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Regenerative Nephrology: From Endogenous Kidney Repair to Bioengineered Organs — Current Evidence, Clinical Applications, and Future Perspectives

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Abstract

The Chronic Kidney Disease (CKD) (About 850 million patients globally, Global Burden of Disease CKD Collaboration 2020) and Acute Kidney Injury (AKI) (About 13 to 15 million cases yearly, KDIGO 2024) continue to be one of the most common causes of morbidity, mortality. Conventional therapies slow disease progression or replace kidney function through dialysis and transplantation but do not restore damaged renal tissue. Regenerative nephrology has emerged as a multidisciplinary field integrating stem cell biology, developmental nephrology, tissue engineering, extracellular vesicle biology, gene editing, and precision medicine to repair or replace injured kidneys. Endogenous tubular repair, Mesenchymal Stromal Cells (MSCs), induced Pluripotent Stem Cells (iPSCs), extracellular vesicles, kidney organoids, kidney-on-chip systems, decellularized scaffolds, three-dimensional bioprinting, bioartificial and wearable kidneys, and genetically engineered xenotransplantation together define the current translational landscape. Early-phase clinical trials of MSC and extracellular-vesicle therapies show encouraging safety but inconclusive efficacy; kidney organoids and gene-editing platforms remain largely preclinical; bioartificial kidneys and pig-to-human kidney xenotransplantation have entered first-in-human feasibility studies. Major obstacles include cellular immaturity, poor vascularization, manufacturing standardization, immune compatibility, fibrosis reversal, and regulatory classification. In this review, the key principles, therapeutic potential, problems and challenges, as well as future prospects of regenerative nephrology are discussed in the context of the emerging paradigm of biological regeneration versus traditional renal replacement therapies.

Keywords: Regenerative Nephrology; Kidney Regeneration; Mesenchymal Stromal Cells; Kidney Organoids; Gene Editing; Tissue Engineering; Bioartificial Kidney; Extracellular Vesicles; Precision Medicine; Chronic Kidney Disease; Acute Kidney Injury; Xenotransplantation

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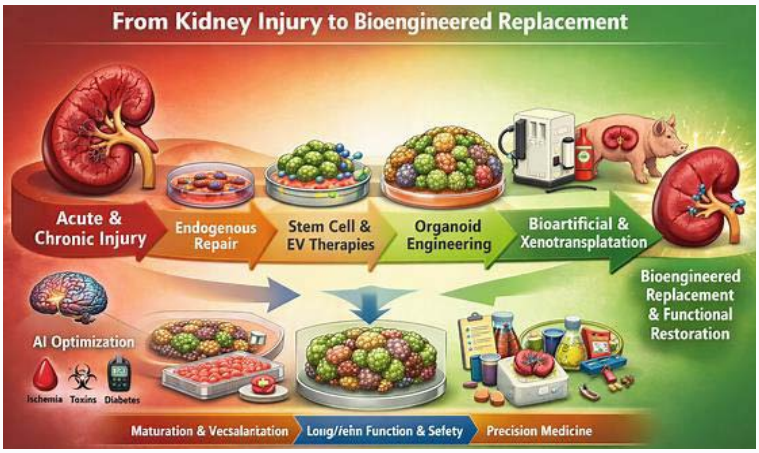

Graphical Abstract: Transition from Kidney Injury to Bioengineered Replacement.
This visual abstract represents the entire process continuum of regeneration from acute/chronic injuries to bio-engineered restoration of functionality. This arrow-flowchart represents the path from natural regeneration, stem cells and extracellular vesicles therapy, organoid engineering and finally bio-artificial or xenogeneic transplantation techniques. These icons of AI optimization, gene editing and precision medicine represent the use of technologies in regenerative nephrology.

Abbreviations

AKI: Acute Kidney Injury; CKD: Chronic Kidney Disease; ESKD: End-Stage Kidney Disease; MSC: Mesenchymal Stromal/Stem Cell; iPSC: induced Pluripotent Stem Cell; ESC: Embryonic Stem Cell; EV: Extracellular Vesicle; miRNA: microRNA; NPC: Nephron Progenitor Cell; UB: Ureteric Bud; MM: Metanephric Mesenchyme; CAKUT: Congenital Anomalies of the Kidney and Urinary Tract; SASP: Senescence-Associated Secretory Phenotype; TGF-β: Transforming Growth Factor-beta; BMP: Bone Morphogenetic Protein; VEGF: Vascular Endothelial Growth Factor; HGF: Hepatocyte Growth Factor; RAD: Renal Tubule Assist Device; WAK: Wearable Artificial Kidney; CRISPR: Clustered Regularly Interspaced Short Palindromic Repeats; PKD: Polycystic Kidney Disease; ADPKD: Autosomal Dominant Polycystic Kidney Disease; FSGS: Focal Segmental Glomerulosclerosis; DKD: Diabetic Kidney Disease; AI: Artificial Intelligence; GMP: Good Manufacturing Practice

