlike the genome, which characterises a relatively stable set of an organism's genetic information, the proteome is a dynamic system that varies depending on cell type, the tissue microenvironment, physiological state and pathological processes [3, 8].

A cell's functional activity is determined not only by the presence of the relevant genes, but also by the level of protein expression, their localisation, interactions and post-translational modifications. It is proteins that directly perform most of the structural, enzymatic and regulatory functions within the cell; therefore, proteome analysis provides information on the actual state of a biological system [4]. Modern proteomic technologies make it possible to investigate changes in protein composition during pathological conditions, to identify the molecular

mechanisms of diseases and to determine potential biomarkers [38]. The genome reflects the potential for biological processes to occur, whilst the proteome characterises the outcome of their functional realisation at the level of protein molecules. However, this relationship is not direct, as there are numerous regulatory levels between genetic information and proteome formation, including the control of transcription, translation, protein degradation and post-translational modifications [36]. This is precisely why proteomic analysis can provide additional information about the functional state of a cell, which cannot be fully obtained through genomic or transcriptomic studies alone.

Proteomics is used to investigate the mechanisms underlying disease development, to identify diagnostic and prognostic markers, and to determine potential therapeutic targets. This field has become particularly significant in the study of tumour processes, immune, metabolic and other pathological conditions, where changes in protein profiles may reflect specific impairments in cellular function. In the context of pathological anatomy, proteomics is regarded as an additional tool for the molecular characterisation of tissues, which can complement traditional morphological and immunohistochemical methods. For forensic medicine, the significance of proteomic studies lies in the ability to analyse the protein profiles of biological samples and obtain additional information about their condition and origin. Proteomics represents one of the avenues for the transition from a descriptive assessment of biological structures to a comprehensive molecular analysis of functional changes.

The purpose of the study was to analyse current scientific data on the potential applications of proteomic technologies in forensic medicine and pathological anatomy, summarise their diagnostic potential, methodological advantages and limitations, and identify the prospects for integrating these methods into modern molecular approaches to the study of biological specimens and pathological processes.

Materials and methods. The study was conducted as a narrative review of current scientific publications devoted to the potential applications of proteomics technologies in forensic medicine and pathological anatomy. A literature search was carried out in the international scientometric databases PubMed/MEDLINE, Scopus and Web of Science, covering original research articles, review articles and methodological papers published in peer-reviewed scientific journals in English from 01.01.2020 till 01.09.2025. The last search query was performed on September 11, 2025.

For explanation. Searching within the PubMed database the following verbatim search query was used: 'proteomics', 'mass spectrometry', 'LC-MS/MS', 'MALDI imaging', 'spatial proteomics', 'forensic medicine', 'forensic

pathology', 'pathological anatomy' and 'molecular pathology'. The logical operators 'AND' and 'OR' were used to formulate the search queries, which enabled the identification of publications focusing on the use of proteomic methods for the analysis of biological samples, tissue characterisation, the identification of protein biomarkers and molecular diagnostics.

Similar search strategies were subsequently used in other databases - Web of Science and SCOPUS. This extensive collection of keywords ensured a broad and exhaustive search that captured the recent experimental trials, morphological and clinical discoveries and advances and the newest fundamental data regarding the mass spectrometric proteomics application, protein identification methods, the analysis of proteomic profiles of biological materials, and the use of proteomic approaches in pathological diagnosis.

The inclusion criteria for the review were strictly defined to ensure high-quality and relevant studies. Only original research articles, systematic reviews, and meta-analyses published in peer-reviewed journals were considered for inclusion. Emphasis was placed on studies published in English, which were prioritized for their broader accessibility and relevance to the international scientific

community. Studies published in Ukrainian were also analyzed but not included in the review due to their insignificant scientific value and irrelevant scientific contribution when compared with that in foreign publications.

Publications that did not correspond to the research topic, did not contain a sufficient description of methodological approaches, as well as conference abstracts and materials that had not undergone a peer-review process, were excluded.

The selected sources were analysed through a qualitative synthesis of the data obtained, identifying the current state of proteomic technologies, their diagnostic potential, key advantages, limitations, and prospects for integration into the practice of forensic medicine and pathological anatomy.

