Journal of Proteomics 316 (2025) 105442

Contents lists available at ScienceDirect

Journal of Proteomics

journal homepage: www.elsevier.com/locate/jprot

Comprehensive biobanking strategy with clinical impact at the European Cancer Moonshot Lund Center☆

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☆ This article is part of a Special issue entitled: '20 Years of the Mexican Proteomics Society' published in Journal of Proteomics.

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https://doi.org/10.1016/j.jprot.2025.105442
Received 17 January 2025; Received in revised form 26 March 2025; Accepted 12 April 2025
Available online 15 April 2025

A R T I C L E I N F O

Keywords:
Biobanking
Proteomics
Precision oncology
Multi-omics
Artificial intelligence
Machine learning

A B S T R A C T

This white paper presents a comprehensive biobanking framework developed at the European Cancer Moonshot Lund Center that merges rigorous sample handling, advanced automation, and multi-omic analyses to accelerate precision oncology.

Tumor and blood-based workflows, supported by automated fractionation systems and standardized protocols, ensure the collection of high-quality biospecimens suitable for proteomic, genomic, and metabolic studies. A robust informatics infrastructure, integrating LIMS, barcoding, and REDCap, supports end-to-end traceability and realtime data synchronization, thereby enriching each sample with critical clinical metadata. Proteogenomic integration lies at the core of this initiative, uncovering tumor- and blood-based molecular profiles that inform cancer heterogeneity, metastasis, and therapeutic resistance. Machine learning and AI-driven models further enhance these datasets by stratifying patient populations, predicting therapeutic responses, and expediting the discovery of actionable targets and companion biomarkers. This synergy between technology, automation, and high-dimensional data analytics enables individualized treatment strategies in melanoma, lung, and other cancer types. Aligned with international programs such as the Cancer Moonshot and the ICPC, the Lund Center's approach fosters open collaboration and data sharing on a global scale. This scalable, patient-centric biobanking paradigm provides an adaptable model for institutions aiming to unify clinical, molecular, and computational resources for transformative cancer research.

1. Executive summary

Biobanking transforms from a static repository into a dynamic, integrative system central to advancing precision medicine. The European Cancer Moonshot Lund Center is implementing a comprehensive framework that ensures rigorous sample integrity and traceability contributing to this transformation. This framework incorporates cutting-edge technologies, including proteomics and digital pathology, to enhance cancer research and treatment, particularly in Melanoma and Lung Cancer.

This White Paper presents a two-step procedural framework to ensure high-quality performance and robust traceability using electronic surveillance in clinical cancer studies. The process spans from surgical tumor isolation and blood sampling to storage and analysis, incorporating barcoding and stepwise scanning within an electronic software environment to uphold traceability and sample integrity through the following measures:

Sample Origin: The origin of each sample is rigidly documented, capturing comprehensive details about the patient, tumor type, and collection conditions and the clinical data of patients. This ensures traceability and contextual accuracy, aligning closely with the hospital and the Principal Investigator (PI), ensuring patient integrity.

Sample Processing: By standardized procedures for sampling, sample preparation, and molecular pathology analysis implemented using efficient and reproducible SOPs and protocols with electronic surveillance, laboratories achieve consistency and accuracy in molecular testing, to ensure sample integrity. Automation and Robotics in these process steps is crucial to ensure consistency and reproducibility with quality.

This white paper is intended for oncology researchers, healthcare providers, and biobank managers dedicated to advancing cancer research through robust biobanking practices. Collaboration with clinical centers across the globe following unified standards and principles creates a reliable framework for consistent, high-quality outcomes, an essential foundation for maximizing patient benefits.

2. Expedited development process

This white paper presents an integrated framework for biobanking strategies at the European Cancer Moonshot Lund Center, designed to advance patient care by bridging clinical data with proteomics and multi-omics data integration. By emphasizing sample quality, traceability, and cutting-edge molecular and digital pathology, this paper establishes a blueprint for modern biobanking that supports precision medicine.

2.1. Key Highlights

- **Sample Integrity and Traceability**: Robust electronic surveillance systems, including Laboratory Information Management Systems (LIMS) and 2D barcoding, ensure stringent tracking and high-quality preservation of biological samples from collection to analysis. These tools mitigate risks of degradation and data fragmentation, enabling reproducibility in downstream analyses.
- **Advanced Automation and Scalability**: Automated workflows for tumor tissues and blood fractionation enhance processing efficiency while preserving sample integrity. High-throughput systems allow scalable operations essential for multi-center collaborations, addressing the growing demand for standardized biobank resources.
- **ProteoGenomics-Driven Precision Medicine**: Integrating spatial proteomics, transcriptomics, and tumor microenvironment analysis enables actionable insights into tumor biology. This approach bridges the gap between genomic data and clinical applications, providing a functional molecular understanding for therapy choice optimization and monitoring.
- **Global Collaboration**: The Lund Biobank aligns with international cancer initiatives, including the Cancer Moonshot Program and the International Cancer Proteogenome Consortium (ICPC), fostering unified research standards and expanding the reach of biomarker discovery efforts.

2.2. Translational Impact

This framework directly addresses existing gaps in cancer research by linking advanced biobanking workflows to clinical outcomes. By integrating proteomics and digital pathology with detailed real-time clinical data, the proposed strategies empower oncologists to:

- Identify and validate actionable biomarkers for early diagnosis and treatment selection.
- Monitor therapeutic responses and detect resistance mechanisms in a non-invasive manner.
- Tailor therapies for individual patients, based on dynamic proteome and tumor microenvironment characteristics.
- Apply artificial intelligence and machine learning leveraging from multi-omic datasets, to enhance the predictive power of clinical biomarkers enabling better risk assessment and personalized intervention strategies.

2.3. Visions for Cancer Patient Benefit

The European Cancer Moonshot Lund Center demonstrates that

biobanking is no longer a static resource but a dynamic, integrative system driving innovation in oncology. By adopting these guidelines, researchers and clinicians worldwide can replicate this success, pushing the boundaries of precision medicine to include functional molecular insights that improve patient outcomes.

This paper calls for the importance of adopting standardized biobanking practices, international collaboration, and the integration of advanced analytical tools to ensure that cutting-edge cancer research translates into real-world clinical benefits. Together, we can transform precision oncology and deliver equitable, effective care to all cancer patients;

(i) by integrating blood-based proteomics with imaging, clinicians may be able to detect therapy resistance earlier, allowing timely treatment changes that improve patient outcomes and reduce unnecessary toxicities.
(ii) real-time analysis of tumor heterogeneity also promotes patients to receive personalized therapies, minimizing side effects and maximizing efficacy.

3. Introduction

Biobanks play a foundational role in modern cancer research, enabling the systematic collection, storage, and analysis of biological samples [1–3]. High-quality biospecimens are essential for understanding cancer biology, identifying novel biomarkers, and advancing precision medicine. At the European Cancer Moonshot Lund Center, biobanking is integrated with cutting-edge proteomics, molecular, and digital pathology to address unmet needs in oncology research [4,5].