Introduction

Kidney disease is a major and growing global health burden. CKD and AKI are associated with substantial morbidity, premature mortality, and escalating healthcare costs, and current therapeutic strategies remain largely supportive rather than restorative. Pharmacological approaches slow disease progression but do not reverse established renal fibrosis, the final common pathway of most progressive nephropathies [1]. Dialysis and kidney transplantation remain the standard renal replacement therapies for ESKD, but dialysis carries substantial cardiovascular morbidity and transplantation is constrained by donor shortage, lifelong immunosuppression, and chronic allograft dysfunction [2].

The traditional view of the adult mammalian kidney as a terminally differentiated, non-regenerative organ has been revised over the past two decades. Experimental work has shown that the injured kidney possesses a substantial but limited regenerative capacity for tubular repair through dedifferentiation, proliferation, and redifferentiation of surviving epithelial cells [3].

Regenerative nephrology has emerged as a field seeking not only to preserve residual renal function but to restore damaged kidney tissue through biological repair and tissue replacement, drawing on stem cell therapy, extracellular vesicle-based interventions, iPSC technology, kidney organoids, tissue engineering, gene editing, xenotransplantation, and bioartificial kidneys [4]. This review summarizes the historical evolution, biological foundations, principal therapeutic platforms, clinical translation, and future perspectives of regenerative nephrology (Table 1).

Historical Evolution of Regenerative Nephrology

The main discoveries in the field of tissue engineering were those involving the application of cells, scaffolding, and biological information to restore tissue function [5]. The advent of pluripotent human cells through the development of human embryonic stem cells was one such discovery [5], whereas the discovery of the conversion of somatic cells into pluripotent stem cells via induced reprogramming helped researchers to circumvent ethical problems and patient-specific modeling [5]. In parallel, studies of the injured kidney overturned the assumption that nephron loss was irreversible, demonstrating that surviving tubular epithelial cells retain substantial capacity for dedifferentiation and repair after ischemic or toxic injury [5]. These two lines of investigation, pluripotent stem cell biology and intrinsic renal repair, form the conceptual foundation of contemporary regenerative nephrology (Figure 1) (Table 2) [4].

Kidney Development and Endogenous Renal Repair

Most regenerative strategies aim to recapitulate the developmental programs that build the kidney. The metanephros arises from reciprocal induction between the ureteric bud and the metanephric mesenchyme, and nephron progenitor cells within the cap mesenchyme retain the capacity to generate every epithelial nephron segment except the collecting duct; their depletion shortly before birth and during late fetal development leaves humans without a nephron progenitor reserve in adult life, a key reason why nephron loss in adults is generally irreversible [14].

Table 1: Historical milestones in regenerative nephrology.

Period	Milestone	Significance	Ref.
1990s	Emergence of tissue engineering principles	Established combining cells, scaffolds, and biological signals for tissue restoration	[5]
1998	Human embryonic stem cell lines derived	Provided first pluripotent human cell source	[6]
2006-2007	Induced pluripotent stem cells generated	Enabled patient-specific regenerative medicine and disease modeling	[7]
2000s	Intrinsic tubular repair mechanisms characterized	Showed kidney repair does not depend solely on circulating stem cells	[3]
2013	First bioengineered kidney transplantation model	Demonstrated feasibility of whole-organ tissue engineering	[8]
2015	Human kidney organoids generated from iPSCs	Created platforms for disease modeling and drug testing	[9,10]
2022–2025	First genetically modified pig kidney xenotransplantation into human's studies	Marked entry of gene-edited xenotransplantation into human study	[11]

Table 2: Stem cell platforms investigated in regenerative nephrology.

