

Review

Precision Medicine in Liver and Lung Transplantation: Integrating Immunology, Regenerative Therapies, and Computational Advances

Tamer A. Addissouky *

New Burg El-Arab Hospital, Ministry of Health, Alexandria, Egypt; E-Mails: tedesoky@gmail.com; tedesoky@science.menofia.edu.eg; ORCID: 0000-0003-3797-9155

* **Correspondence:** Tamer A. Addissouky; E-Mails: tedesoky@gmail.com; tedesoky@science.menofia.edu.eg; ORCID: 0000-0003-3797-9155

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Abstract

Liver and lung transplantation remain among the most intricate and resource-intensive arenas in modern medicine, challenged by organ scarcity, immunological complexities, and the persistent threat of rejection. According to recent WHO and UNOS reports, approximately 100,000 patients globally await liver transplants annually, with only 30-40% receiving transplants, resulting in waitlist mortality rates of 15-20%. Similarly, lung transplant demand exceeds supply by a factor of 4:1, with 5-year survival rates remaining at 60-65%. This article outlines the evolving landscape of liver and lung transplantation, with a focus on the intersection of immunological science, regenerative medicine, and computational advances. It aims to synthesize current challenges and emerging therapeutic strategies, emphasizing the transformative potential of precision medicine and advanced immunomodulation techniques. Recent decades have witnessed a paradigm shift from standardized immunosuppression toward individualized, data-driven care. Advances in molecular immunology have revealed complex cellular interactions and rejection pathways, informing targeted therapies such as extracorporeal photopheresis (ECP), immune checkpoint modulation, and the engineering of regulatory T cells. Regenerative medicine, including mesenchymal stem cells, iPSC-derived tissues, and gene editing, offers new avenues for organ repair and tolerance induction. Meanwhile, artificial intelligence and digital health platforms enable predictive modeling, risk



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stratification, and real-time monitoring, optimizing patient selection and management. Nanotechnology and advanced diagnostics, such as liquid biopsy and single-cell sequencing, further refine graft surveillance and intervention. These developments are situated within an ethical, regulatory, and economic context, underscoring the need for global collaboration and equitable access. The future of liver and lung transplantation lies in the convergence of precision immunology, regenerative strategies, and computational innovation. Interdisciplinary, personalized approaches promise to enhance graft survival, patient outcomes, and the sustainable integration of cutting-edge therapies into global healthcare systems.

Keywords

Precision medicine; liver and lung transplantation; immunomodulation; regenerative medicine; artificial intelligence in transplantation

1. Background

Liver and lung transplantation are among the most complex and resource-intensive procedures in modern medicine [1, 2]. These interventions often serve as the only viable treatment for patients with end-stage organ failure. Despite significant advancements, transplantation remains fraught with challenges, including organ scarcity, immunological complications, and logistical hurdles [3, 4].

1.1 Global Burden and Statistics

Recent WHO and UNOS data reveal stark realities in transplantation [3, 4]:

1.1.1 Liver Transplantation

Approximately 100,000 patients globally await liver transplants annually, with only 30-40% receiving transplants. Lung transplantation: Demand exceeds supply by a 4:1 ratio, with 5-year survival rates at 60-65% [5, 6]. Waitlist mortality: 15-20% for liver transplant candidates, 25-30% for lung transplant candidates. Geographic disparities: Up to 10-fold variation in transplantation rates between developed and developing regions [4].

The increasing prevalence of chronic diseases such as hepatitis, pulmonary fibrosis, and chronic obstructive pulmonary disease has substantially raised the global demand for viable organs, outpacing supply and exacerbating waitlist mortality rates [6-9].

1.2 Current Challenges

1.2.1 Immunological Complexity

Transplantation introduces a foreign organ into a recipient's body, triggering a cascade of immunological reactions [10, 11]. The human immune system is finely tuned to recognize and eliminate non-self-elements, posing a formidable barrier to long-term graft survival [12, 13]. Major

histocompatibility complex (MHC) mismatches, minor antigen disparities, and preformed donor-specific antibodies are critical determinants of early and late transplant outcomes [11, 14].

1.2.2 Rejection Mechanisms

Rejection remains a leading cause of graft loss post-transplantation [15, 16]:

- Hyperacute rejection: Mediated by pre-existing antibodies, occurs within minutes to hours.
- Acute cellular rejection: Driven by T-cell activation, it typically arises within weeks.
- Chronic rejection: Characterized by progressive fibrosis and vascular changes, can manifest months or years after transplantation.

1.3 Paradigm Shift: From Conventional to Precision Medicine

1.3.1 Historical Perspective

Traditional transplant medicine has relied mainly on standardized immunosuppressive protocols and clinical algorithms [17, 18]. While these approaches have improved short-term outcomes, they fail to account for the unique immunological and genetic profiles of individual patients [19, 20].

1.3.2 Emerging Technological Interventions

The past decade has witnessed an explosion of technologies enabling more profound insights into transplant immunobiology [21, 22]. High-throughput sequencing, advanced imaging, and computational modeling now facilitate unprecedented characterization of donor and recipient biology [23, 24].

1.3.3 Personalized Approach Rationale

Precision medicine aims to move beyond the "one-size-fits-all" paradigm [19, 20]. By integrating genetic, molecular, and clinical data, clinicians can stratify patients based on risk, predict treatment response, and customize immunosuppression [25, 26].

2. Immunological Foundations

2.1 Molecular Immunology of Transplantation

2.1.1 Cellular Interactions

The immunological response to allografts is orchestrated by a complex interplay of immune cells [10, 12]. Dendritic cells, as professional antigen-presenting cells, play a pivotal role in initiating and modulating the response [27]. They capture donor antigens and present them to recipient T cells, which, upon activation, proliferate and differentiate into effector subsets.

2.1.2 Immune Recognition Mechanisms

Allograft recognition occurs via direct and indirect pathways [12, 13]:

- **Direct pathway:** Recipient T cells recognize donor MHC molecules on donor antigen-presenting cells.

- **Indirect pathway:** Recipient antigen-presenting cells process and present donor-derived peptides to T cells.
- **Semi-direct allorecognition:** Recipient dendritic cells acquire intact donor MHC-peptide complexes.

2.2 Tolerance Induction Strategies

Establishing immune tolerance remains the "holy grail" of transplantation [28, 29]. Current strategies include:

2.2.1 Preclinical Success vs Clinical Limitations

While preclinical models demonstrate promising results with mixed chimerism achieving 80-90% tolerance rates, clinical translation faces significant challenges [28-30]:

- **Mixed chimerism:** Requires intensive conditioning, achieving only 15-30% success in clinical trials.
- **Regulatory T-cell infusion:** Shows 50-70% efficacy in Phase I/II trials but faces scalability issues [28, 29].
- **Costimulatory blockade:** Demonstrates safety but limited long-term efficacy (40-60% success rates) [31].

2.2.2 Clinical Trial Outcomes

Recent landmark studies provide insight into tolerance strategies [28, 29]:

- **ONE Study (EU):** Multi-center trial of regulatory cell therapies showing 45% reduction in rejection episodes.
- **ITN trials (US):** Immune Tolerance Network studies demonstrating feasibility but limited scalability.
- **Challenge in sensitized recipients:** Particularly problematic in lung transplants, where 60-80% of recipients have pre-existing sensitization.

2.3 Advanced Immunomodulation Techniques

Recent advances in immunomodulation have introduced several promising therapeutic approaches with varying degrees of clinical implementation and success rates as presented in Table 1 [31, 32].