The increasing demand for reproducible and scalable cancer studies requires robust biobanking workflows [6]. Challenges include maintaining sample integrity, ensuring traceability across clinical centers, and integrating diverse data streams, such as histopathology, imaging, and proteomic analysis [7]. Proteomics has emerged as a transformative tool for uncovering protein-level anomalies that drive tumor development, progression, and therapeutic resistance [8]. Recent advancements in proteomic technologies have addressed previous limitations in sensitivity, reproducibility, and scalability, further enabling their application in clinical settings [9,10]. At the 2024 HUPO World Congress, global leaders in proteomics emphasized that the technology

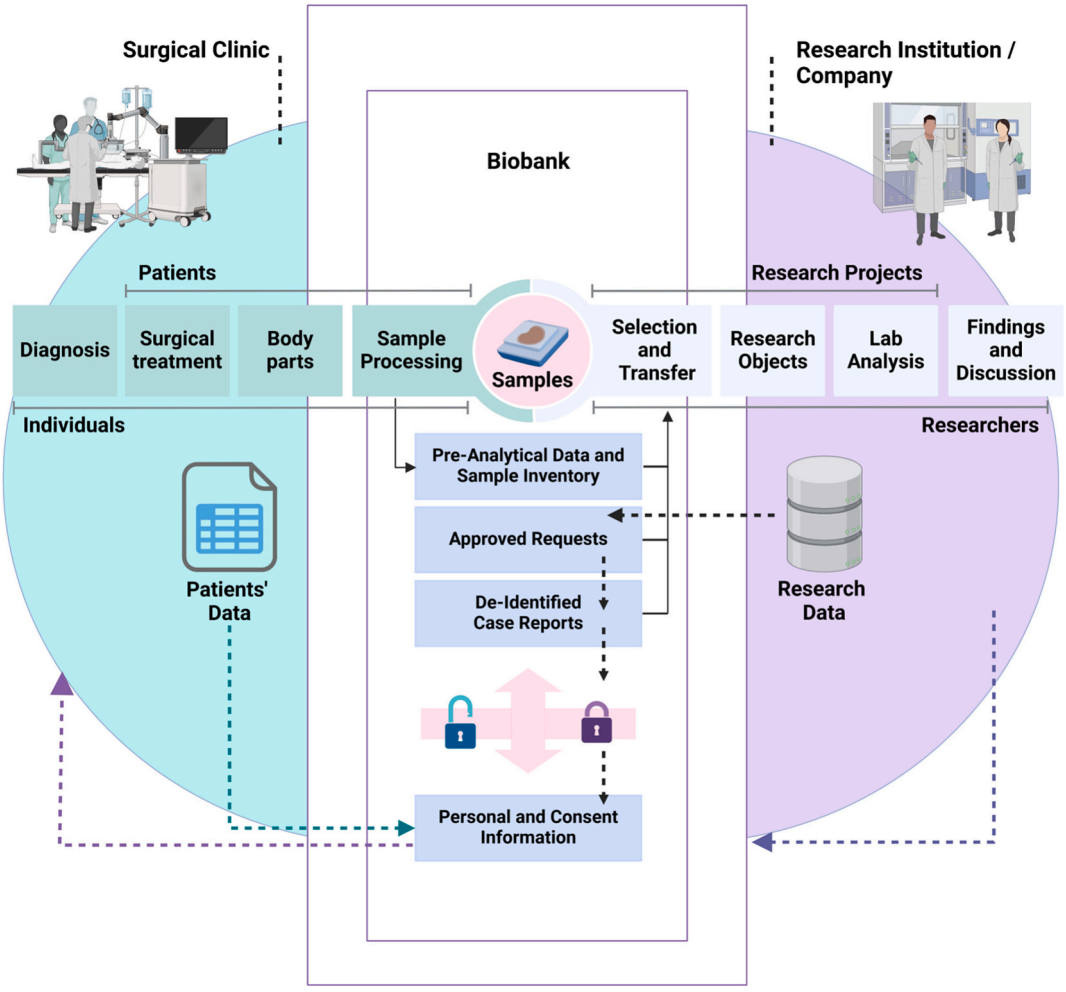

Fig. 1. Schematic overview of the integrated clinical–research workflow for melanoma patients.
This diagram depicts the end-to-end process of patient diagnosis, surgical treatment, and sample handling within a biobanking ecosystem. On the left, patients undergo diagnosis and surgical procedures at a clinical facility, generating body parts and related biospecimens. These samples are then funneled into biobank operations, which manage collection, processing, and secure storage under standardized protocols. Associated patient information is safeguarded through personal and consent information management and de-identification processes to protect privacy. The biobank stores pre-analytical data and maintains a sample inventory, granting approved requests for researchers while supplying de-identified case reports that ensure confidentiality. On the right, research institutions and companies receive selected specimens, integrating them with research objects for lab analysis and subsequent findings and discussion. Resulting research data—encompassing proteomic, histopathologic, and genomic insights—are fed back to clinical teams to inform treatment decisions. Overall, this workflow underscores the synergy between clinical care and cutting-edge research, driving continuous improvements in cancer diagnostics, prognostics, and therapeutics.

has now matured to a level where it can drive clinical decisions and advance precision medicine.

This consensus marks a turning point: proteomics is uniquely positioned to deliver functional molecular data that complement genomic and transcriptomic analyses [11,12]. By identifying actionable protein biomarkers and understanding post-translational modifications (PTMs), proteomics bridges the gap between molecular insights and clinical applications, providing direct evidence of disease state, therapeutic targets, and treatment responses [13].

At the European Cancer Moonshot Lund Center, our mission is to conduct cancer research that delivers tangible benefits to all patients, ensuring equity, innovation, and clinical impact. By coupling advanced biobanking practices with state-of-the-art proteomics workflows, we aim to support large-scale multi-omic studies through integrative proteogenomic analysis to identify clinically actionable biomarkers [11,14–16]. We strive to push precision medicine toward functional molecule data–driven frameworks, utilizing proteomic data to guide treatment choices, predict therapeutic resistance, and enable tailored interventions. Additionally, we are committed to driving translational oncology by linking molecular and histological-level findings to clinical outcomes to improve patient care [17]. Through international collaborations, we align with global initiatives such as the Cancer Moonshot program and the ICPC to standardize proteomics for clinical applications, fostering innovation and advancing precision oncology worldwide.

Fig. 1 illustrates the overarching workflow for melanoma patient treatment and sample management, from initial diagnosis and surgical intervention to biobanking, multi-omic research, and final clinical insights. This diagram highlights the collaborative nature of oncology research by underscoring how clinical and research teams work together to maintain sample integrity, manage patient data securely, and integrate diverse datasets to improve patient outcomes.

By leveraging mature proteomic technologies and our mission-driven approach, the European Cancer Moonshot Lund Center advances functional molecular insights into clinical practice through a robust biobanking framework. This framework reshapes precision medicine by enabling tailored therapies to the dynamic proteome and the true biological state of each patient, ensuring that groundbreaking cancer research translates into meaningful improvements for patients worldwide.

4. Challenges in biobanking for precision oncology

Biobanking is a cornerstone of cancer research and precision oncology, providing access to high-quality biological samples for molecular and proteomic analyses. However, several challenges persist, including limited scalability, fragmented data integration, and the insufficient translation of molecular findings into actionable clinical biomarkers. Addressing these challenges is critical to unlock the full potential of biobanking to deliver insights that drive precision medicine. We tackle these gaps through a robust, scalable biobanking framework that integrates real-time clinical data and supports high-throughput, reproducible multi-omic analyses. This innovative approach enables the development of actionable biomarker discovery, directly contributing to improved patient outcomes and advancing precision oncology. Maintaining up-to-date clinical registries is essential for defining standardized endpoints and ensuring consistent data collection across studies. Thus, this standardization enhances the reliability of research findings and supports the development of effective healthcare interventions.

To exemplify and to fully understand the evolving complexity of malignant tumors and biobanking implementations, within our lung cancer program, it is crucial to analyze primary tumors and multiple metastatic lesions in different organs from the same patient, particularly given that therapeutic resistance may be associated with increased heterogeneity [18]. Access to metastatic tumors in different organs, such as the brain, the liver, or the adrenal gland, will allow a better understanding of how the microenvironment controls tumor plasticity and promotes metastasis within patients. In this context, our multicenter rapid research autopsy program [19], intends to procure representative multisite tissue samples from small cell lung cancer patients promptly after death. To avoid protein degradation, all rapid research autopsies within the framework of this program are performed within four hours of the patient's death by an on-call multidisciplinary team. With a biobanking workflow ensuring sample integrity by electronic surveillance, multi-site representative samples allow the integration of multiple parallel analyses, including multi-omics and IHC-based approaches. Cell lines and xenograft models can also be established from the multisite fresh tumor specimens collected within the program's framework [19,20].