Cell source	Advantages	Limitations	Ref.
Embryonic stem cells	Unlimited proliferation, pluripotency	Ethical concerns, tumor risk	[6]
Induced pluripotent stem cells	Patient-specific, avoids embryo use	Genomic instability, maturation limits	[7]
Bone marrow MSCs	Most studied, immunomodulatory	Invasive harvest, donor-age effects	[12]
Mesenchymal stem cells (MSCs)	Potential long-term benefits	Insufficient long-term data	[13]
Renal progenitor cells	Kidney-specific regenerative potential	Isolation and identity remain debated	[14]

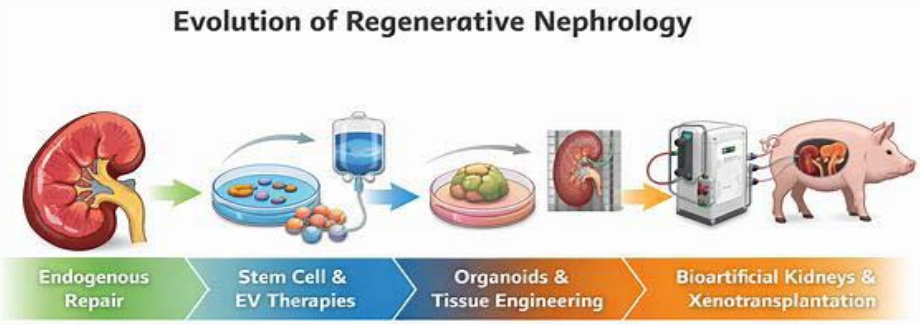

Figure 1: Evolution of regenerative nephrology. The diagram above represents the process of recovery of the kidney, which ranges from self-healing to the bioengineering method. This ranges from self-tubular regeneration to the use of stem cell therapy and extracellular vesicles therapy through the generation of organoids to the artificial kidney technology and finally xenotransplantation. The arrows connecting each stage represent the continuous process of kidney therapy from cellular to organ level.

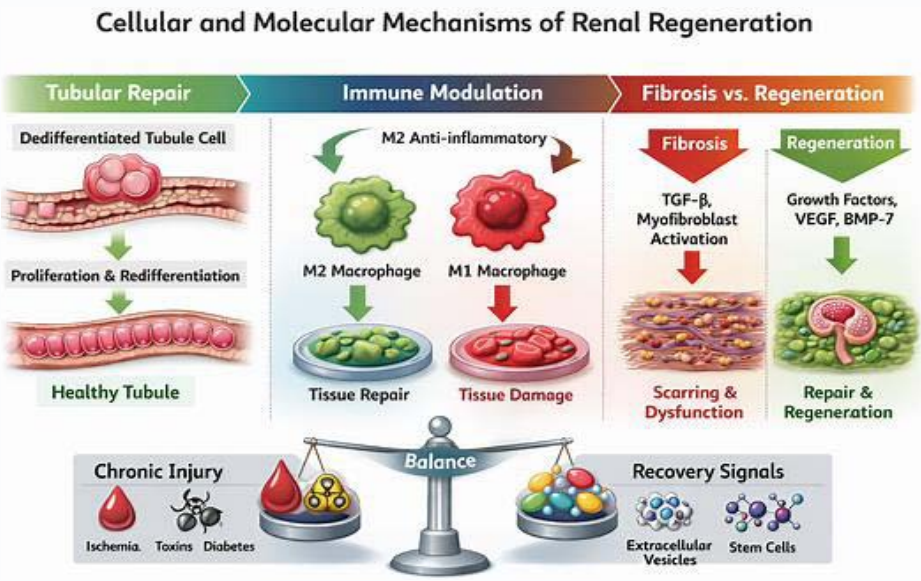

Figure 2: Cellular and molecular mechanisms of renal regeneration. Above is the diagram of how tubular epithelial cells de-differentiate, proliferate, and re-differentiate through the injury process involving the regulation of immune modulation and growth factors. M1 and M2 macrophages show the correlation between inflammation and healing, whereas the opposing mechanisms of fibrosis and regeneration show the mechanisms of action of TGF-*β*, VEGF, and BMP-7. Figure 2 above shows how oxidative stress and senescence determine the final effect of renal injury.

Following acute injury, renal recovery is now understood to reflect repair of surviving tissue rather than generation of new nephrons. Tubular Epithelial Cells undergo de-differentiation, migration, proliferation, and re-differentiation, where they temporarily express developmental genes before reverting to an epithelial state [3, 15]. The process is regulated by the interaction of immune cells, endothelial cells, fibroblasts, and pericytes, where pro-inflammatory macrophages clear dead cellular material while anti-inflammatory macrophages promote new vessels formation and proliferation of epithelial cells, and lack of which leads to progressive scarring and CKD [16]. Cellular senescence has emerged as a further mechanism linking AKI to CKD: senescent tubular cells secrete a senescence-associated secretory phenotype that perpetuates inflammation and impairs regeneration [17, 18].