Table 1 Comprehensive Comparison of Advanced Immunomodulation Techniques in Liver and Lung Transplantation.

Technique	Mechanism of Action	Clinical Applications	Sample Sizes	Efficacy Data	Advantages	Limitations	Key References
Extracorporeal Photopheresis (ECP)	Photoactivation-induced leukocyte apoptosis, promotion of tolerogenic APCs, and Treg expansion	Steroid-resistant acute rejection, chronic allograft dysfunction, and GVHD prevention	n = 150-300 per study	60-80% response rate in refractory rejection; 70% reduction in chronic rejection progression	Minimal systemic toxicity, preserves immune competence, reduces steroid dependence	Time-intensive procedure, requires specialized equipment, variable response rates	[30, 33-37]
Regulatory T-cell Therapy	Direct infusion of expanded Tregs, immune suppression via IL-10/TGF- β secretion, and contact-dependent inhibition	Tolerance induction, rejection prevention, and autoimmune complications	n = 20-50 (Phase I/II)	Phase I/II trials show a 50-70% reduction in rejection episodes	Antigen-specific tolerance, reduced immunosuppression requirements	Cell preparation complexity, potential for in vivo instability, and limited expansion capacity	[28, 29, 32]
CAR-Treg Engineering	Genetically modified Tregs with chimeric antigen receptors for enhanced specificity	Targeted tolerance to specific alloantigens, precision immunomodulation	n = 10-25 (preclinical/early clinical)	Preclinical studies show 80-90% graft survival improvement	Enhanced specificity, prolonged persistence, reduced off-target effects	Manufacturing complexity, potential immunogenicity, long-term safety unknown (investigational phase)	[32, 38]
Immune Checkpoint Modulation	PD-1/CTLA-4 pathway manipulation, T-cell exhaustion induction, and co-stimulation blockade	Prevention of chronic rejection, tolerance maintenance protocols	n = 30-100 per study	40-60% improvement in long-term graft survival	Precise immune regulation, combination therapy potential	Risk of over-immunosuppression, malignancy concerns, and autoimmune complications (investigational phase)	[31, 39-41]

Mesenchymal Stem Cell Therapy	Immunomodulation via paracrine signaling, tissue repair, and anti-inflammatory cytokine production	Acute rejection treatment, chronic allograft dysfunction, ischemia-reperfusion injury	n = 50-150 per study	30-50% reduction in rejection episodes, improved graft function	Tissue regenerative properties, low immunogenicity, and multiple administration routes	Variable potency, limited persistence, standardization challenges	[38, 42, 43]
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Note: CAR-Treg and immune checkpoint modulation are primarily in preclinical or early investigational phases for transplantation applications. Efficacy data vary between liver and lung transplant applications, with generally higher response rates observed in liver transplantation.

2.3.1 Extracorporeal Photopheresis (ECP)

Extracorporeal Photopheresis (ECP) employs photoactivation-induced leukocyte apoptosis and promotion of tolerogenic antigen-presenting cells [33-37]. In clinical applications for steroid-resistant acute rejection and chronic allograft dysfunction, ECP demonstrates response rates of 60-80% in refractory rejection cases and a 70% reduction in chronic rejection progression in studies with sample sizes ranging from 150 to 300 patients per study.

2.3.2 Regulatory T-cell Therapy

Regulatory T-cell Therapy involves direct infusion of expanded regulatory T cells for tolerance induction and rejection prevention [28, 29, 32]. Phase I/II trials with sample sizes of 20-50 patients show a 50-70% reduction in rejection episodes. The therapy offers antigen-specific tolerance and reduced immunosuppression requirements, though it faces challenges in cell preparation complexity and potential in vivo instability.

2.3.3 CAR-Treg Engineering

CAR-Treg Engineering represents genetically modified regulatory T cells with chimeric antigen receptors for enhanced specificity in targeted tolerance to specific alloantigens [32, 38]. Currently in the preclinical to early clinical phases, with sample sizes ranging from 10 to 25 patients, preclinical studies demonstrate an 80-90% improvement in graft survival. While offering enhanced specificity and prolonged persistence, manufacturing complexity and potential immunogenicity remain significant limitations.

2.3.4 Immune Checkpoint Modulation

Immune Checkpoint Modulation focuses on manipulating the PD-1/CTLA-4 pathway and inducing T-cell exhaustion to prevent chronic rejection [31, 39-41]. Studies with sample sizes of 30-100 patients have demonstrated a 40-60% improvement in long-term graft survival. Though offering precise immune regulation and combination therapy potential, concerns exist regarding over-immunosuppression risk and malignancy complications.

2.3.5 Mesenchymal Stem Cell Therapy

Mesenchymal Stem Cell Therapy utilizes immunomodulation via paracrine signaling and tissue repair properties for acute rejection treatment and chronic allograft dysfunction [38, 42, 43]. Studies involving 50-150 patients per study have shown a 30-50% reduction in rejection episodes and improved graft function. The therapy offers tissue regenerative properties and low immunogenicity, with multiple administration routes; however, variable potency and limited persistence present challenges to standardization.

3. Regenerative Medicine Strategies

3.1 Stem Cell Innovations

3.1.1 Mesenchymal Stem Cell Applications

Mesenchymal stem cells (MSCs) possess potent immunomodulatory and regenerative properties [42, 43]. In transplantation, MSCs have been shown to modulate immune responses, reduce rejection, and promote tissue repair. Clinical trials demonstrate the safety and potential efficacy of MSC infusions in liver and lung transplant recipients, particularly in the context of refractory rejection and chronic allograft dysfunction [38, 43].

3.1.2 Regulatory and Cost Challenges in iPSC and Gene-Edited Tissues

The deployment of iPSCs and gene-edited tissues in transplantation faces significant hurdles [44-47]:

Regulatory Framework. FDA/EMA require extensive safety data for gene-edited products with current approval timelines of 8-12 years for novel cell therapies [46, 47]. The cost of regulatory compliance ranges from \$50-100 million per product, necessitating standardized Good Manufacturing Practice (GMP) protocols.

Economic Considerations. iPSC-derived hepatocytes are estimated to carry costs of \$100,000-\$500,000 per patient treatment, while gene-edited organs are projected to have initial costs of \$1-\$2 million per transplant [44-47]. Infrastructure requirements demand \$10-50 million per specialized center, with insurance coverage remaining uncertain for experimental therapies.

3.1.3 Cellular Reprogramming Techniques

The ability to reprogram somatic cells into induced pluripotent stem cells (iPSCs) has opened new avenues for regenerative medicine [44, 45]. Patient-specific induced pluripotent stem cells (iPSCs) can be differentiated into hepatocytes, alveolar epithelial cells, and other relevant cell types for organ repair or replacement [44, 45, 48].

3.1.4 Gene Editing Approaches

Gene editing technologies, such as CRISPR/Cas9, facilitate precise modification of cellular genomes [46, 47]. In transplantation, gene editing can be used to eliminate immunogenic antigens, enhance resistance to ischemia-reperfusion injury, and manipulate immune cell function [49-51].

3.2 Organ Preservation and Regeneration

3.2.1 Machine Perfusion Innovations

Ex vivo machine perfusion represents a transformative approach to organ preservation [52-56]. By providing continuous oxygenation and nutrient delivery, machine perfusion maintains organ viability and function outside the body as presented in Table 2 [23, 24, 57]. Both normothermic and

hypothermic perfusion techniques enable the real-time assessment of organ quality, delivery of therapeutic agents, and repair of marginal grafts before transplantation.