4.1. Sample quality and integrity

One of the foremost challenges lies in ensuring sample quality and integrity. Biological samples, particularly tumor tissues and blood fractions, are prone to rapid molecular degradation if not handled and preserved under rigorous conditions. Proteins, RNA, and metabolites degrade quickly, compromising the quality of downstream analyses, including proteomics and genomic studies. Rapid and standardized workflows, such as snap-freezing tumor tissues in liquid nitrogen immediately after surgical resection, are essential to maintain molecular fidelity. The critical role of high-quality biospecimens in proteogenomic characterization highlights the importance of preserving sample integrity to ensure accurate and reproducible data generation [21].

4.2. Traceability and data management

Another significant challenge involves sample traceability and data integration. Linking biospecimens to patient metadata, including demographics, clinical parameters, and outcomes, is essential for translational research. However, fragmented data management systems across clinical centers can hinder sample traceability and multi-omic data integration. Advances in LIMS and barcode-based tracking technologies, such as those employed at the European Cancer Moonshot Lund Center, address these issues by ensuring end-to-end traceability of each sample. This linkage enables researchers to correlate molecular findings with clinical outcomes, creating a comprehensive and actionable dataset.

Effective data sharing is crucial for advancing cancer research but faces several challenges. Privacy and ethical concerns arise from handling sensitive patient information, requiring strict confidentiality and compliance with regulations like the General Data Protection Regulation (GDPR). Technological challenges, such as data standardization and interoperability, hinder seamless collaboration among research institutions. Additionally, obtaining informed consent for data use, especially for unforeseen purposes, remains complex yet essential for maintaining patient trust. At the European Cancer Moonshot Lund Center, robust measures including GDPR-compliant platforms such as REDCap and secure LIMS are employed to ensure patient confidentiality and facilitate secure international data sharing. Addressing these challenges necessitates collaborative efforts among policymakers, researchers, and patient communities to establish ethical, secure, and efficient data-sharing frameworks.

4.3. Scalability and automation

Scalability is another major hurdle, particularly for multi-center biobanking initiatives where large volumes of biospecimens need to be processed and stored without compromising quality. Manual workflows are labor-intensive, error-prone, and unsustainable for high-throughput studies. The implementation of automated systems, robotics, and high-density storage solutions has addressed these

limitations in advanced biobanks. For instance, semi-automated workflows and liquid-handling systems enable efficient processing and aliquoting of blood fractions, minimizing freeze-thaw cycles and preserving sample integrity for proteomic studies. The integration of such technologies, as demonstrated by initiatives like the Clinical Proteomic Tumor Analysis Consortium (CPTAC), has proven essential for achieving scalable and reproducible biobanking operations [22].

4.4. Bridging the gap between research and clinical application

Bridging the gap between research and clinical application remains a key challenge in precision oncology. While biobanks facilitate fundamental discoveries, translating these findings into clinically actionable biomarkers is often hindered by a lack of validated targets and standardized protocols. Proteomics, as a mature technology, offers a unique opportunity to address this challenge by providing functional molecular insights that complement genomic data. Blood-derived proteomic biomarkers, such as circulating tumor proteins (CTPs), have shown promise for early cancer detection and therapy monitoring, as previously demonstrated [23,24]. However, integrating proteomic technologies into clinical workflows requires further standardization and validation to ensure their reliability in real-world settings.

Finally, global collaboration and harmonization of biobanking practices present both opportunities and challenges. International initiatives, such as the ICPC, emphasize the need for unified protocols, data-sharing agreements, and ethical standards across institutions. Harmonization enables cross-institutional studies, expands sample diversity, and accelerates biomarker discovery. However, disparities in infrastructure, resources, and regulatory frameworks across regions must be addressed to ensure equitable access to biobanking resources.

Addressing these challenges requires a multi-faceted approach that combines technological innovation, standardized workflows, ethical governance, and international collaboration. By implementing advanced automation, robust traceability systems, and proteomic-driven analyses, biobanks can bridge the gap between research and clinical practice. The REDCap database serves as a real-time engine that synchronizes our multi-center clinical study activities with barcoding systems, ensuring seamless alignment throughout our clinical research.

Initiatives like those at the European Cancer Moonshot Lund Center exemplify how modern biobanking can meet these challenges, supporting the development of precision oncology strategies that benefit patients worldwide.

5. Clinical biorepositories

This white paper highlights the role of biobanking in cancer research and the infrastructure required to uphold sample integrity throughout the collection, storage, and analysis process. Cancer biobanks facilitate the investigation of genetic, epigenetic, and proteomic characteristics that drive malignancies, providing insights essential for personalized medicine.

Advanced biobank systems ensure rigorous sample tracking through electronic surveillance, using both 2D and 1D barcoding and hospital and laboratory scanners. Integrated software solutions enable comprehensive tracking, allowing every sample's journey to be monitored and ensuring data integrity and reliability for high-impact research.

Electronic surveillance is a cornerstone of this approach, ensuring that each step of the workflow is standardized and meticulously monitored. Procedures for sampling, sample preparation, and analysis follow reproducible standard operating procedures (SOPs) and protocols. These protocols are designed to be adaptable, accommodating a diverse range of tumor types while maintaining consistency across samples.

The integration of automated systems and digital tracking tools ensures precise documentation and monitoring at every stage from collection to analysis. This not only enhances reliability and accuracy but also streamlines data sharing and collaboration across multiple clinical centers. The robust electronic infrastructure supports scalability and preserves the integrity and traceability of patient samples throughout the process.

To maintain complete traceability and contextual accuracy, the origin of each sample is carefully documented. Detailed records, including patient demographics, tumor type, collection date, and collection conditions, are consistently updated. This ensures alignment with hospital protocols and PI oversight, adhering to ethical and procedural standards.

By capturing comprehensive information at the point of collection, the sample's integrity and relevance to clinical and research objectives are safeguarded. This systematic approach not only supports seamless tracking and analysis but also provides critical context, enabling meaningful insights into tumor biology and patient outcomes.

Cancer incidence continues to rise worldwide, underscoring the challenges in early detection and effective treatment. Advances in molecular biology and genomics have unveiled new insights into the pathogenesis of various cancers—including melanoma—yet the discovery of reliable biomarkers for diagnosis and targeted therapy remains a critical unmet need. Protein expression profiling has emerged as a promising tool in this context [14–17], allowing researchers to map complex cellular processes and identify protein-level anomalies linked to cancer progression, as recently demonstrated in small cell lung cancer [19,20].

By leveraging cutting-edge immunohistochemical techniques and advanced proteomics in collaboration with globally recognized research centers, this approach holds potential to reveal actionable biomarkers that could transform melanoma treatment [14–16]. The current research, involving clinical centers across Hungary and Sweden, aims to bridge gaps in translational oncology by integrating detailed tissue analysis with real-world clinical insights.

Here, we outline our methodology, discuss the pivotal role of biobanks in sample preservation, and examine the implications of this research for identifying prognostic and therapeutic targets. We also address the ethical considerations inherent in genetic studies and data handling, ensuring full compliance with rigorous standards to protect patient privacy. This paper is intended for oncology professionals, researchers, and stakeholders striving to remain at the forefront of oncology research and clinical innovations.

In partnership with the NIH under the Cancer Moonshot program, the European Cancer Moonshot Lund Center (http://www.cancermoonshotlund.com/) is contributing to the largest global cancer initiative in history [https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative]. This international collaboration unites universities, hospitals, research institutes, and industry partners to share expertise and resources in the fight against cancer, accelerating breakthroughs in prevention, diagnosis, and treatment.

Recognizing that integrated, cross-institutional collaboration is vital for scientific progress, Lund University's senior management has positioned this partnership as a strategic priority. The Lund Center's state-of-the-art biobank facility supports large-scale research through a semi-automated workflow that employs a 384-tube high-density sample format. High-speed sample array robots manage small aliquot volumes (50–70 μL) and conduct cherry-picking processes essential for wide-ranging cancer and cardiovascular studies. By combining automated sample handling, significant ultra-low-temperature storage, and clinical integration, the European Cancer Moonshot Lund Center biobank drives innovation in precision medicine.