Molecular Pathways Governing Regeneration

Kidney regeneration depends on developmental signaling networks that also govern fibrosis when dysregulated (Figure 2). Transforming growth factor-beta is a central mediator of renal fibrosis, and myofibroblast activation from multiple cellular origins has been directly demonstrated in human kidney tissue; because global inhibition of these pathways impairs physiological repair, selective modulation rather than total inhibition is the current therapeutic goal [19, 20]. Reversing established fibrosis, rather than merely slowing its progression, remains an unmet objective of anti-fibrotic drug development [21]. Cellular senescence and its secretory phenotype represent an additional, partially independent target for combination therapy [17, 18]. Mitochondrial dysfunction is a further common pathway of tubular injury, given the heavy reliance of proximal tubular cells on oxidative phosphorylation; restoring mitochondrial function, including through transfer of functional mitochondria from mesenchymal stromal cells, is an emerging regenerative strategy, particularly in diabetic kidney disease [22,23].

Stem Cell-Based Therapies

Stem cell therapy remains the most extensively investigated regenerative approach in nephrology (Figure 3). Mesenchymal

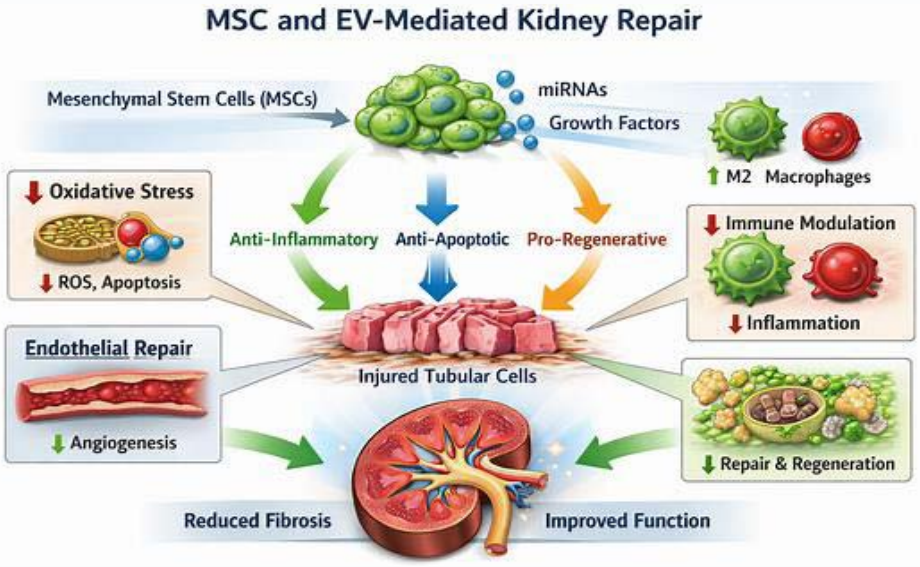

Figure 3: MSC and EV mediated kidney repair. The diagram above shows how paracrine signaling through the EVs of the MSCs helps promote kidney repair. The MSCs secrete the EVs that carry microRNA and growth factors with an anti-inflammatory, anti-apoptotic, and tissue-repairing effect on the injured tubular cells. The squares illustrate how oxidative stress is reduced, endothelial cells repaired, and immunomodulation achieved to improve kidney function and limit fibrosis.

Table 3: Extracellular vesicle and regenerative strategies.

Platform	Mechanism	Indications studied	Ref.
MSC-derived microvesicles	Paracrine anti-inflammatory, anti-apoptotic signaling	Acute tubular injury (preclinical)	[27]
EV-mediated kidney regeneration	Anti-inflammatory, anti-fibrotic paracrine effects	AKI and CKD models	[28]
Standardized EV characterization	Position statement defining EV nomenclature and study criteria	Field-wide methodology standard	[26]
EV clinical translation	Cell-free regenerative therapy	AKI, CKD (early translational)	[29]

Stromal Cells (MSCs), multipotent fibroblast-like cells isolated from bone marrow, adipose tissue, umbilical cord, placenta, or dental pulp, account for the majority of clinical trials in this field [12]. Only a minority of infused MSCs engraft permanently in the kidney; their principal effects are attributed instead to paracrine signaling that reduces inflammation, oxidative stress and apoptosis, and promotes endothelial repair in models of ischemic acute renal failure [24]. Early clinical experience with autologous MSCs in living-related kidney transplantation has demonstrated feasibility and an acceptable safety profile [13], and broader reviews of cell therapy for the kidney describe encouraging safety with more variable evidence of efficacy attributable to differences in cell source, dose, timing, and route of administration [25].