Table 2 Regenerative Medicine and Gene Editing Strategies: Therapeutic Applications and Clinical Translation Status.

Therapeutic Strategy	Technology Platform	Target Applications	Development Stage	Clinical Outcomes	Regulatory Status	Challenges & Solutions	Key References
iPSC-Derived Hepatocytes	Induced pluripotent stem cell differentiation, organoid culture	Liver tissue engineering, hepatocyte replacement therapy, and drug screening	Phase I/II clinical trials (n = 20-40)	20-30% improvement in liver function scores, reduced need for re-transplantation	FDA breakthrough therapy designation	Maturation challenges, scalability issues; Solution: Advanced bioreactor systems, 3D culture optimization	[44, 45, 48, 58]
CRISPR/Cas9 Gene Editing	Programmable nucleases, base editing, prime editing	HLA modification, disease gene correction, and xenograft humanization	Preclinical to Phase I (n = 10-25)	Successful HLA knockout in 90% of treated cells, reduced immunogenicity	Under regulatory review	Off-target effects, delivery challenges; Solution: Improved guide RNA design, lipid nanoparticle delivery	[46, 47, 49-51]
Lung Organoids	3D culture systems, airway stem cell expansion	Lung repair, cystic fibrosis treatment, personalized drug testing	Preclinical development	Functional airway tissue generation, 60% survival in animal models	Research-stage	Limited vascularization, immature phenotype; Solution: Co-culture systems, vascular integration	[48, 58-60]
Decellularized Scaffolds	Organ decellularization and recellularization protocols	Whole organ engineering, biological scaffolds	Phase I clinical trials (n = 5-15)	Successful transplantation in small animal models, with biocompatibility confirmed	Early clinical investigation	Incomplete cellular repopulation, limited function; Solution: Enhanced seeding protocols, growth factor incorporation	[52-56, 61-63]
Machine Perfusion Systems	Normothermic/hypothermic perfusion, oxygenators	Organ preservation, viability assessment, therapeutic delivery	Clinical implementation	25-30% increase in transplantable organs, improved graft function	FDA/EMA-approved devices	Cost and complexity; Solution: Automated systems, portable devices, AI-guided optimization	[23, 24, 52-57]

3.2.2 Current Clinical Implementation

Adoption rates show 40-60% of transplant centers now use machine perfusion, resulting in a 25-30% increase in transplantable organs [52-56]. Cost considerations range from \$50,000 to \$100,000 per perfusion system, while outcome improvements demonstrate a 15-25% reduction in primary non-function rates [23, 24, 57].

3.2.3 Decellularized Scaffolds

Decellularized Scaffolds employ organ decellularization and recellularization protocols for whole organ engineering and biological scaffolds [52-56]. Currently in Phase I clinical trials with sample sizes of 5-15 patients, successful transplantation has been achieved in small animal models, confirming biocompatibility [61-63]. However, incomplete cellular repopulation and limited function remain challenges, addressed through enhanced seeding protocols and growth factor incorporation as presented in Figure 1.



Figure 1 Evolution from Empirical Treatment to Precision Medicine in Transplantation.

The timeline depicts the transition from empirical, standardized transplant care to an integrated precision medicine model. Key technologies (machine perfusion, regenerative cells, ECP), diagnostics (cfDNA, single-cell), and computational layers (AI/XAI, federated learning) converge to enable adaptive, patient-specific interventions and improved long-term outcomes.

4. Computational Transformation

4.1 Artificial Intelligence Applications

4.1.1 Predictive Modeling

Artificial intelligence (AI) is revolutionizing transplantation through predictive modeling [22, 64-66]. Machine learning algorithms analyze vast datasets to identify risk factors for graft rejection, infection, and other complications. These models support clinical decision-making by providing individualized risk assessments, guiding immunosuppression, and optimizing patient management [39-41].

4.1.2 AI Implementation Challenges

Despite promising applications, AI in transplantation faces significant challenges [22, 64-66]:

4.1.3 Interpretability and Bias Issues

Many AI models lack explainability, which limits their clinical acceptance due to the "black box problem" [65, 66]. Dataset bias often underrepresents minority populations and rare conditions, while cross-center variability means models trained at one center may not generalize to others. Temporal drift causes model performance to degrade over time due to changing patient populations and practices [39-41].

4.1.4 Proposed Solutions

Development of explainable AI (XAI) methods for clinical transparency, implementation of federated learning to address data sharing constraints, continuous model validation and updating protocols, and standardization of data collection and preprocessing methods [67, 68].

4.1.5 Machine Learning Algorithms

Machine learning techniques, including supervised and unsupervised learning, enable the extraction of complex patterns from clinical, genomic, and imaging data as presented in Table 3 [65, 66]. These algorithms facilitate early detection of rejection, prediction of graft outcomes, and identification of optimal donor-recipient matches [69-71].

Table 3 Artificial Intelligence and Digital Health Applications in Transplant Medicine: Current Status and Future Prospects.

AI Application Domain	Technology/Algorithm	Clinical Implementation	Performance Metrics	Current Limitations	Future Developments	Key References
Rejection Prediction	Machine learning (Random Forest, SVM, Neural Networks)	Real-time monitoring systems, biomarker integration	85-92% accuracy, 0.88-0.94 AUC, 72-85% sensitivity	Limited generalizability across centers, data quality dependencies, and interpretability issues	Deep learning integration, multi-modal data fusion, continuous learning algorithms	[22, 64-66, 68, 72, 73]
Risk Stratification	Ensemble methods, gradient boosting, deep neural networks	Pre-transplant assessment, personalized immunosuppression	Risk score accuracy: 80-88%, improved clinical decision-making by 35%	Static models, limited dynamic risk assessment, and bias in training data	Real-time adaptive algorithms, incorporation of omics data, and federated learning	[23, 24, 39-41, 57]
Donor-Recipient Matching	Optimization algorithms, graph neural networks	Organ allocation systems, compatibility scoring	15-25% improvement in graft survival, reduced cold ischemia time	HLA-centric focus, limited inclusion of molecular compatibility, cross-center variability	Multi-dimensional compatibility scoring, AI-driven organ sharing networks	[69-71, 74-76]
Image Analysis	Convolutional neural networks, computer vision	Histopathological diagnosis, radiological assessment	90-95% accuracy in rejection diagnosis, 80% reduction in diagnostic time	Requires large annotated datasets and interpretability challenges	Automated grading systems, real-time surgical guidance, predictive imaging	[77-80]

4.1.6 Rejection Prediction

Rejection Prediction utilizes machine learning algorithms, including Random Forest, SVM, and Neural Networks, for real-time monitoring systems and biomarker integration [22, 64-66]. Performance metrics show 85-92% accuracy, 0.88-0.94 AUC, and 72-85% sensitivity [68, 72, 73]. Current limitations include limited generalizability across centers, data quality dependencies, and issues with interpretability. Future developments focus on integrating deep learning, multi-modal data fusion, and continuous learning algorithms.

4.1.7 Risk Stratification

Risk Stratification employs ensemble methods, gradient boosting, and deep neural networks for pre-transplant assessment and personalized immunosuppression [39-41]. The risk score accuracy ranges from 80% to 88%, with improved clinical decision-making by 35% [23, 24, 57]. Static models and limited dynamic risk assessments present challenges, while bias in training data remains a significant problem. Future advances include the development of real-time adaptive algorithms, the incorporation of omics data, and the application of federated learning approaches.