In summary, cancer research that emphasizes comprehensive tumor characterization is reshaping clinical care. Detailed exploration of tumor pathology, encompassing molecular, cellular, and spatial profiling, not only refines our understanding of cancer but also inspires the next generation of targeted therapies. This shift from conventional, one-size-fits-all approaches to highly individualized care promises improved patient outcomes and a future where treatments are tailored to the unique biology of each tumor. Tumor pathology remains at the forefront

of this transformation, paving the way for precision medicine and delivering new hope in the global fight against cancer.

Fig. 2 highlights the European Cancer Moonshot Lund Center's advanced biobanking infrastructure, featuring automated systems, high-density sample formats, and specialized freezing units essential for large-scale cancer research and personalized medicine initiatives.

6. Integrative tumor and blood-based sample handling for precision oncology

Comprehensive cancer studies integrate analyses of tumor tissues and blood-derived samples, offering multidimensional insights that guide diagnostics, therapeutic strategies, and biomarker discovery. At the European Cancer Moonshot Lund Center, this dual approach is central to understanding cancer biology and advancing precision medicine.

Characterizing tumor tissues remains crucial for identifying molecular drivers of cancer progression and therapy resistance. Landmark studies, such as those from The Cancer Genome Atlas (TCGA) and CPTAC, have demonstrated how multi-omic profiling of tumor tissues, including genomic and proteomic analyses, can uncover clinically actionable biomarkers and therapeutic targets [21,25,26]. These studies have been instrumental in linking molecular alterations to clinical outcomes, paving the way for personalized therapies.

Blood-derived samples complement tissue analysis by offering a minimally invasive means to study the systemic effects of cancer. CTPs, extracellular vesicles, and immune-related biomarkers in blood provide critical insights into cancer progression, metastasis, and therapeutic responses. The utility of blood-based multi-analyte tests in detecting cancers at early stages has been previously demonstrated, emphasizing the clinical potential of circulating biomarkers for diagnostics [23]. Similarly, the tumor burden and immune response can effectively be monitored over time, by blood-based molecular profiling including proteomics [27].

The integration of tumor and blood-based analyses allows researchers to link tissue-specific molecular changes with systemic biomarkers, offering a comprehensive view of cancer biology. Recent studies have emphasized how circulating biomarkers, when analyzed alongside tumor tissue data, improve our ability to predict therapeutic responses and monitor treatment efficacy in real time [24,28].

At the Lund Center, this combined approach enables the identification of biomarkers across multiple levels—genomic, proteomic, and systemic—enhancing our understanding of tumor heterogeneity and its broader implications for patient care [29,30].

Histopathological analysis is the starting point of the process of tumor characterization often begins with, where tissue samples are microscopically examined to assess cellular morphology, tumor grade, and architectural features. This analysis provides foundational information, including tumor type, degree of differentiation, and specific markers that may suggest aggressive potential or likelihood of metastasis. Through histopathology, pathologists establish the baseline classification but also provides information on initial treatment strategies.

Genome & Proteome-molecular profiling, beyond morphology, has become essential in modern tumor pathology. Advanced sequencing technologies, allow pathologists to identify mutations, gene rearrangements, and other molecular alterations driving tumor growth. Molecular profiling not only uncovers cancer-driving mutations but also identifies actionable functional expressions that may respond to targeted therapies. These actionable targets support personalized treatments that are more likely to be effective, minimizing unnecessary exposure to less

Fig. 2. Photographic overview of the European Cancer Moonshot Lund Center's biobanking facilities. Top left: Official logo of the European Cancer Moonshot Lund Center. **Top center:** Semi-automated equipment for processing 384-tube high-density sample plates, illustrating the precision and scalability of the facility's workflow. **Top right:** Interior view of a high-capacity storage system where samples are kept at ultra-low temperatures, ensuring sample integrity for large-scale studies.**Bottom left:** Research staff monitor data in real time using electronic surveillance systems and digital scanners, ensuring robust sample tracking and documentation. **Bottom right:** A corridor lined showing the loading unit and the storage designed for large-volume biobanking with a total capacity of 5 million samples, highlighting secure, temperature-controlled storage.

effective therapies.

Tumor microenvironment (TME) analysis has become a priority in pathology, focusing on the cells and structures surrounding the tumor. The TME, which includes immune cells, stromal cells, blood vessels, and the extracellular matrix, plays an influential role in tumor progression, immune evasion, and therapeutic response [17]. Analyzing the TME can reveal whether a tumor may respond to immune-based therapies, as the function or merely the presence or absence of specific immune cells can indicate the tumor's immune landscape. Understanding the TME helps clinicians select treatment strategies that address both the tumor and its supportive environment.

Spatial omics is an emerging technique that enables pathologists to map gene and protein expression across different regions of a tumor, preserving spatial context. Tumors are inherently heterogeneous, with distinct areas often displaying unique molecular and cellular behaviors. Spatial omics provides insight into this heterogeneity, revealing molecular "hotspots" of activity such as immune-infiltrated zones or hypoxic areas. This spatial information is invaluable for identifying zones that may require different therapeutic approaches or for predicting which areas might resist treatment.

Functional imaging techniques, including PET scans, MRI, and CT, complement tumor pathology by providing visual assessments of tumor size, structure, and location in vivo. Imaging techniques can include the use of molecular biomarkers that highlight specific functional characteristics, like glucose metabolism, allowing for a non-invasive look at tumor activity and real-time tracking of treatment effects. When combined with blood-based proteomic biomarkers, imaging can validate blood biomarkers by correlating circulating proteins with imaging-derived tumor characteristics. In addition, the use of non-invasive blood markers and imaging together can monitor treatment response to assess therapy efficacy in real time. This integrated approach enables a dynamic understanding of cancer progression, linking functional imaging with systemic molecular insights.

By integrating tumor characterization with blood-based profiling, the European Cancer Moonshot Lund Center delivers a truly multidimensional view of cancer biology, capturing tumor heterogeneity at the genomic, proteomic, and spatial levels. This dual approach enables the identification of circulating biomarkers that offer systemic, non-invasive insights into tumor biology, while tissue-specific analyses provide a deeper understanding of molecular and cellular mechanisms driving cancer progression and therapy resistance. Linking these findings enhances clinical relevance, as blood-based markers can monitor treatment response, detect minimal residual disease, and assess immune system dynamics in real-time.

Functional protein expression plays a particularly critical role in this framework by providing dynamic, functional insights into protein expression and PTMs complement static genetic and transcriptomic data. By leveraging proteomics-driven characterization of both tumor tissues and blood-derived samples, the Lund Center advances precision medicine strategies that reflect the true biological and systemic state of each patient. This comprehensive approach ensures that therapies are not only targeted but also tailored to the evolving molecular profile of the disease, offering transformative potential for improving patient outcomes.