Induced pluripotent stem cells offer patient-specific, ethically uncontroversial pluripotent cells that can be directed toward podocytes, proximal tubular cells, collecting duct cells, nephron progenitors, and kidney organoids [7], but genomic instability, epigenetic variability, tumorigenicity, and manufacturing complexity remain unresolved. Embryonic stem cells retain the greatest pluripotency but are limited by ethical, immunological, and regulatory constraints and have been largely superseded by iPSC approaches for translational work [6]. Resident renal progenitor-like populations remain of interest as autologous, kidney-intrinsic regenerative candidates within the developmental niche described above, although their contribution to physiological repair is debated [14].

Cell-Free Regenerative Therapies: Extracellular Vesicles and the Secretome

Because much of the therapeutic benefit of MSC administration is mediated by secreted factors rather than cell engraftment, Extracellular Vesicles (EVs), including exosomes, micro vesicles, and apoptotic bodies, mRNAs, proteins, and lipids, have emerged as a leading cell-free alternative; a position statement from the International Society for Extracellular Vesicles has standardized minimal criteria for their study [26]. MSC-derived micro vesicles protect against acute tubular injury in preclinical models, attenuating apoptosis and inflammation [27]. Broader reviews describe how stem-cell-derived EVs contribute to kidney regeneration through anti-inflammatory, anti-apoptotic, and anti-fibrotic paracrine signaling [28], and clinical-translation reviews have outlined the therapeutic application of extracellular vesicles across a range of kidney diseases, including AKI and CKD [29]. Compared with cellular therapy, EV-based approaches offer lower immunogenicity, easier storage, and greater potential for standardized pharmaceutical-scale manufacture, though defined potency assays and reproducible isolation protocols remain unresolved regulatory and manufacturing challenges (Table 3).

Kidney Organoids, Kidney-on-Chip Systems, and Tissue Engineering

Most studies involving kidney organoids have focused on nephron progenitor-derived lineages, for example, podocytes, proximal tubules, and distal tubules. Nevertheless, the primary drawback of early kidney organoids was the absence of the collecting duct lineage derived from ureteric bud progenitors, which are necessary for proper water and electrolytes transport. Therefore, the lack of functionality of collecting system limits both the physiological and translational capabilities of these platforms. New research findings include

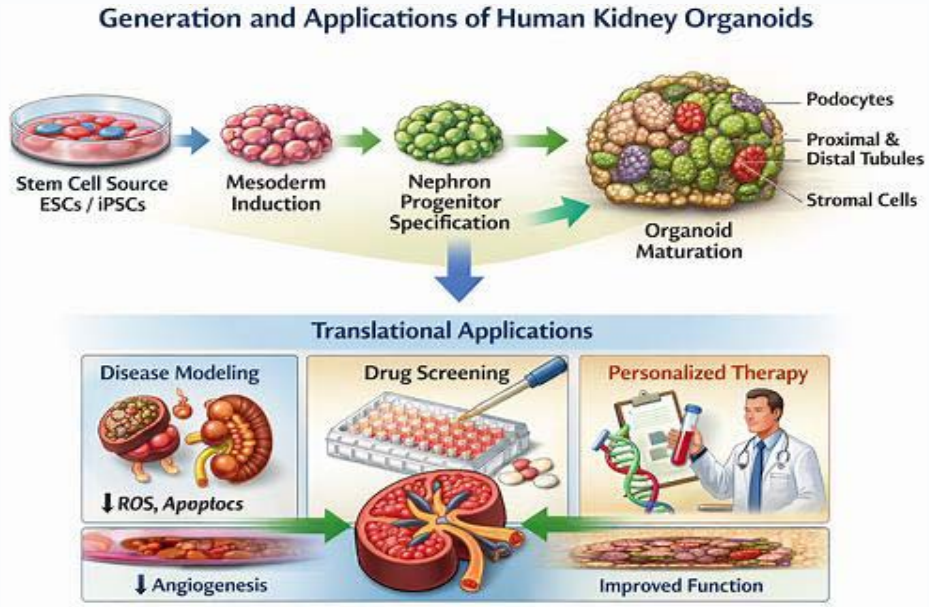

Figure 4: Generation and applications of human kidney organoids. The top figure demonstrates the process of differentiation of pluripotent stem cells starting from mesodermal induction followed by nephrogenic progenitor induction and organoid formation, which results in the formation of organoids containing podocyte, tubular epithelium, and stromal cell compartments. Conversely, the bottom figure demonstrates the application of the method for disease modeling (polycystic kidney disease, Alport syndrome), nephrotoxicity testing of drugs, and personalized medicine.