4.1.8 Donor-Recipient Matching

Donor-recipient matching utilizes optimization algorithms and graph neural networks for organ allocation systems and compatibility scoring [41, 69, 70]. Implementation shows 15-25% improvement in graft survival and reduced cold ischemia time [74-76]. Current limitations include an HLA-centric focus, limited inclusion of molecular compatibility, and cross-center variability. Future developments encompass multi-dimensional compatibility scoring and AI-driven organ sharing networks.

4.2 Digital Health Integration

4.2.1 Real-Time Monitoring Systems

Digital health technologies enable continuous, real-time monitoring of transplant recipients [81-84]. Wearable devices, implantable sensors, and remote monitoring platforms collect physiological, biochemical, and behavioral data. These data streams facilitate early detection of complications, prompt intervention, and personalized care adjustments [83, 84].

4.2.2 Telemedicine Platforms

Telemedicine expands access to specialized transplant care, particularly in underserved regions [85]. Virtual consultations, remote monitoring, and digital education tools support pre- and post-transplant management. Telehealth platforms facilitate multidisciplinary collaboration, patient engagement, and continuity of care across geographic barriers [86, 87].

5. Extracorporeal Photopheresis (ECP)

5.1 Mechanism of Action

ECP exerts its effects through the selective modulation of immune cell populations [33-37]. The procedure involves three key steps:

1. **Collection:** Patient's peripheral blood mononuclear cells are collected via apheresis.
2. **Treatment:** Cells are exposed to 8-methoxypsoralen and UVA light, inducing DNA cross-linking.
3. **Reinfusion:** Treated cells are returned to the patient, where they undergo apoptosis.

5.1.1 Molecular Pathways

ECP influences multiple molecular pathways involved in immune regulation [33-37]:

- **Apoptosis induction:** Photochemically induced DNA damage triggers intrinsic and extrinsic apoptotic pathways.
- **Tolerogenic signaling:** Clearance of apoptotic cells by macrophages promotes anti-inflammatory cytokine production.
- **Regulatory T-cell expansion:** Enhanced differentiation and proliferation of CD4⁺CD25⁺FoxP3⁺ regulatory T cells.
- **Cytokine modulation:** Decreased IL-1 β , TNF- α , and increased IL-10, TGF- β production.

5.2 Clinical Implementation

5.2.1 Standardized Protocols

ECP protocols must be standardized for optimal therapeutic efficacy with treatment frequency of 2 consecutive days every 2-4 weeks initially, then monthly maintenance [33-37]. Duration requires a minimum of 6-12 months, with response-guided extension. Patient selection focuses on steroid-resistant rejection, chronic allograft dysfunction, and high immunological risk cases, with regular monitoring of rejection markers and immunosuppressive drug levels.

5.2.2 Organ-Specific Applications

Liver Transplantation. Liver Transplantation applications include steroid-resistant acute cellular rejection with a 65-75% response rate, chronic ductopenic rejection showing 40-50% stabilization of liver function, and recurrent autoimmune hepatitis achieving 60-70% remission rates [33-37]. The protocol involves an intensive phase consisting of eight treatments over four weeks, followed by maintenance.

Lung Transplantation. Lung Transplantation applications encompass bronchiolitis obliterans syndrome (BOS) with 45-55% stabilization or improvement, chronic lung allograft dysfunction (CLAD) showing 35-45% functional improvement, and acute cellular rejection achieving a 70-80% response rate in steroid-resistant cases. The protocol requires a more intensive regimen due to higher rejection rates with 12 treatments over 6 weeks.

5.2.3 Long-term Outcomes

Long-term studies demonstrate that ECP can reduce rejection rates, preserve graft function, and improve patient survival [33-37]. The therapy is well-tolerated, with a favorable safety profile and minimal infectious complications. Response rates include acute rejection at 60-80%, chronic rejection at 40-60% stabilization, infectious complications at <5% serious adverse events, and long-term survival benefit showing 15-25% improvement in 5-year graft survival.

6. Translational Research Perspectives

6.1 Interdisciplinary Approach

Advances in transplantation immunology drive the development of novel therapies and diagnostics [38, 88]. Cross-disciplinary collaboration accelerates the translation of fundamental immunological discoveries into clinical interventions, fostering innovation and improving patient outcomes. Integrating computational sciences enables the analysis of complex, high-dimensional datasets [23, 68]. Bioinformatics, machine learning, and systems biology approaches reveal novel biomarkers, therapeutic targets, and predictive models, bridging the gap between data generation and clinical application [68, 72, 73].

6.2 Emerging Therapeutic Strategies

6.2.1 Combination Immunomodulatory Approaches

Combining immunomodulatory agents offers synergistic benefits, targeting multiple rejection pathways simultaneously [31, 32]:

- **Dual checkpoint blockade + Treg infusion:** Phase I trials show 60-70% response rates.
- **MSCs combined with ECP:** 45-55% improvement in chronic rejection outcomes.
- **Tolerogenic DC therapy + costimulatory blockade:** Preclinical data suggest 80% tolerance induction.

6.2.2 Personalized Treatment Protocols

The integration of genomic, proteomic, and clinical data enables the development of tailored immunosuppression and supportive therapies [77, 89]. Dynamic risk assessment and adaptive management optimize patient outcomes while reducing adverse effects [74, 78].

7. Technological Innovations

7.1 Advanced Diagnostic Technologies

7.1.1 Liquid Biopsy

Liquid biopsy enables non-invasive assessment of graft health through analysis of circulating cell-free DNA, microRNAs, and extracellular vesicles [21, 83]. These biomarkers provide real-time insights into graft injury, immune activation, and early rejection, enabling timely intervention [84].

Current Applications. Current Applications include donor-derived cfDNA with 85-90% accuracy for detecting acute rejection, microRNA profiling with 80-85% specificity for chronic rejection, and exosome analysis as an emerging biomarker with 75-80% sensitivity [83, 84]. Implementation allows point-of-care testing within 2-4 hours.

7.1.2 Single-Cell Sequencing Technologies

Single-cell sequencing provides high-resolution insights into cellular composition and functional states of the immune system [21, 23]. In transplantation, single-cell analysis reveals heterogeneity in immune cell populations, identifies unique rejection signatures, and uncovers novel therapeutic targets [24, 73].

7.2 Nanotechnology Applications

7.2.1 Nanoparticle-Based Drug Delivery

Nanoparticle-based drug delivery systems enable precise targeting of immunosuppressive agents to specific immune cells or graft sites [50, 51]. This approach reduces systemic toxicity, enhances therapeutic efficacy, and enables controlled release of drugs in response to local cues.

7.2.2 Nanoscale Monitoring Systems

Nanoscale sensors and imaging probes enable real-time monitoring of cellular interactions within the graft microenvironment as presented in Table 4 [49, 90]. These technologies provide dynamic insights into immune cell trafficking, antigen presentation, and tissue remodeling.

Table 4 Implementation Barriers and Proposed Solutions in Precision Transplant Medicine.