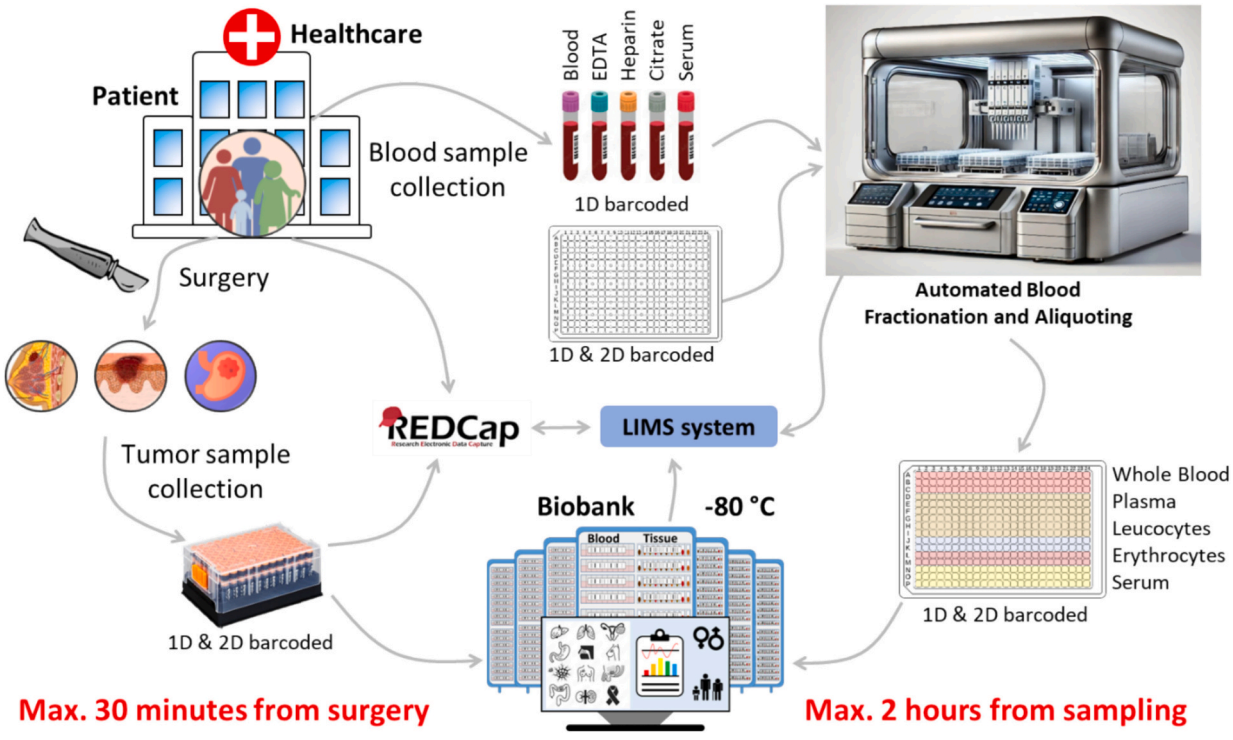

Fig. 3. Schematic overview of the integrated tissue and blood sampling workflow at the European Cancer Moonshot Lund Center. Patient-derived tumor tissue and blood samples are collected, processed, and tracked under stringent timelines to ensure high-quality biospecimens: Tumor samples are resected during surgery and transferred to the biobank within 30 min. Tumor portions are allocated for both clinical histopathology and downstream molecular analyses. Blood tubes (e.g., EDTA, Na-citrate, Na-heparin, serum) are drawn from the patient at the hospital. Each tube is time-stamped and labeled for sample integrity and traceability. Within two hours of blood drawing, blood tubes are fractionated using high-throughput robotic systems. This step produces multiple aliquots (e.g., plasma, serum, buffy coat, red blood cells) in a 384-well format for large-scale analyses. Aliquots are stored at ultra-low temperatures. The standardized 70 μL format enables minimal freeze–thaw cycles, improving sample stability for proteomics, genomics, and multi-omic research. Sample information (patient ID, clinical data, collection details) is recorded in REDCap. REDCap securely interfaces with the LIMS, enabling comprehensive sample metadata management. The LIMS manages sample inventories and barcode tracking, coordinating data flows between the clinical site, REDCap, and the automated lab instrumentation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

7. Tumor and blood-based workflows

A robust biobanking framework begins at the point of patient care, where optimized clinical workflows ensure the collection of high-quality biospecimens. At the European Cancer Moonshot Lund Center, tumor tissues and blood samples are collected, processed, and stored under stringent conditions to preserve their molecular integrity for downstream analyses (Fig. 3) [6,31,32]. This integrated process underpins the identification of clinically actionable biomarkers via proteomic and multi-omic studies, thereby advancing precision medicine.

The tumor and blood sampling workflows are central to precision oncology, ensuring that biospecimens are managed under rigorous protocols from the moment of surgical resection or blood draw (Fig. 3). By maintaining the highest quality of molecular and functional integrity, these specimens are ideally suited for proteomics, genomics, and other multi-omic approaches. The linkage of each sample to patient clinical data provides a robust foundation for generating actionable insights into cancer biology and response to therapy.

7.1. Tumor tissue workflow

The tumor tissue workflow begins in the operating room, where careful handling of resected tissue ensures suitability for downstream research. Immediately post-resection, the tissue is split into two portions: one is sent for clinical histopathology to evaluate the tumor's histological features, and the other is designated for biobanking. This dual allocation meets critical clinical needs while preserving high-value tissue for molecular and proteomic research.

To minimize molecular degradation, the biobanking portion undergoes snap-freezing in liquid nitrogen within 30 min of surgical removal. This rapid preservation is vital for maintaining protein, RNA, and DNA integrity, which can degrade rapidly under suboptimal conditions. Snap-frozen tissues are stored in cryotubes at ultra-low temperatures (−80 °C or in liquid nitrogen), ensuring their long-term stability (Fig. 3). These preserved samples support high-sensitivity analyses, ranging from proteomic profiling to RNA sequencing and genomics, and enable the discovery of potential therapeutic targets and biomarkers.

In parallel, a separate tumor portion is formalin-fixed and paraffin-embedded (FFPE) for long-term archival storage. FFPE processing preserves tissue architecture and morphology, facilitating detailed histopathological assessment of cellular features, tumor grade, and marker expression. FFPE samples also support immunohistochemical studies to identify clinically relevant proteins, making them indispensable for retrospective investigations that rely on stable, well-preserved tissue (Fig. 4).

Advanced laboratory workflows and automated tracking systems support both freezing and FFPE processes. Each sample is labeled with a 2D barcode and integrated into a LIMS, ensuring comprehensive traceability from collection to analysis. By associating tissue samples with patient metadata (e.g., demographics, tumor characteristics, and treatment history), researchers gain a 360-degree view of tumor biology, further enhancing translational potential.

7.2. Blood sampling and fractionation

Blood-derived biospecimens represent a complementary resource to solid tumor tissue, offering a systemic perspective on cancer progression, therapy response, and immune modulation. At the European Cancer Moonshot Lund Center, blood collection follows a standardized,