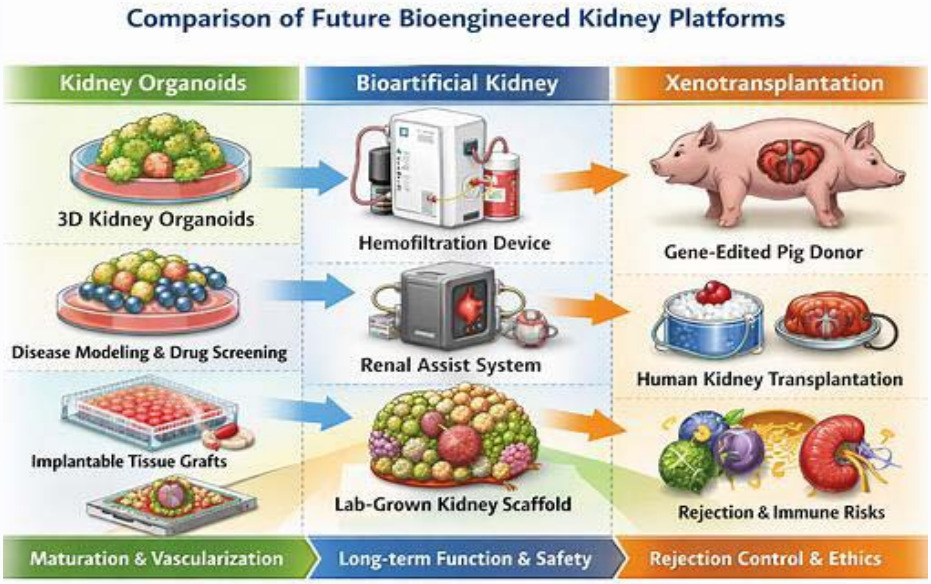

Figure 5: Comparison of future bioengineered kidney platforms. The comparative analysis will look at the three popular regenerative medical techniques such as kidney organoids, bioartificial kidneys, and xenotransplantation. Each of the sections has an overview of the technological options and their advantages and disadvantages such as organoid formation and vascularization, safety and functionality of the bioartificial kidney, and rejection of the xenotransplant.

different methods to include ureteric bud and nephron progenitors in kidney organoids to create complete and draining organoids that represent the structure of kidney better. For instance, the fusion technique between the distal nephrons and ureteric buds creates an organoid with a properly working collecting system, whereas the creation of perfusable 3D model of ureteric buds and collecting ducts demonstrates the potential of engineering such drainage system. Despite these promising results, there are still many obstacles to overcome in order to achieve the development of mature vascularized organoid with the working collecting system. Overcoming these limitations will be crucial to make progress in clinical applications of kidney organoids in nephrology [10]. Patient- and stem-cell-derived organoids have been used to reconstitute glomerular-capillary-wall function and to model polycystic kidney disease and other genetic nephropathies, and to test nephrotoxic and therapeutic compounds [30, 31]. Current organoids remain developmentally immature and poorly vascularized, though incorporating endothelial networks improves maturation and physiological relevance [32]; kidney-on-chip systems combine microfluidic engineering with human renal cells to reproduce physiological flow and are increasingly used for

Table 4: Kidney organoid and Kidney-on-Chip platforms.

Platform / Approach	Key Features / Applications	Ref.
iPSC-derived kidney organoids	Recapitulate nephrogenesis, model human kidney development	[9, 10]
Podocyte organoids	Mature podocytes reconstituting glomerular-capillary wall function	[30]
Patient-derived cystic organoids	Model polycystic kidney disease and cystogenesis	[31]
Vascularized kidney organoids	Improved maturation and perfusion, bioengineered vascularization	[32]
Kidney-on-chip systems	Microfluidic devices mimicking nephron physiology	[33]
Biomaterial scaffolds	Provide supportive extracellular matrix for cell growth	[34]
Whole-organ decellularized scaffolds	Retain native architecture for recellularization	[35]
3D bioprinting	Layer-by-layer fabrication of renal tissue constructs	[36]

Table 5: Bioartificial kidneys, wearable devices, and xenotransplantation.