Barrier Category	Specific Challenges	Global Impact	Proposed Solutions	Implementation Models
Data Security & Privacy	HIPAA compliance, international data sharing, and blockchain implementation	Limits collaborative research, affects global registry development	Federated learning platforms, homomorphic encryption, secure multi-party computation	EU GDPR framework, US HIPAA-compliant systems, blockchain consortia
Cost & Economic Access	High therapy costs (\$100K-\$2 per patient), limited insurance coverage	Creates healthcare disparities, limits adoption in developing countries	Value-based care models, government subsidies, and international funding initiatives	UK NHS precision medicine program, German SHI reimbursement models
Equity & Global Access	Geographic disparities, technological infrastructure gaps	10-fold variation in transplant access between regions	Telemedicine networks, technology transfer programs, and capacity building	WHO Global Observatory, NOTTO international partnerships
Regulatory Harmonization	Inconsistent approval processes, varying safety standards	Delays in global therapy access, increased development costs	International regulatory consortia, mutual recognition agreements	ICH guidelines, FDA-EMA parallel review processes
Infrastructure Requirements	Need for specialized centers, equipment, and training	Limited scalability, concentrated in urban centers	Hub-and-spoke models, mobile units, and AI-assisted remote monitoring	Mayo Clinic One virtual care, Cleveland Clinic global network

8. Clinical Implementation Framework

8.1 Barriers and Solutions

8.1.1 Data Security & Privacy

Data Security & Privacy challenges include HIPAA compliance, international data sharing, and blockchain implementation, which limit collaborative research and affect global registry development [91, 92]. Proposed solutions involve federated learning platforms, homomorphic encryption, and secure multi-party computation, with implementation models including EU GDPR framework, US HIPAA-compliant systems, and blockchain consortia.

8.1.2 Cost & Economic Access

Cost & Economic Access barriers encompass high therapy costs (\$100K-\$2M per patient) and limited insurance coverage, creating healthcare disparities and limiting adoption in developing countries [3, 4]. Solutions include value-based care models, government subsidies, and international funding initiatives, with implementation models such as the UK NHS precision medicine program and German SHI reimbursement models.

8.1.3 Equity & Global Access

Equity & Global Access challenges involve geographic disparities and technological infrastructure gaps, resulting in 10-fold variation in transplant access between regions [3, 4]. Solutions encompass telemedicine networks, technology transfer programs, and capacity building, implemented through the WHO Global Observatory and NOTTO international partnerships.

8.2 Ethical Considerations

The rapid pace of technological innovation in transplantation raises critical ethical questions regarding equitable access to advanced therapies reaching diverse populations, informed consent for adequately explaining complex novel interventions, long-term implications of unknown effects from genetic and cellular modifications, and resource allocation balancing innovation costs with healthcare accessibility [89, 91].

8.3 Future Research Directions

8.3.1 Integration of Emerging Technologies

Future research will focus on integrating novel technologies such as synthetic biology, quantum computing, and advanced robotics into transplantation practice [74, 76]. These frontiers promise to further personalize care, expand the donor pool, and improve long-term outcomes.

8.3.2 Overcoming Implementation Barriers

Key research priorities include data standardization through the development of interoperable platforms for multi-center collaboration, biomarker validation via large-scale studies to establish

clinical utility, and cost-effectiveness through health economic analyses to support reimbursement decisions. Additionally, regulatory science involves adaptive trial designs for accelerated approval pathways [89, 91].

9. Computational Modeling

9.1 Predictive Analytics

9.1.1 Advanced Machine Learning Approaches

Machine learning algorithms continue to evolve, incorporating deep learning, reinforcement learning, and ensemble methods [92, 93]. These approaches enhance prediction of rejection, infection, and other complications, supporting proactive clinical management [68, 72].

9.1.2 Long-Term Forecasting Models

Predictive analytics enable simulation of treatment scenarios and long-term forecasting of graft survival, quality of life, and healthcare utilization [74, 75]. These tools support resource planning, patient counseling, and continuous improvement of transplantation programs.

9.2 Data Integration Strategies

9.2.1 Multi-Omics Integration

The integration of genomics, transcriptomics, proteomics, and metabolomics provides a comprehensive view of transplant biology [23, 24]. Multi-omics data support biomarker discovery, provide mechanistic insights, and facilitate the development of personalized interventions [68, 73].

9.2.2 Privacy-Preserving Analytics

Advancements in privacy-preserving analytics, such as federated learning and homomorphic encryption, enable secure analysis of sensitive patient data [76, 91]. These techniques support collaborative research while maintaining patient confidentiality and regulatory compliance.

10. Conclusions

This review underscores the transformative potential of precision medicine in liver and lung transplantation, highlighting the convergence of advanced immunological insights, regenerative medicine, and computational innovations. The integration of these multidisciplinary strategies enables a shift from empirical, standardized care to personalized, data-driven interventions that can enhance graft survival, reduce rejection rates, and improve patient quality of life.

Key findings include:

- **AI-driven approaches** show 85-92% accuracy in rejection prediction but face interpretability and bias challenges.
- **Regenerative therapies** demonstrate promising preclinical results but require regulatory framework development and cost reduction strategies.

- **Advanced immunomodulation** techniques like ECP achieve 60-80% response rates in refractory cases.
- **Global disparities** in access remain significant, with 10-fold variation in transplantation rates between regions.

The application of technologies such as extracorporeal photopheresis, gene editing, machine learning, and digital health platforms has already begun to reshape both clinical practice and research paradigms. However, these advances also present significant challenges, including data integration complexities, ethical considerations, global inequities in access, and the need for robust clinical validation.

11. Recommendations

To realize the full potential of precision medicine in liver and lung transplantation, the following strategic recommendations are proposed:

11.1 Research Priorities

1. **Large-scale, multi-center clinical trials** of emerging immunomodulatory and regenerative therapies with standardized outcome measures and a minimum 5-year follow-up.
2. **Investment in interoperable digital infrastructure** and multi-omics platforms for effective data integration and personalized risk stratification.
3. **Biomarker validation studies** with sample sizes >1000 patients to establish clinical utility and cost-effectiveness.

11.2 Implementation Strategies

4. **Foster interdisciplinary collaboration** between immunologists, bioengineers, computational scientists, and clinicians through funded consortium programs.
5. **Develop adaptive regulatory pathways** for accelerated approval of breakthrough therapies while maintaining safety standards.
6. **Establish value-based care models** that incentivize long-term outcomes over procedural volume.

11.3 Global Health Initiatives

7. **Create international data sharing consortia** with standardized protocols and privacy-preserving analytics.
8. **Implement hub-and-spoke telemedicine networks** to extend specialist care to underserved regions.
9. **Develop technology transfer programs** and capacity building initiatives for low-resource settings.

11.4 Policy and Economics

10. **Address cost barriers** through government subsidies, insurance coverage expansion, and innovative financing models.

11. **Ensure equitable access** through quota systems and international cooperation agreements.
12. **Harmonize regulatory standards** through international working groups and mutual recognition agreements.

Future research should prioritize translating preclinical breakthroughs into standardized protocols, expanding the integration of multi-omics, and fostering interdisciplinary collaboration to address persistent barriers. The field must remain vigilant regarding long-term safety, cost-effectiveness, and societal implications of novel therapies while ensuring that technological innovations benefit diverse patient populations globally.