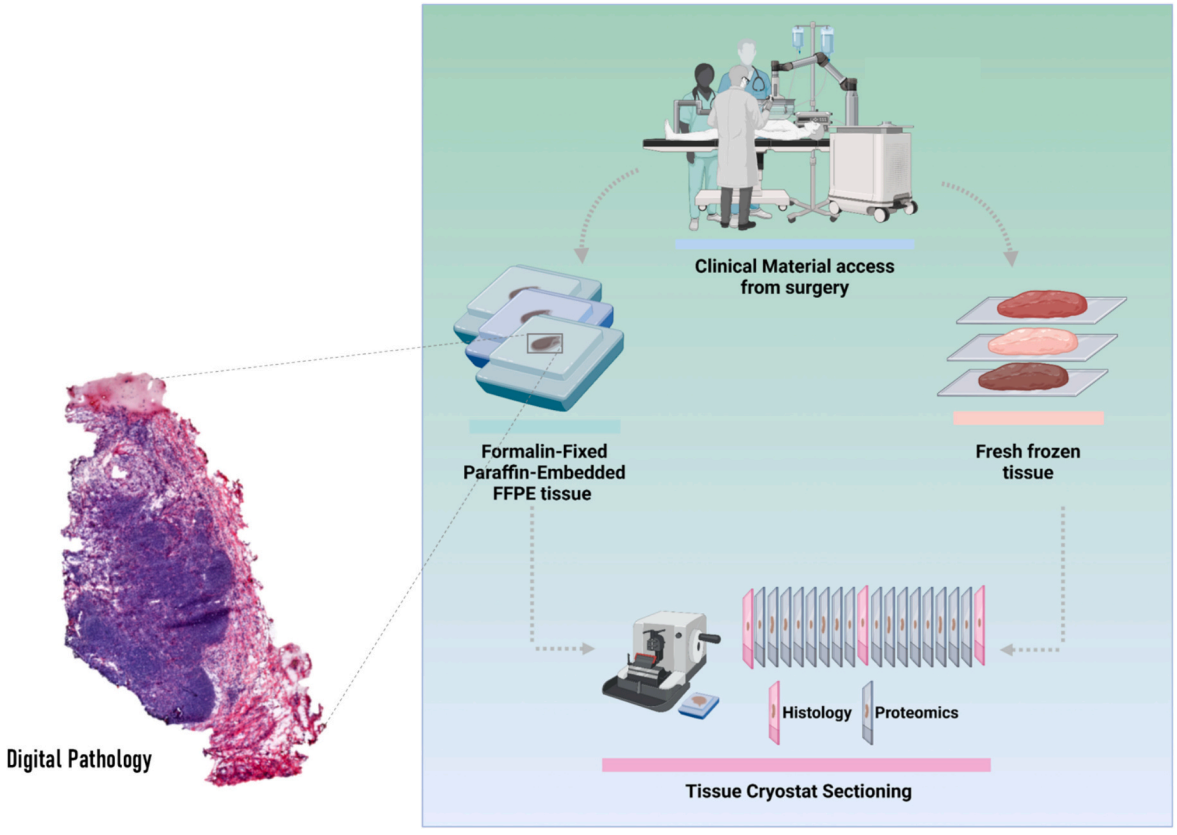

Fig. 4. Schematic representation of tissue workflows for histology and multi-omic analyses. H&*E*-stained tumor section showing morphological features; every 5th section is assessed for tumor content, immune infiltration, stromal phenotype characterization and necrosis. Tissue derived from surgery is allocated into fresh-frozen and FFPE formats for parallel histopathological and molecular analyses. The preparation for proteomics and multi-omics starts with tissue sectioning and staining, enabling efficient annotation of tumor and stromal regions.

automated workflow designed to maintain sample quality and reproducibility.

Blood is drawn into five specialized tubes, supporting EDTA (whole blood, plasma), Na-citrate (coagulation assays), Na-heparin (cellular analyses), and serum preparation. Each tube is transported under carefully tracked conditions to the biobank facility, ensuring arrival within a critical processing window (Fig. 3).

Upon laboratory receipt, the blood undergoes automated fractionation using high-throughput liquid-handling systems, typically within two hours. This process produces several key fractions:

- **Whole blood:** retains all cellular and plasma constituents.
- **Plasma:** used for proteomic and metabolic analyses.
- **Serum:** essential for biomarker discovery and validation.
- **Buffy coat:** a leukocyte-rich fraction suitable for genomic and transcriptomic profiling.
- **Red blood cells:** used in hemoglobin-related studies, membrane proteomics, and metabolic analyses.

Each fraction is dispensed in standardized 70 μL aliquots into Thermo Scientific Matrix™ 384-well plates, storing two patients' samples on a single plate. A single patient can yield up to 192 aliquots per sampling timepoint, covering all blood fractions. These aliquots are stored at −80 °C in automated LiCONiC freezers, enabling both high-density storage and precise "cherry-picking" for retrieval. By minimizing freeze–thaw cycles through small aliquots, sample quality is safeguarded for downstream proteomic and multi-omic investigations.

Blood-derived biospecimens are particularly advantageous for identifying circulating biomarkers such as CTPs, extracellular vesicles, cytokines, and immune mediators, that reflect the dynamic interplay between the tumor and the host environment. Such markers enable non-invasive tracking of therapeutic responses, monitoring of disease progression, and early detection of emerging treatment resistance.

7.3. Longitudinal follow-up and sampling

Incorporating a longitudinal follow-up dimension into biobanking workflows significantly enhances the ability to monitor disease progression, therapeutic response, and relapse dynamics. At the European Cancer Moonshot Lund Center, we emphasize the collection of samples across multiple time points, including pre-treatment, immediate post-treatment, and regular follow-up intervals. This temporal sampling approach provides invaluable insights into the evolving molecular landscape of cancer, enabling the identification of biomarkers predictive of treatment response or resistance [33].

The longitudinal follow-up protocol involves systematic collection and standardized processing of biospecimens at clearly defined clinical milestones. Tumor biopsies, blood samples, and other relevant biological fluids are obtained at baseline, immediately after therapeutic interventions, and at subsequent intervals to capture dynamic molecular changes. Integrated with comprehensive clinical data, these serial samples facilitate a robust, temporal correlation of molecular markers with clinical outcomes, supporting personalized patient management and precision oncology strategies. By maintaining meticulous records and employing automated tracking systems, each longitudinal sample is securely linked to corresponding patient metadata. This process ensures data integrity and traceability, essential for high-impact translational research.

7.4. Integration of non-invasive sampling approaches

Adopting less invasive sampling methods, such as saliva and urine tests, significantly enhances patient comfort, compliance, and accessibility. Saliva samples offer a non-invasive approach for biomarker discovery, particularly beneficial for early detection of cancers like head and neck malignancies. Urine samples similarly represent a non-invasive alternative, enabling detection and monitoring of tumor-derived biomarkers.

Despite the promising potential and clinical value of these less invasive methods, the gold standard for tumor characterization within clinical practice remains tissue-based pathological diagnosis. At the European Cancer Moonshot Lund Center, tumor characterization predominantly leverages histopathology enhanced by Digital Pathology, and increasingly incorporates advanced AI-driven imaging and analytics. Integrating both conventional and novel approaches provides a comprehensive framework to enhance early detection, monitor therapeutic efficacy, and facilitate precision oncology.

8. Integrated workflows for histology and proteomics

The preparation of biological samples is a cornerstone for obtaining high-quality, reproducible results in proteomic and multi-omic studies. Standardized workflows have been developed to preserve the integrity of various biomolecules—proteins, PTMs, metabolites, and nucleic acids—and to ensure robust data generation [30,31,34–36]. By leveraging state-of-the-art methodologies and published best practices, these workflows serve as guidelines for effective sample handling.

8.1. Tissue sectioning and histology-guided sample preparation

Tissue sectioning strategies at the Lund Center are optimized to balance morphological preservation for histological evaluation with the acquisition of high-quality material for downstream molecular analyses. This dual emphasis ensures that multi-omic data accurately reflects tumor characteristics.

For fresh-frozen tissues samples are cut at 10–15 μm thickness using a cryostat to maintain molecular integrity. Every fifth section is stained with hematoxylin and eosin (H&E) for histopathological assessment, which examines tumor content, immune cell infiltration, and necrotic regions (Fig. 4). These assessments verify tissue quality and guide the selection of sections representing the tumor for multi-omic analyses [34].

In the FFPE tissue workflow, archived tissues are sectioned at 6–8 μm thickness and routinely stained with H&E. The slides are digitized for automated annotation of tumor and stromal areas via deep-learning algorithms [17]. Digital segmentation precisely maps histological features, enabling targeted molecular analyses of defined regions. FFPE slides also enable quantitative proteomics and PTM-focused studies when paired with optimized antigen-retrieval protocols (e.g., Tris-EDTA) that mitigate the effects of formalin-induced crosslinking [36–38]. These protocols further support downstream multi-omic applications, including proteogenomic integration (Fig. 4).

For even higher spatial resolution, specific tumor and stromal compartments can be isolated via laser capture microdissection (Fig. 5). This technique is particularly valuable for dissecting heterogeneous tumor regions and clarifying the contributions of distinct cell populations within the tumor microenvironment [17]. The resulting spatially resolved proteomic data significantly enhance our understanding of tumor biology.

By adopting these optimized sectioning and histology-guided workflows, the Lund Center preserves morphological integrity and ensures that tissue is suitable for proteomic, genomic, and spatial analyses. This integrated approach is critical for unraveling tumor heterogeneity and advancing precision oncology.