Technology	Development stage	Main advantage	Ref.
Renal tubule assist device	Clinical evaluation completed	Metabolic/endocrine function beyond dialysis	[38]
Implantable bioartificial kidney (silicon nanopore)	Translational/preclinical	Potential continuous renal replacement	[40]
Wearable artificial kidney	Early clinical studies	Mobility, continuous therapy	[39]
Genetically engineered pig kidney xenotransplantation	Early human trials	Addresses donor organ shortage	[41,42]

nephrotoxicity screening and personalized drug-response testing [33] (Figure 4).

Tissue-engineering approaches, including biomaterial scaffolds engineered to provide the complex, instructive extracellular environments required for cell growth and repair, aim to construct transplantable renal tissue [34]. Whole-organ decellularized-scaffold engineering and orthotopic transplantation of bioengineered kidney constructs have demonstrated proof-of-concept feasibility in animal models (Figure 5) [35], and three-dimensional bioprinting technology now permits layer-by-layer construction of tissue-like structures, though reproducing whole-kidney vascular and nephron complexity remains a major barrier (Table 4) [36].

Bioartificial Kidneys, Wearable Devices, Xenotransplantation, and Gene Editing

Renal assist devices combining hollow-fiber filtration cartridges with cultured human proximal tubular cells were the first bioartificial systems to enter clinical evaluation, replacing uremic renal function in animal models with a tissue-engineered device [37]; a subsequent randomized study in critically ill patients with acute renal failure demonstrated feasibility and biological activity [38]. Wearable artificial kidney prototypes have undergone early human pilot testing and could improve mobility and continuous clearance [39], while silicon nanopore membrane technology underlies implantable device concepts aiming to combine passive filtration with a living renal epithelial bioreactor, though durability and long-term biocompatibility remain unresolved [40].

Xenotransplantation using genetically engineered pigs has advanced from early failures due to hyperacute rejection toward recent first-in-human kidney xenografts, enabled by CRISPR-Cas9 inactivation of porcine endogenous retroviruses [41] and by prolonged xenograft survival achieved through combined genetic modification [42]. These advances build on strategies to overcome major immunological barriers, including hyperacute rejection driven by natural antibodies against carbohydrate antigens (α-Gal, CMAH, GGTA1), acute humoral and cellular xenograft rejection, and the need for transgene expression of human complement regulatory proteins (CD46, CD55, CD59) to mitigate complement-mediated injury. CRISPR-Cas9 technology, first described as a programmable RNA-guided DNA endonuclease [43], together with newer prime-editing platforms capable of precise sequence insertion, deletion, and replacement without double-strand breaks [44], has opened a parallel path toward correcting inherited nephropathies. Genetic kidney diseases, including polycystic kidney disease, Alport syndrome, and podocyte-specific disorders, remain compelling targets for such correction [45], and pluripotent-stem-cell-based disease modeling continues to inform how these mutations might best be targeted [46], although efficient and safe renal-targeted delivery remains a major unresolved obstacle (Table 5).

Clinical Applications and Translational Trial Evidence

Early-phase human trials of MSC therapy in CKD (e.g., NCT07240987, NCT06752577) and diabetic kidney disease (NCT07039318) have demonstrated feasibility and short-term safety, though definitive efficacy awaits adequately powered randomized studies (Table 6). Importantly, trial NCT07039318 is still listed as an ongoing double-blind RCT.

Acute Kidney Injury (AKI) remains the most clinically accessible target for regenerative therapy because tubular epithelial cells retain substantial repair capacity. Mesenchymal Stromal Cell (MSC) administration accelerates repair and reduces apoptosis and inflammation in preclinical models of ischemic renal failure [24], and early-phase human trials in kidney transplantation have demonstrated feasibility and safety [13]. Stem-cell–based clinical translation has increasingly focused on MSCs, which combine regenerative and immunomodulatory properties relevant to kidney disease and transplantation. Early phase studies have demonstrated feasibility and short-term safety [4], whereas experimental and clinical data show that MSCs can regulate innate and adaptive immunity, reduce inflammation, and induce regulatory immune phenotypes [48]. These immunomodulatory properties provide the rationale for considering MSCs as a complement to the conventional immunosuppressive therapy; however, evidence of their efficacy in

Table 6: Current clinical indications for regenerative nephrology (with trial identifiers).