Abbreviations

AI	Artificial Intelligence
BOS	Bronchiolitis Obliterans Syndrome
CAR	Chimeric Antigen Receptor
cfDNA	Cell-Free DNA
CLAD	Chronic Lung Allograft Dysfunction
CTLA-4	Cytotoxic T-Lymphocyte-Associated Protein 4
ECP	Extracorporeal Photopheresis
EMA	European Medicines Agency
FDA	Food and Drug Administration
GMP	Good Manufacturing Practice
GVHD	Graft-Versus-Host Disease
HLA	Human Leukocyte Antigen
ICH	International Conference on Harmonisation
iPSC	Induced Pluripotent Stem Cell
LAG-3	Lymphocyte-Activation Gene 3
MHC	Major Histocompatibility Complex
MSC	Mesenchymal Stem Cell
NF-κB	Nuclear Factor Kappa B
NOTTO	National Organ and Tissue Transplant Organisation
PD-1	Programmed Cell Death Protein 1
PET	Positron Emission Tomography
SPECT	Single-Photon Emission Computed Tomography
STAT	Signal Transducer and Activator of Transcription
Treg	Regulatory T Cell
UNOS	United Network for Organ Sharing
WHO	World Health Organization
XAI	Explainable Artificial Intelligence

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The corresponding author completed the study protocol and was the primary organizer of data collection and the manuscript's draft and revision process. The corresponding author wrote the article and ensured its accuracy.

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Competing Interests

The author hereby declares that they have no competing interests.

Data Availability Statement

All data are available and sharing is available as well as publication.

AI-Assisted Technologies Statement

In the revision of this manuscript, we utilized the AI language model GPT-4.1 to assist with language refinement and to adjust certain references. The AI tool was used solely to improve clarity and consistency, and all intellectual content, analysis, and interpretations remain the original work of the corresponding author. The use of AI assistance has been fully disclosed in accordance with the journal's policy.

References

1. Papamichalis P, Oikonomou KG, Xanthoudaki M, Valsamaki A, Skoura AL, Papathanasiou SK, et al. Extracorporeal organ support for critically ill patients: Overcoming the past, achieving the maximum at present, and redefining the future. *World J Crit Care Med.* 2024; 13: 92458.
2. Manek P, Madkaiker A, Gandhi H, Trivedi V, Prajapati J, Jain A, et al. Current status, challenges, and solution for heart transplantation in public sector hospital. *Indian J Transplant.* 2024; 18: 352-359.
3. Ehtuish EF. Perspective chapter: Self-sufficiency and equitable access in organ, tissue, and cell transplantation. *IntechOpen*; 2024. doi: 10.5772/intechopen.1007602.
4. Symeou S, Avramidou E, Papalois V, Tsoulfas G. Global transplantation: Lessons from organ transplantation organizations worldwide. *World J Transplant.* 2025; 15: 99683.
5. Kapnadak SG, Raghu G. Lung transplantation for interstitial lung disease. *Eur Respir Rev.* 2021; 30: 210017.
6. Swartz K, Mansour A, Alsunaid S. Lung transplant for chronic obstructive pulmonary disease. *Semin Respir Crit Care Med.* 2024; 45: 611-618.

7. Rieder F, Nagy LE, Maher TM, Distler JH, Kramann R, Hinz B, et al. Fibrosis: Cross-organ biology and pathways to development of innovative drugs. *Nat Rev Drug Discov.* 2025; 24: 543-569.
8. Greene CM, Abdulkadir M. Global respiratory health priorities at the beginning of the 21st century. *Eur Respir Rev.* 2024; 33: 230205.
9. Chavda VP, Bezbaruah R, Ahmed N, Alom S, Bhattacharjee B, Nalla LV, et al. Proinflammatory cytokines in chronic respiratory diseases and their management. *Cells.* 2025; 14: 400.
10. Kosuta I, Kelava T, Ostojic A, Sesa V, Mrzljak A, Lalic H. Immunology demystified: A guide for transplant hepatologists. *World J Transplant.* 2024; 14: 89772.
11. Khalil MAM, Sadagah NM, Hediki I, Tan J, Al-Qurashi SH. Donor-specific antibodies against HLA-C, HLA-DP and HLA-DQ and their implications in kidney transplantation. *World J Transplant.* 2025; 15: 99952.
12. Charmetant X, Pettigrew GJ, Thaunat O. Allorecognition unveiled: Integrating recent breakthroughs into the current paradigm. *Transpl Int.* 2024; 37: 13523.
13. Krishnamurthy P, Potter V, Dazzi F. Molecular basis of transplantation. *Mol Hematol.* 2024. doi: 10.1002/9781394180486.ch26.
14. Xie S, Xu C, Zhu Z, Qin C, Song X, Wang X, et al. Influence of CDC-XM and HLA compatibility on clinical outcomes in kidney transplant recipients during the post-operative recovery period: A retrospective analysis. *Exp Ther Med.* 2025; 29: 99.
15. Tsai CY, Lee CY, Chen JH, Chiang CK. Chronic antibody-mediated rejection and plasma cell ER Stress: Opportunities and challenges with calcineurin inhibitors. *Int J Mol Sci.* 2025; 26: 2711.
16. Diebold M, Mayer KA, Hidalgo L, Kozakowski N, Budde K, Böhmig GA. Chronic rejection after kidney transplantation. *Transplantation.* 2025; 109: 610-621.
17. Yokoyama M, Imai D, Wolfe S, George L, Sambommatsu Y, Khan AA, et al. Transplant immunology in liver transplant, rejection, and tolerance. *Livers.* 2024; 4: 420-434.
18. Slominska A, Loban K, Kinsella EA, Ho J, Sandal S. Supportive care in transplantation: A patient-centered care model to better support kidney transplant candidates and recipients. *World J Transplant.* 2024; 14: 97474.
19. Delgado CF, Ferretti MT, Carnevale A. Beyond one-size-fits-all: Precision medicine and novel technologies for sex-and gender-inclusive COVID-19 pandemic management. In: *Innovating Health Against Future Pandemics.* Elsevier; 2024. pp. 133-156.
20. Prabhakar PK. Advancements in precision medicine: Tailoring healthcare to individual needs. In: *Biomedical Research Developments for Improved Healthcare.* IGI Global Scientific Publishing; 2024. pp. 310-326.
21. Addissouky TA. Nanopore sequencing of cell-free DNA: An emerging liquid biopsy approach for brain tumor molecular profiling. *J Exp Pathol.* 2024; 5: 49-60.
22. Olawade DB, Marinze S, Qureshi N, Weerasinghe K, Teke J. The impact of artificial intelligence and machine learning in organ retrieval and transplantation: A comprehensive review. *Curr Res Transl Med.* 2025; 73: 103493.
23. Vitorino R. Transforming clinical research: The power of high-throughput omics integration. *Proteomes.* 2024; 12: 25.
24. Saliba A, Du Y, Feng T, Garmire L. Multi-omics integration in nephrology: Advances, challenges, and future directions. *Semin Nephrol.* 2024; 44: 151584.
25. Addissouky TA. Precision medicine for personalized cholecystitis care: Integrating molecular diagnostics and biotherapeutics. *Bull Natl Res Cent.* 2024; 48: 89.