As this is a review article based on the analysis of publicly available literature, ethical approvals were not required for this study. The study protocol was performed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Hence, a total of 504 articles were selected. After removing duplicates and those not meeting the inclusion criteria, a portion was selected for full-text review. Therefore, 45 manuscripts were determined to meet the inclusion criteria (Table 1).

Table 1

Simplified PRISMA Flow

Stage	Description	Number of Records/Studies
1. Identified	Total number of records identified through database searching and other sources	504
2. Duplicates Removed	Number of records removed before screening (e.g., duplicates)	126
3. Screened (Title/Abstract)	Number of records screened after duplicates were removed	378
4. Assessed for Eligibility (Full-text)	Number of full-text articles assessed for eligibility against the inclusion/exclusion criteria	116
5. Included in Review	Total number of primary studies finally included in the systematic review	45

Results of the study and their discussion.

Forensic medical practice requires obtaining the most comprehensive information possible from biological samples, particularly in cases where traditional investigative methods are limited due to insufficient sample quantity, sample degradation or the complexity of the expert assessment. Proteomics is regarded as a promising field of molecular analysis that complements classical forensic medical approaches by investigating the specific protein profiles of biological materials [26]. Unlike DNA analysis, which is predominantly used for individual identification, proteomic methods provide additional information regarding the biological origin of the sample, its tissue origin and the functional state of the material under investigation [37]. Parker et al. (2021) note that proteins are an important component of biological evidence and can be used to identify biological fluids and tissues due to the specific proteomic characteristics of the cells from which they originate [28].

One of the most advanced areas of forensic proteomics is the identification of biological fluids, in particular blood, saliva and semen. Traditional methods for determining the origin of biological traces, including immunological reactions and enzymatic tests, are of great practical value; however, their informative value may be reduced in cases of material degradation or the presence of complex mixed samples [30]. The use of mass spectrometric proteomic platforms allows for the analysis of the totality of proteins and peptides characteristic of a specific type of biological substrate, enabling a more comprehensive characterisation of the trace.

A separate promising area is the application of proteomics to the study of bone tissue and the analysis of human remains in forensic medicine. Bone is a biological substrate in which protein components can be preserved for a long time, making them promising targets for proteomic analysis [16]. Research into the bone tissue proteome is based on the identification of specific protein profiles and potential biomarkers that

can be used to characterise remains, in particular to estimate the post-mortem interval and age at the time of death. Mickleburgh et al. (2021) demonstrated that decomposition processes, taphonomic factors and individual biological differences influence the preservation of proteins in bone; however, certain protein components may hold promise for the development of forensic proteomics methods [23].

The use of proteomics to estimate the post-mortem interval (PMI) is one of the most promising areas of modern forensic molecular diagnostics. Following death, predictable biochemical changes occur in tissues, including protein degradation, changes in enzyme activity and disruption of cellular homeostasis. These processes can give rise to temporal patterns in changes to the proteomic profile, which could potentially be used as molecular markers to estimate the time elapsed since death. Zissler et al. (2021) note that post-mortem protein degradation depends on a complex set of factors, including temperature, environmental conditions, microbial activity and tissue characteristics, all of which must be taken into account when developing proteomic models for determining PMI [44].

Proteomics in forensic medicine represents a promising area of molecular research that can complement traditional forensic methods in cases involving the identification of biological fluids, the analysis of degraded remains and the assessment of post-mortem changes. At present, most proteomic approaches are at the stage of active development and validation; however, the results obtained indicate significant potential for their integration into a comprehensive system of forensic medical examination of biological samples.

In modern pathological anatomy, there is a gradual shift from a predominantly morphological assessment of pathological changes towards comprehensive molecular analysis of tissues [22]. Histological analysis remains the primary method of morphological diagnosis; however, in a number of cases—particularly when examining tumours with similar morphological characteristics—it needs to be supplemented by methods capable of assessing the molecular features of the pathological process [39]. Proteomics, owing to its ability to simultaneously analyse a large number of protein components, is regarded as one of the promising areas of molecular pathology, enabling the characterisation of changes in tissue protein composition, the identification of pathologically associated protein profiles, and the search for potential biomarkers.