Disease	Main approach under study	Current evidence	Ref.
Acute kidney injury	MSCs, extracellular vesicles	Phase I/II; encouraging safety; ongoing trials (e.g., NCT07240987)	[24, 47]
Chronic kidney disease	MSCs, anti-fibrotic strategies	Early-phase, experimental; MSC trials (NCT06752577)	[15, 21]
Diabetic kidney disease	MSC therapy	Double-blind RCT ongoing (NCT07039318)	[23, 25]
Kidney transplantation	MSCs, immune modulation	Early trials; feasibility shown	[13, 48]
ESKD	Bioartificial kidney, xenotransplantation	Translational/early human	[37, 41, 42]

Table 7: Major challenges in regenerative nephrology and proposed solutions.

Challenge	Current limitation	Potential solution	Ref.
Organ complexity	Complete kidney reconstruction not achieved	Developmental-biology-guided engineering, AI optimization	[9, 10, 14]
Cell/organoid immaturity	Limited adult-level function	Vascularization, metabolic conditioning	[32]
Fibrosis	Limits regeneration in advanced CKD	Anti-fibrotic and senolytic strategies	[17, 18, 20, 21]
Poor cell engraftment/survival	Variable therapeutic effect	Biomaterial carriers, extracellular vesicles	[26, 34]
Immune/xenogeneic rejection	Barrier to allo-/xenotransplantation	Gene editing, immune tolerance induction	[41, 42, 48]
Manufacturing standardization	Regulatory uncertainty	GMP-based production, potency assays	[47, 49]

Table 8: Future roadmap of regenerative nephrology.

Time horizon	Expected advances	Remaining barriers	Ref.
2025–2030	Expanded MSC/EV trials; improved organoids; AI-based modeling	Standardization, regulatory approval	[47, 49, 50]
2030–2040	Vascularized organoids; improved bioartificial kidney systems	Functional maturation, implantation	[32, 36, 40]
2040–2050	Integrated bioengineered kidneys; refined xenotransplantation	Long-term safety, accessibility, ethics	[41, 42, 49, 52]

clinical practice has yet to be proven by well-designed clinical trials. Simultaneously, the use of kidney organoids derived from pluripotent stem cells has emerged as a complementary approach for disease modeling, genetic modification, and precision medicine applications, especially in inherited nephropathies [45, 46]. Thus, the use of stem cell technology represents two different approaches to translational research in regenerative nephrology: clinical use of MSCs for tissue regeneration and immune modulation and organoid platforms for basic and translational research (Table 7).

Precision Medicine, Artificial Intelligence, and Future Directions

AI-assisted multimodal integration of imaging, genomics, transcriptomics, proteomics, and clinical data may enable individualized regenerative treatment selection, including to predict AKI onset from continuous clinical data streams [50, 51], and is expected to contribute to organoid optimization, biomarker discovery, and individualized selection of regenerative therapy (Table 8).

Realizing this vision requires overcoming several categories of obstacle. Biologically, achieving mature, vascularized, functionally complete renal tissue at nephron-appropriate scale remains unresolved [9, 10, 14]. Clinically, cell-therapy manufacturing lacks standardization of cell source, dose, and administration route [47]. Immunologically, allogeneic and xenogeneic products face rejection risk that gene editing and immune-tolerance strategies may mitigate [42, 48]. Regulatory and ethical frameworks must evolve to classify combination biological-device products and ensure long-term safety surveillance, an imperative underscored by past calls to clarify the benefits and risks of stem-cell therapy [49] and to counter the marketing of unproven stem-cell interventions to vulnerable patients [52].

Conclusions

Regenerative nephrology has progressed from descriptive studies of intrinsic tubular repair to an increasingly translational field encompassing cellular therapy, cell-free extracellular vesicle therapeutics, developmental tissue engineering, and functional organ replacement. Mesenchymal stromal cell and extracellular vesicle therapies have reached early-phase clinical testing with encouraging safety but unproven definitive efficacy; kidney organoids and gene-editing platforms remain largely preclinical; and bioartificial kidneys and genetically engineered pig kidney xenotransplantation have entered early human experience. The kidney remains among the most structurally and functionally complex organs to regenerate, and clinically meaningful restoration of renal function will likely require integration of stem-cell biology, biomaterials engineering, gene editing, and artificial intelligence rather than any single technology. Continued rigorous multicenter clinical trials, standardized manufacturing under Good Manufacturing Practice (GMP), harmonized regulatory frameworks, and long-term safety surveillance will determine whether regenerative nephrology evolves from an experimental discipline into routine clinical practice.

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