26. Hamdy NM, Basalious EB, El-Sisi MG, Nasr M, Kabel AM, Nossier ES, et al. Advancements in current one-size-fits-all therapies compared to future treatment innovations for better improved chemotherapeutic outcomes: A step-toward personalized medicine. *Curr Med Res Opin.* 2024; 40: 1943-1961.
27. Peter A, Vermeulen M, Van Delen M, Dams A, Peeters S, De Reu H, et al. Physiological oxygen levels in the microenvironment program ex vivo-generated conventional dendritic cells toward a tolerogenic phenotype. *Cells.* 2025; 14: 736.
28. Wolner L, William-Olsson J, Podesser BK, Zuckermann A, Pilat N. Tolerogenic therapies in cardiac transplantation. *Int J Mol Sci.* 2025; 26: 3968.
29. Ohm B, Giannou AD, Harriman D, Oh J, Jungraithmayr W, Zazara DE. Chimerism and immunological tolerance in solid organ transplantation. *Semin Immunopathol.* 2025; 47: 27.
30. Herenda V, Rebić D, Hamzić-Mehmedbašić A, Ribić-Mrkonja A, Odobašić M. When there is no need for immunosupresives: Combined bone marrow and kidney transplantation. *IntechOpen;* 2024. doi: 10.5772/intechopen.1006524.
31. Zhang J, Feng S, Geng Y, Wang X, Wang Z, Liu Y. Anti-inflammatory phenotypes of immune cells after myocardial infarction and prospects of therapeutic strategy. *Naunyn Schmiedebergs Arch Pharmacol.* 2025. doi: 10.1007/s00210-025-04167-y.
32. Lei T, Wang Y, Zhang Y, Yang Y, Cao J, Huang J, et al. Leveraging CRISPR gene editing technology to optimize the efficacy, safety and accessibility of CAR T-cell therapy. *Leukemia.* 2024; 38: 2517-2543.
33. Du G, Dou C, Sun P, Wang S, Liu J, Ma L. Regulatory T cells and immune escape in HCC: Understanding the tumor microenvironment and advancing CAR-T cell therapy. *Front Immunol.* 2024; 15: 1431211.
34. Ning J, Wang Y, Tao Z. The complex role of immune cells in antigen presentation and regulation of T-cell responses in hepatocellular carcinoma: Progress, challenges, and future directions. *Front Immunol.* 2024; 15: 1483834.
35. Palma M, Qi B. Advancing phage therapy: A comprehensive review of the safety, efficacy, and future prospects for the targeted treatment of bacterial infections. *Infect Dis Rep.* 2024; 16: 1127.
36. Batinić J, Dreta B, Rinčić G, Mrdeža A, Jakobac KM, Krišto DR, et al. Outcomes of Ixazomib Treatment in Relapsed and Refractory Multiple Myeloma: Insights from Croatian Cooperative Group for Hematologic Diseases (KROHEM). *Medicina.* 2024; 60: 1905.
37. Mallenahalli Neeekantappa V, Kamath A, Bharathi Rajaduraivelpandian P. Safety profile of monoclonal antibodies and subsequent drug developments in the treatment of paroxysmal nocturnal hemoglobinuria. *Medicina.* 2024; 60: 379.
38. Wu S, Lin M, Ji M, Wang T. Exploring core knowledge in interdisciplinary research: Insights from topic modeling analysis. *Appl Sci.* 2024; 14: 10054.
39. Sharaby I. AI-driven approach for diagnosis of renal transplant rejection based on biomarkers identification and integration. Louisville, Kentucky: University of Louisville; 2024; Paper 4486.
40. Al Moussawy M, Lakkis ZS, Ansari ZA, Cherukuri AR, Abou-Daya KI. The transformative potential of artificial intelligence in solid organ transplantation. *Front Transplant.* 2024; 3: 1361491.
41. Di Teodoro G. Toward personalized medicine and transparent decision-making with Machine Learning Models for complex diseases: A focus on HIV-1 and type 2 Diabetes. Roma, Italy: Sapienza Università di Roma; 2024.

42. Eskandari SK, Daccache A, Azzi JR. Chimeric antigen receptor Treg therapy in transplantation. *Trends Immunol.* 2024; 45: 48-61.
43. Addissouky TA, El Sayed IET, Ali MM, Wang Y, El Baz A, Elarabany N, et al. Oxidative stress and inflammation: Elucidating mechanisms of smoking-attributable pathology for therapeutic targeting. *Bull Natl Res Cent.* 2024; 48: 16.
44. Liu C, Shi C, Wang S, Qi R, Gu W, Yu F, et al. Bridging the gap: How patient-derived lung cancer organoids are transforming personalized medicine. *Front Cell Dev Biol.* 2025; 13: 1554268.
45. Goecke T, Ius F, Ruhparwar A, Martin U. Unlocking the future: Pluripotent stem cell-based lung repair. *Cells.* 2024; 13: 635.
46. Lasorsa F, Rutigliano M, Milella M, d'Amati A, Crocetto F, Pandolfo SD, et al. Ischemia-reperfusion injury in kidney transplantation: Mechanisms and potential therapeutic targets. *Int J Mol Sci.* 2024; 25: 4332.
47. Stimmeder S, Leber B, Sucher R, Stiegler P. Genetic modulation: Future trends toward graft optimization during machine perfusion. *Transplantation.* 2024; 108: 614-624.
48. Eskandar K. Bioimpressão no Transplante de Órgãos: Dos modelos Experimentais às Perspectivas Clínicas. *Braz J Transplant.* 2025; 28: e1825.
49. Zhao X, Ma Y, Lei Z. Advanced optical imaging technology in the near infrared window for cell tracking in vivo. *Coord Chem Rev.* 2024; 521: 216178.
50. Rezaei Z, Wang N, Rodriguez ADJA, Higashi S, Shin SR. Biosensors in biomedical research: Bridging cell and tissue engineering and real-time monitoring. *Curr Opin Biomed Eng.* 2025; 34: 100582.
51. Xiong Y, Mi B, Liu G, Zhao Y. Microenvironment-sensitive nanozymes for tissue regeneration. *Biomaterials.* 2024; 309: 122585.
52. Chullo G, Panisello-Rosello A, Marquez N, Colmenero J, Brunet M, Pera M, et al. Focusing on ischemic reperfusion injury in the new era of dynamic machine perfusion in liver transplantation. *Int J Mol Sci.* 2024; 25: 1117.
53. Yang S, Hou W, Liu L. Progress in preservation of intestinal grafts by oxygenated hypothermic machine perfusion. *Transplant Rev.* 2024; 38: 100802.
54. López-Martínez S, Simón C, Santamaria X. Normothermic machine perfusion systems: Where do we go from here? *Transplantation.* 2024; 108: 22-44.
55. Addissouky TA, El Sayed IET, Ali MM, Alubiady MHS. Optical insights into fibrotic livers: Applications of near-infrared spectroscopy and machine learning. *Arch Gastroenterol Res.* 2024; 5: 1-10.
56. Addissouky TA, El Sayed IE, Ali MM, Wang Y, El Baz A, Khalil AA, et al. Can vaccines stop cancer before it starts? Assessing the promise of prophylactic immunization against high-risk preneoplastic lesions. *J Cell Immunol.* 2023; 5: 127-140.
57. Zhou Y, Que T, Yu L, Que S, Xu J, Liu Z. Current understanding on inferior quality of liver grafts by donation after circulatory death based on multi-omics data. *Front Immunol.* 2025; 16: 1548735.
58. Ho BX, Teo AKK, Ng NHJ. Innovations in bio-engineering and cell-based approaches to address immunological challenges in islet transplantation. *Front Immunol.* 2024; 15: 1375177.
59. Shiwarski DJ, Hudson AR, Tashman JW, Bakirci E, Moss S, Coffin BD, et al. 3D bioprinting of collagen-based high-resolution internally perfusable scaffolds for engineering fully biologic tissue systems. *Sci Adv.* 2025; 11: eadu5905.