The protein composition of tissue is the result of complex interactions between gene expression, the regulation of protein synthesis, post-translational modifications and the cellular microenvironment. Therefore, changes in the proteome may reflect functional disturbances that arise during the development of pathology, even in cases where morphological changes are not sufficiently specific.

Mass-spectrometric proteomic approaches enable the investigation of a wide range of proteins in tissue samples, the identification of differences between normal and pathological tissues, and the development of molecular signatures that may have diagnostic or prognostic significance [40].

Proteomics has become particularly significant in oncopathology, where one of the key tasks is the differential diagnosis of tumours, the determination of their molecular characteristics, and the search for markers associated with the prognosis of the disease. Despite significant advances in immunohistochemical methods, certain tumour processes may exhibit similar morphological features and require additional molecular verification. The analysis of protein profiles using modern proteomic technologies enables the identification of differences between tumour subtypes, the investigation of mechanisms of tumour progression, and the identification of potential therapeutic targets [21, 41].

In clinical pathology, proteomic studies are actively used to investigate the molecular characteristics of various types of neoplasms, including the identification of protein signatures associated with cell proliferation, invasiveness, metastatic potential and response to treatment [42]. At the same time, most proteomic markers remain at the research evaluation stage and require further clinical validation before they can be widely introduced into routine pathological practice.

One of the most promising areas of development in proteomics within pathological anatomy is MALDI imaging mass spectrometry (MALDI-IMS) and other methods of spatial proteomics [1, 15]. Unlike traditional proteomic analysis, which involves the extraction of proteins from tissue, spatial proteomics methods allow the distribution of molecules to be investigated directly within a tissue section whilst preserving the morphological context. Combining a molecular map of the tissue with its histological structure provides the opportunity for a deeper understanding of the spatial organisation of pathological processes, including tumour heterogeneity, the interaction of tumour cells with the microenvironment, and the localisation of specific molecular changes.

MALDI imaging mass spectrometry is regarded as a promising tool for integrating molecular information with traditional histopathology. Recent studies demonstrate the potential of this approach for tissue classification, the investigation of tumour processes, and the identification of molecular markers that may complement standard diagnostic criteria. At the same time, the widespread application of the method in clinical practice is limited by the need to standardise sample preparation protocols, ensure the reproducibility of results, and develop validated algorithms for interpreting the molecular data obtained [29].

An important area of focus for pathological anatomy is the application of proteomics to formalin-fixed, paraffin-embedded (FFPE) tissue samples, which constitute the bulk of the archived material in pathological anatomy laboratories. For a long time, the use of FFPE samples in proteomic studies was limited due to the chemical modification of proteins during fixation; however, the development of modern extraction methods and mass spectrometric analysis has significantly expanded the scope of their application. Analysis of FFPE material enables retrospective studies, the investigation of rare pathological processes, and the search for biomarkers based on large archival tissue collections [5, 27].

Proteomics in pathological anatomy provides an additional level of molecular information that complements traditional morphological and immunohistochemical methods. Its application enables a more in-depth characterisation of pathological processes, improves differential diagnosis and lays the foundation for the development of molecularly oriented pathology. The further development of proteomic technologies paves the way for the creation of a common molecular platform capable of uniting the approaches of forensic medicine and pathological anatomy [12, 18]. Despite the differences in the practical objectives of these disciplines, the subject of their research is biological structures, changes in which are reflected at the level of the molecular composition of tissues and cells.

In forensic medicine, these tasks include determining the origin of biological samples, analysing post-mortem changes and identifying complex forensic evidence, whilst in pathological anatomy the main focus is on characterising pathological processes and identifying molecular markers of disease. Proteomics enables these processes to be investigated at a common level, through the analysis of changes in protein composition and the functional state of biological systems.

One promising area is the integration of proteomics with other molecular analysis platforms, in particular genomics and transcriptomics. A comprehensive multi-omics approach allows the integration of information on genetic alterations, gene expression levels and the end products of gene expression, namely proteins [10, 32]. Such integration can provide a more complete understanding of the mechanisms underlying pathological processes, as well as enhance the informative value of analyses of complex biological objects in forensic medical investigations. At the same time, it must be borne in mind that the relationship between different levels of molecular organisation is not direct; therefore, the interpretation of the data obtained requires a comprehensive analysis.