8.2. Biobank standards delivers the human melanoma proteome atlas

Standardized biobank-driven sample processing was pivotal for generating the Human Melanoma Proteome Atlas, which combines mass spectrometry–based proteomics and histopathology to analyze 505 tumor samples from 232 patients. Encompassing more than 15,500 proteoforms and achieving ~74 % proteome coverage, this project

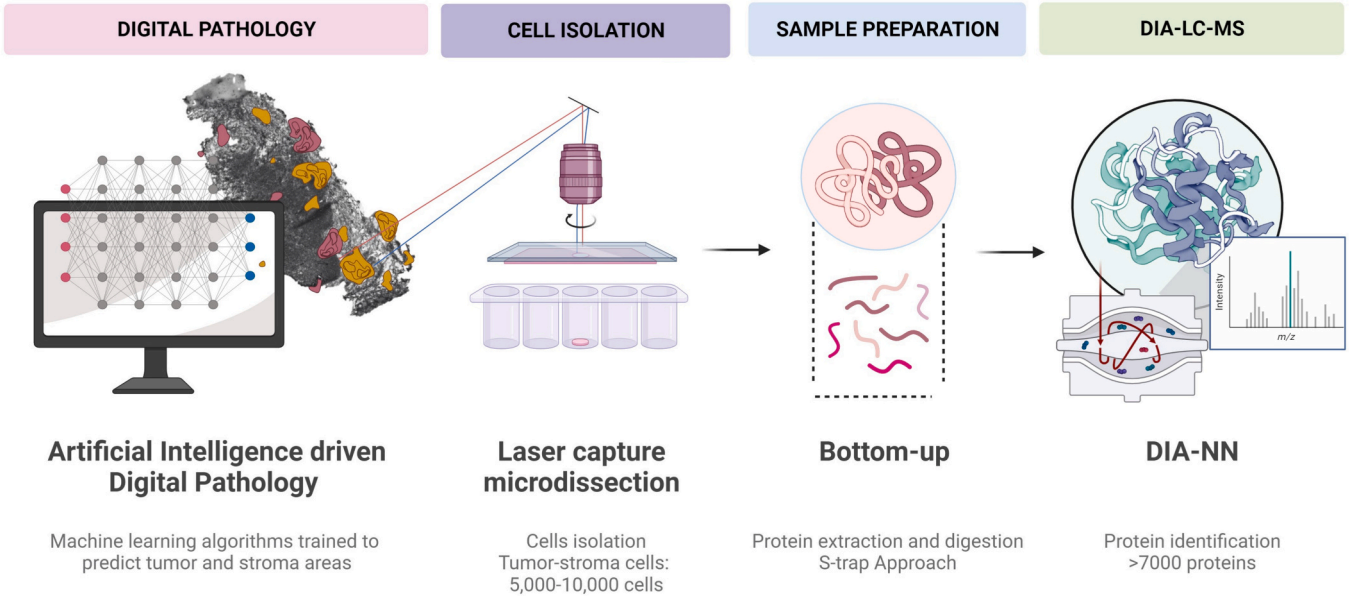

Fig. 5. Workflow for digital pathology followed by special proteomics of intratumor regions. Artificial intelligence–driven digital pathology predicting tumor and stromal compartments. Laser capture microdissection isolates intratumor annotated regions including tumor clones and stromal cells directly into collection tubes for downstream proteomic analyses. Bottom-up proteomics workflow using S-Trap protein digestion and subsequent data-independent acquisition (DIA) LC–MS This workflow yields spatially resolved proteomic insights that link molecular heterogeneity to functional tumor biology.

identified key driver mutations (e.g., BRAF V600E, NRAS Q61) and mapped critical PTMs, highlighting intratumor heterogeneity and dynamic protein expression.

Notably, the atlas also offers a first-in-kind plasma proteome profile for melanoma patients, bridging tissue-level and systemic insights. As a globally recognized benchmark for melanoma research [11,12,29], it advances biomarker discovery, therapeutic monitoring, and precision oncology. Moreover, the underlying principles are broadly applicable to other malignancies, as demonstrated by the publicly accessible dataset (https://www.tnmplot.com/melanoma) [39]. This initiative exemplifies how biobank-standardized workflows can drive impactful research across the spectrum of cancer diseases.

9. Data analysis and bioinformatics: Integrating multi-Omic data with AI and machine learning

The integration of multi-omic datasets—spanning proteomics, genomics, metabolomics, and histopathology—has become pivotal for understanding cancer biology and propelling precision medicine. At the European Cancer Moonshot Lund Center, advanced data analysis pipelines and bioinformatics strategies enable the processing, analysis, and interpretation of vast biological datasets. By incorporating cutting-edge tools, including AI and machine learning, the Lund Center not only extracts actionable insights but also develops predictive models for patient stratification, treatment outcomes, and biomarker discovery.

9.1. Proteomic data analysis: Statistical and AI driven approaches

The first critical step in multi-omic data analysis is rigorous preprocessing to ensure accuracy, reproducibility, and comparability. Regardless of the omic layer—proteomics, genomics, transcriptomics, or metabolomics—each raw dataset undergoes stringent quality control to filter out outliers, correct batch effects, and eliminate technical noise. To unify these data layers for downstream analyses, the Lund Center employs custom R-based bioinformatics pipelines. By harmonizing data handling and processing, researchers can uncover molecular patterns, functional relationships, and biomarkers across multiple omic layers, advancing the goals of precision oncology.

Proteomic data analysis at the Lund Center begins by identifying, quantifying, and normalizing up to 8000 proteins from raw MS spectra, yielding high-quality datasets for downstream exploration (Fig. 6). Statistical methods (e.g., linear modeling, pathway enrichment) uncover dysregulated proteins and biological processes linked to disease progression and treatment response. In parallel, AI-driven approaches from machine learning algorithms (e.g., random forests, SVMs) to deep learning architectures (e.g., CNNs), mine these datasets for non-linear patterns, enabling patient stratification and predictive modeling of therapy outcomes. Crucially, AI models also integrate EHR data, correlating clinical parameters, histopathology, and multi-omic profiles to forecast disease recurrence and guide personalized treatments. Recently, it was demonstrated an AUC of ~0.85 when applying gradient-boosting models to predict early-stage melanoma recurrence [40]. Together, these complementary statistical and AI-driven techniques streamline biomarker discovery, enhance risk assessment, and improve patient outcomes, solidifying the Lund Center's role at the forefront of precision oncology.

10. Biobanking considerations and future progression

The European Cancer Moonshot Lund Center has developed a comprehensive and scalable biobanking framework that directly addresses critical unmet needs in current biobanking systems. By integrating advanced workflows for tumor tissue and blood sample collection, processing, and storage, the center ensures the generation of high-quality biospecimens that preserve molecular integrity for downstream proteomic, genomic, metabolomic, and spatial analyses. This infrastructure is further strengthened by real-time integration with clinical data, enabling researchers to seamlessly correlate molecular findings with patient demographics, clinical histories, and treatment outcomes. For skin and other visible tumor types, clinical data collection should include photographs of primary tumors and metastases, as well as dermoscopic images. Incorporating both clinical and dermoscopic images enhances diagnostic accuracy and aids in monitoring treatment responses.