60. Stoian A, Adil A, Biniazan F, Haykal S. Two decades of advances and limitations in organ recellularization. *Curr Issues Mol Biol*. 2024; 46: 9179-9214.
61. Liu H, Xing F, Yu P, Lu R, Ma S, Shakya S, et al. Biomimetic fabrication bioprinting strategies based on decellularized extracellular matrix for musculoskeletal tissue regeneration: Current status and future perspectives. *Mater Des*. 2024; 243: 113072.
62. Sun M, Tang L, Yang X, Lu J, He H, Lin J, et al. Advancements of biomaterials in oral tissue engineering: Past, present, and future. *Beni Suef Univ J Basic Appl Sci*. 2024; 13: 104.
63. Wang M, Hong Y, Fu X, Sun X. Advances and applications of biomimetic biomaterials for endogenous skin regeneration. *Bioact Mater*. 2024; 39: 492-520.
64. Mizera J, Pondel M, Kepinska M, Jerzak P, Banasik M. Advancements in artificial intelligence for kidney transplantology: A comprehensive review of current applications and predictive models. *J Clin Med*. 2025; 14: 975.
65. Chafai N, Bonizzi L, Botti S, Badaoui B. Emerging applications of machine learning in genomic medicine and healthcare. *Crit Rev Clin Lab Sci*. 2024; 61: 140-163.
66. Pantanowitz L, Pearce T, Abukhiran I, Hanna M, Wheeler S, Soong TR, et al. Nongenerative artificial intelligence in medicine: Advancements and applications in supervised and unsupervised machine learning. *Mod Pathol*. 2025; 38: 100680.
67. Chen YM, Hsiao TH, Lin CH, Fann YC. Unlocking precision medicine: Clinical applications of integrating health records, genetics, and immunology through artificial intelligence. *J Biomed Sci*. 2025; 32: 16.
68. Lin M, Guo J, Gu Z, Tang W, Tao H, You S, et al. Machine learning and multi-omics integration: advancing cardiovascular translational research and clinical practice. *J Transl Med*. 2025; 23: 388.
69. Westhoff CM, Floch A. Blood group genotype matching for transfusion. *Br J Haematol*. 2025; 206: 18-32.
70. Tiwari A, Mukherjee S. Role of complement-dependent cytotoxicity crossmatch and HLA typing in solid organ transplant. *Rev Recent Clin Trials*. 2024; 19: 34-52.
71. Goktas P, Damadoglu E. Future of allergy and immunology: Is artificial intelligence the key in the digital era? *Ann Allergy Asthma Immunol*. 2025; 134: 396-407.e2.
72. Ogunjobi TT, Ohaeri PN, Akintola OT, Atanda DO, Orji FP, Adebayo JO, et al. Bioinformatics applications in chronic diseases: A comprehensive review of genomic, transcriptomics, proteomic, metabolomics, and machine learning approaches. *Medinformatics*. 2024. doi: 10.47852/bonviewMEDIN42022335.
73. Liu X, Shi J, Jiao Y, An J, Tian J, Yang Y, et al. Integrated multi-omics with machine learning to uncover the intricacies of kidney disease. *Brief Bioinform*. 2024; 25: bbae364.
74. Sen S, Kilic KD. Digital twins in medicine, ai-driven personalized healthcare, and predictive analytics. In: *AI-powered digital twins for predictive healthcare: Creating virtual replicas of humans*. IGI Global Scientific Publishing; 2025. pp. 359-396.
75. Islam MS, Kalmady SV, Hindle A, Sandhu R, Sun W, Sepehrvand N, et al. Diagnostic and prognostic electrocardiogram-based models for rapid clinical applications. *Can J Cardiol*. 2024; 40: 1788-1803.
76. Tyagi AK, Seranmadevi R. Blockchain for enhancing security and privacy in the smart healthcare. In: *Digital Twin and Blockchain for Smart Cities*. Wiley; 2024. pp. 343-370.

77. Yu B, Ma W. Biomarker discovery in hepatocellular carcinoma (HCC) for personalized treatment and enhanced prognosis. *Cytokine Growth Factor Rev.* 2024; 79: 29-38.
78. Cummings JL, Teunissen CE, Fiske BK, Le Ber I, Wildsmith KR, Schöll M, et al. Biomarker-guided decision making in clinical drug development for neurodegenerative disorders. *Nat Rev Drug Discov.* 2025; 24: 589-609.
79. Soltani A, Habibzadeh A, Karimi H, Afra F, Eini S, Nazari H, et al. T-cell responses during cancer immunotherapy through the use of CT, MRI, and PET. In: *Cancer immunotherapy and nanobiotechnology: An interdisciplinary approach*. Cham: Springer; 2024. pp. 429-451.
80. Malviya G, Singh PK. Molecular imaging: From the cellular players to bedside. In: *Evolving Landscape of Molecular Diagnostics*. Elsevier; 2024. pp. 87-120.
81. Kanakaprabha S, Kumar GG, Reddy BP, Raju YR, Rai PCM. Wearable devices and health monitoring: Big data and AI for remote patient care. In: *Intelligent data analytics for bioinformatics and biomedical systems*. Wiley; 2024. pp. 291-311.
82. Abhinav V, Basu P, Verma SS, Verma J, Das A, Kumari S, et al. Advancements in wearable and implantable BioMEMS devices: Transforming healthcare through technology. *Micromachines.* 2025; 16: 522.
83. Song Y, Wang Y, Wang W, Xie Y, Zhang J, Liu J, et al. Advancements in noninvasive techniques for transplant rejection: From biomarker detection to molecular imaging. *J Transl Med.* 2025; 23: 147.
84. Cao C, Yuan L, Wang Y, Liu H, Cuello Garcia H, Huang H, et al. Analysis of the primary factors influencing donor derived cell-free DNA testing in kidney transplantation. *Front Immunol.* 2024; 15: 1435578.
85. Al-Shehri DAA, Altulaih SMA, Alharbi AAM. Leveraging telehealth for medication optimization: Interdisciplinary integration of nursing and pharmacy. *Int J Health Sci.* 2020; 4: 458-477.
86. Bhambri P, Khang A. Managing and monitoring patient's healthcare using AI and IoT technologies. In: *Driving Smart Medical Diagnosis Through AI-Powered Technologies and Applications*. IGI Global Scientific Publishing; 2024. pp. 1-23.
87. Wiedermann CJ. Preserving continuity and trust in primary care: Strategies for implementing team-based models in South Tyrol, Italy. *Int J Environ Res Public Health.* 2025; 22: 477.
88. Khorram-Manesh A, Burkle Jr FM, Goniewicz K. Pandemics: Past, present, and future: Multitasking challenges in need of cross-disciplinary, transdisciplinary, and multidisciplinary collaborative solutions. *Osong Public Health and Res Perspect.* 2024; 15: 267.
89. Lawler M, Keeling P, Kholmanskikh O, Minnaard W, Moehlig-Zuttermeister H, Normanno N, et al. Empowering effective biomarker-driven precision oncology: A call to action. *Eur J Cancer.* 2024; 209: 114225.
90. Chan HW, Kuo DY, Shueng PW, Chuang HY. Visualizing the tumor microenvironment: Molecular imaging probes target extracellular matrix, vascular networks, and immunosuppressive cells. *Pharmaceuticals.* 2024; 17: 1663.
91. Okoli UI, Obi OC, Adewusi AO, Abrahams TO. Machine learning in cybersecurity: A review of threat detection and defense mechanisms. *World J Adv Res Rev.* 2024; 21: 2286-2295.
92. Terven J. Deep reinforcement learning: A chronological overview and methods. *AI.* 2025; 6: 46.
93. Wilson A, Anwar MR. The future of adaptive machine learning algorithms in high-dimensional data processing. *Int Trans Artif Intell.* 2024; 3: 97-107.