Advances in bioinformatic analysis methods have had a significant impact on the development of modern proteomics. Mass spectrometry studies

generate large volumes of complex data, which require specialised algorithms for protein identification, quantitative assessment of changes in protein levels, analysis of molecular interactions, and identification of potentially significant biomarkers. The use of bioinformatics platforms enables the standardisation of proteomic data processing and improves the reproducibility of results, which is a key prerequisite for the transition from experimental research to practical application [9, 20].

A separate promising area is the application of artificial intelligence and machine learning methods to the analysis of proteomic data. Artificial intelligence algorithms can be used to recognise complex patterns in large datasets of molecular information, classify biological samples and build predictive models. In pathological anatomy, such approaches are being investigated to integrate molecular data with the morphological characteristics of tissues, whilst in forensic medicine they can facilitate the analysis of complex proteomic profiles and improve the accuracy of result interpretation [25, 34].

The integration of proteomic technologies with genomic, transcriptomic and information-analytical approaches is shaping a new concept of comprehensive molecular investigation in forensic medicine and pathological anatomy [14, 17]. The promise of this field lies not only in expanding the amount of available biological information, but also in the possibility of obtaining more precise characterisations of pathological and post-mortem processes. At the same time, the widespread implementation of such technologies requires further standardisation of methods, the creation of large reference databases, and confirmation of their practical value in clinical and forensic medical practice.

Despite the significant potential of proteomic technologies in forensic medicine and pathological anatomy, their widespread practical implementation remains limited by a number of methodological, technical and organisational factors. One of the main constraints is the high cost of modern proteomic equipment, in particular mass spectrometry platforms, as well as the need for specialised infrastructure for sample preparation, analysis and data processing [43]. This limits the accessibility of such technologies for many laboratories and necessitates the concentration of resources in specialised centres.

Another significant challenge is the need for highly qualified specialists with expertise in molecular biology, analytical chemistry, mass spectrometry and bioinformatics. The interpretation of proteomic data is a complex process, as the results of the analysis depend on a large number of technical parameters, including the sample preparation method, the conditions under which the mass spectrometry analysis is carried out, and the data processing algorithms.

A significant limitation remains the lack of full standardisation of proteomic methodologies. Differences in protein extraction protocols, tissue sample preparation, the choice of analytical platforms and approaches to statistical analysis can affect the reproducibility of results and complicate the comparison of data between different research groups. This is particularly relevant to forensic medicine, where results have not only scientific but also expert significance and must meet the requirements of admissibility as evidence [9].

Proteomics holds significant potential for the development of forensic medicine and pathological anatomy; its integration into clinical practice requires the resolution of a number of technical, methodological and regulatory issues. Further development in this field will depend on the

standardisation of analytical approaches, improved access to technologies, and the accumulation of evidence regarding their diagnostic and expert value.

Limitations. The following limitations were applied when working with the selected literature sources: Russian-language sources and works published in journals of the Russian Federation and Belarus were excluded.

As English is not the native language of the authors, the artificial intelligence tool 'DeepL Pro' was utilized to improve the stylistic quality and readability of the text. All AI-assisted content was thoroughly reviewed, verified, and edited by the authors, who retain full responsibility for the integrity, scientific accuracy, and final version of the manuscript.

Conclusion

Proteomic technologies represent a promising area of development for forensic medicine and pathological anatomy, as they provide additional information on the molecular composition and functional state of biological samples. Their application broadens the possibilities for identifying biological materials, investigating post-mortem changes, and characterising pathological processes at the molecular level.

In pathological anatomy, proteomics can complement traditional histological and immunohistochemical methods, facilitating the search for biomarkers and refining the diagnostic characteristics of diseases. In forensic medicine, it has the potential to analyse complex forensic specimens, in particular degraded biological materials.

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ORCID: Trach Rosolovska S.V. <https://orcid.org/0000-0001-7322-2200>, Mykolenko A.Z. <https://orcid.org/0000-0002-1845-4882>, Orel Y.M. <https://orcid.org/0000-0002-5871-5397>, Holovata T.K. <https://orcid.org/0000-0001-9989-6510>, Furdela M.Y. <https://orcid.org/0000-0002-6816-8614>.

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