A key strength of the framework lies in its scalability, achieved through cutting-edge automation, standardized protocols, and rigorous

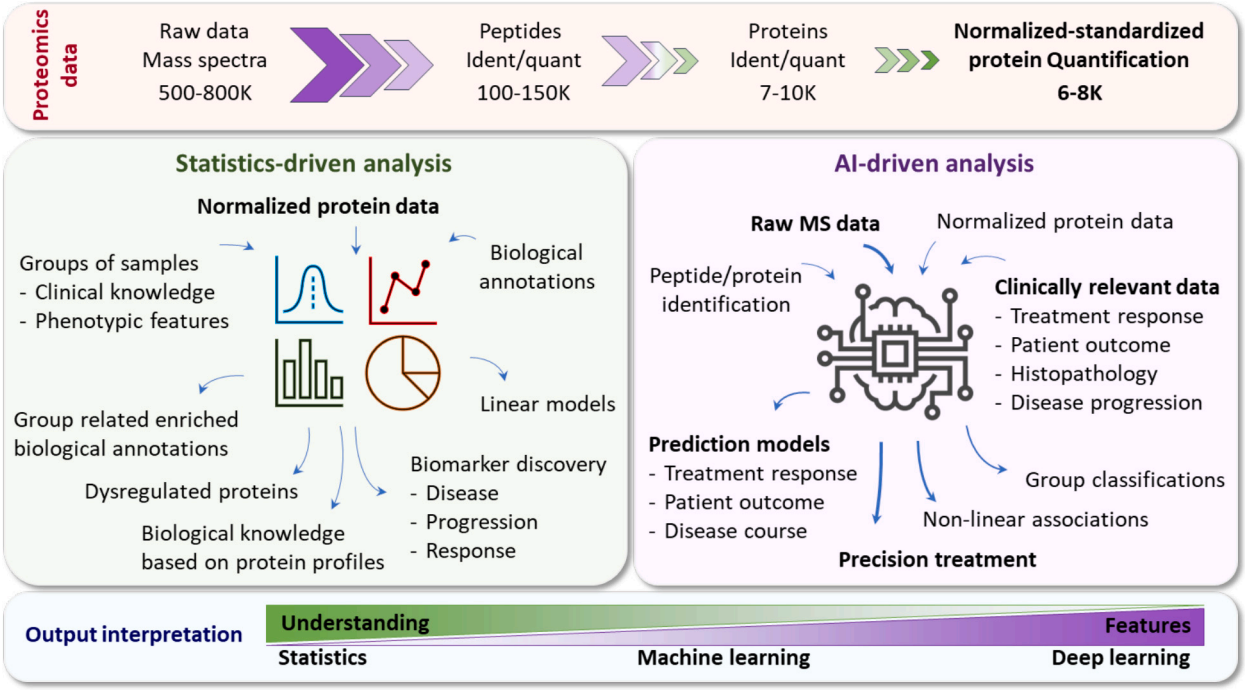

Fig. 6. Bioinformatics in clinical proteomics to impact clinical decision making. The progression from raw mass spectrometry data (500–800 k spectra) to peptide-level identification (100–150 k) and finally protein-level identification (7–10 k). After normalization and standardization, ~6–8 k proteins remain for quantitative analyses. Statistics-Driven Analysis use normalized data after rigorous quality control, significantly dysregulated proteins and pathways are identified in relation to the clinical and phenotypical features of the cohort study. AI-Driven Analysis can analyze data to uncover molecular signatures associated with clinical data. Bottom bar highlights the continuum from statistical approaches (more understanding) to machine and deep learning (more features), underscoring the progressive shift toward complex AI-driven analyses that foster deeper biological interpretations and precision treatments.

quality control measures. This approach ensures reproducibility, minimizes variability, and supports high-throughput multi-omic analyses across large patient cohorts.

Proteomics has emerged as a cornerstone technology within this ecosystem, offering functional molecular insights that bridge the gap between molecular research and clinical practice. As emphasized during the 2024 HUPO World Congress, proteomic technologies have reached a level of maturity that provides the opportunity for clinicians to incorporate basic science-driven predictors into clinical decision making. By integrating proteomics with blood-based biomarkers, histopathology, and genomics, the Lund Center delivers a multidimensional understanding of cancer biology. These approaches facilitate the identification of actionable therapeutic targets, comprehensive patient stratification, disease progression tracking, and therapy monitoring, advancing the precision medicine agenda. To overcome heterogeneity and lack-of-reproducibility across clinical cohorts, further translational validation using real-world-data from independent cohorts.

A major achievement within this framework is the development of the Human Melanoma Proteome Atlas, a landmark effort that mapped the proteomic landscape of melanoma across tumor tissues and plasma samples [40]. This atlas has provided transformative insights into tumor heterogeneity, post-translational modifications, and systemic disease progression, while also serving as a model for data accessibility and global collaboration. Furthermore, the center has developed advanced data analysis platforms, such as MEL-PLOT, which enable interactive visualization and exploration of complex proteomic datasets, democratizing access to multi-omic analyses for researchers worldwide [39].

Leveraging AI-driven analytics and machine learning models, the Lund Center has expanded its capabilities in feature selection, patient stratification, and clinical outcome prediction. Integrating electronic health records with multi-omic datasets enables the development of predictive models that identify high-risk patients, optimize treatment strategies, and improve clinical outcomes [14–16,41]. These innovations underscore the center's commitment to harnessing computational tools to maximize the translational potential of biobanking and omic research.

This white paper highlights the Lund Center's mission-driven approach to advancing precision medicine through state-of-the-art infrastructure, multidisciplinary collaborations, and data-driven insights. By addressing critical unmet needs, including scalability, real-time clinical data integration, and actionable biomarker discovery, the Lund Center has established a paradigm for modern biobanking and multi-omic research. Integrating robust biobanking workflows with global initiatives like the Cancer Moonshot Program and the ICPC enhances collaborative efforts in cancer research, fostering data sharing and accelerating the translation of findings into clinical applications.

Through the integration of standardized protocols, AI-powered analytics, and interactive platforms, the Lund Center ensures that cutting-edge discoveries are translated into individualized therapies reflective of the dynamic proteome and the evolving systemic state of each patient.

Looking ahead, the Lund Center remains committed to expanding the reach and impact of its biobanking and proteomic initiatives. By fostering global collaborations, advancing AI-driven computational strategies, and adhering to rigorous quality standards, the center aims to transform cancer care and improve outcomes for patients worldwide.

Significance

This white paper delineates an end-to-end, high-throughput biobanking strategy at the European Cancer Moonshot Lund Center that merges rigorous sample collection, automated workflows, and advanced molecular profiling. By integrating tissue- and blood-based specimens, the framework captures the full breadth of cancer biology, from genomic and proteomic changes in tumor tissues to dynamic, circulating biomarkers in blood, offering a robust platform for biomarker discovery, patient stratification, and therapy monitoring. The seamless alignment

with global precision oncology initiatives underscores the importance of harmonized, high-quality biobanking operations that accelerate translational research and deliver tangible benefits to cancer patients worldwide.

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We extend our deepest gratitude to the patients who, despite their battles with metastatic melanoma, generously contributed samples for this study. Their invaluable contributions have been instrumental in advancing our understanding of this disease. This research was supported by grants from the Berta Kamprad Foundation, and from the Crafoord Foundation (20240554) form Sweden, and it was done under the auspices of a Memorandum of Understanding between the European Cancer Moonshot Center in Lund and the U.S. National Cancer Institute's ICPC. ICPC encourages international cooperation among institutions and nations in proteogenomic cancer research in which proteogenomic datasets are made available to the public. This work was also done in collaboration with the U.S. National Cancer Institute's CPTAC, and by grants from the National Research Foundation of Korea (MSIP; 2021R1A3B1077371) and the Brain Korea 21 Plus Project of the Republic of Korea. B.D. was supported by the Austrian Science Fund (FWF I3522, FWF I3977, and I4677) and the 'BIOSMALL' EU HORIZON-MSCA-2022-SE-01 project. B.D. and Z.M. were supported by funding from the Hungarian National Research, Development, and Innovation Office (2020-1.1.6-JÖVŐ, TKP2021-EGA-33, FK-143751 and FK-147045). Z.M. was supported by the New National Excellence Program of the Ministry for Innovation and Technology of Hungary (UNKP-20-3, UNKP-21-3 and UNKP-23-5), and by the Bolyai Research Scholarship of the Hungarian Academy of Sciences. Z.M. is also the recipient of the International Association for the Study of Lung Cancer/International Lung Cancer Foundation Young Investigator Grant (2022), MTA-SE Lendület "Momentum" Dermatology Research Group, Hungarian Academy of Sciences and Semmelweis University, Budapest, Hungary

Data availability

No

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