Research Output Journal of Engineering and Scientific Research 4(3): 95-101, 2025

ROJESR Publications Online ISSN: 1115-9790

https://rojournals.org/roj-engineering-and-scientific-research/ Print ISSN: 1115-6155

https://doi.org/10.59298/ROJESR/2025/4.3.95101

Personalized Immunotherapy for Congenital Immune Defects: Precision Approaches to Immune Reconstitution

Kagambira Zimbuga M.

Faculty of Medicine Kampala International University Uganda

ABSTRACT

Congenital immune defects, or primary immunodeficiency disorders (PIDs), represent a diverse group of genetically determined conditions that compromise immune function from birth. Recent advances in genomics, gene editing, and cell-based therapies have catalyzed a shift toward personalized immunotherapy—strategies that target the molecular root cause of each disorder while minimizing off-target effects. This review highlights the current landscape of precision approaches for immune reconstitution, including gene therapy, hematopoietic stem cell transplantation (HSCT), and targeted biologics. Gene therapy using lentiviral vectors and CRISPR/Cas9 has shown success in correcting defects in conditions such as SCID and Wiskott-Aldrich Syndrome. Innovations in HSCT, such as reduced-intensity conditioning and gene-modified autologous transplants, have enhanced safety and efficacy. Additionally, cellular therapies like adoptive T cells and regulatory T-cell infusions are gaining traction for immune modulation. Precision diagnostics—powered by next-generation sequencing and immune profiling—now guide therapy selection and monitoring. While challenges remain in access, long-term safety, and ethical oversight, personalized immunotherapy offers transformative potential for treating congenital immune defects. As the field progresses, integrating individualized interventions with global health equity will be key to maximizing impact and improving outcomes for affected children.

Keywords: Congenital immune defects, Personalized immunotherapy, Gene therapy, Hematopoietic stem cell transplantation, Immune

INTRODUCTION

Congenital immune defects, also known as primary immunodeficiency disorders (PIDs), represent a diverse and expanding group of over 450 rare genetic conditions that result from defects in the development, regulation, or function of various components of the immune system [1]. These disorders manifest early in life, although some may not become clinically evident until later childhood or even adulthood. Affected individuals are predisposed to recurrent, severe, and sometimes life-threatening infections, as well as autoimmune manifestations, chronic inflammation, and an increased risk of malignancies [2]. The clinical heterogeneity and overlapping phenotypes of PIDs often complicate diagnosis and management. In recent years, significant progress has been made in understanding the genetic and molecular basis of these disorders, driven largely by advances in next-generation sequencing (NGS) and systems immunology [3,7]. These tools have not only improved diagnostic accuracy but have also laid the groundwork for personalized immunotherapy, a rapidly evolving field that aims to tailor interventions to the unique immunological and genetic profile of each patient [4]. Traditional treatment options for PIDs, such as antimicrobial prophylaxis, immunoglobulin replacement therapy, and allogeneic hematopoietic stem cell transplantation (HSCT), have been instrumental in improving survival. However, they often provide symptomatic relief rather than addressing the root cause of the immune dysfunction [5,6]. Personalized immunotherapy encompassing gene therapy, gene editing, targeted biologics, and customized stem cell-based

strategies seeks to correct or modulate the immune defect at its source [7]. These precision approaches aim not only to restore immune competence but also to reduce treatment-related toxicities, prevent complications, and improve long-term quality of life. This review provides a comprehensive overview of the current and emerging personalized immunotherapeutic strategies for congenital immune defects. It emphasizes advances in gene therapy, HSCT, and immune modulation, while also addressing the diagnostic innovations, ethical considerations, and future directions necessary to optimize immune reconstitution in affected individuals.

Pathophysiology and Classification of Congenital Immune Defects

The pathophysiology of congenital immune defects is rooted in inherited mutations that disrupt key pathways involved in immune cell development, differentiation, signaling, or effector function. These disruptions lead to qualitative or quantitative deficiencies in various components of innate and adaptive immunity, resulting in a wide spectrum of clinical phenotypes. Congenital immune defects are broadly categorized into five major groups: Combined immunodeficiencies (CID): These involve defects affecting both T and B lymphocyte development or function [8]. A classic example is Severe Combined Immunodeficiency (SCID), often referred to as a "pediatric emergency" due to its early onset and fatal course if untreated [9]. Predominantly antibody deficiencies: These disorders, such as X-linked agammaglobulinemia (XLA) and Common Variable Immunodeficiency (CVID), are characterized by impaired B cell development or antibody production, leading to recurrent bacterial infections [10,11]. Phagocytic disorders: Conditions like Chronic Granulomatous Disease (CGD) result from defects in neutrophil function, impairing the ability to kill pathogens and leading to granuloma formation and recurrent abscesses [12]. Complement deficiencies: These impair the innate immune response and predispose individuals to infections with encapsulated bacteria, as well as autoimmune phenomena [13]. Immune dysregulation syndromes: Examples include Immune dysregulation, Polyendocrinopathy, Enteropathy, X-linked (IPEX) syndrome and Autoimmune Lymphoproliferative Syndrome (ALPS), where mutations affect immune tolerance mechanisms, resulting in autoimmunity, lymphoproliferation, and tissue damage [14,15]. Accurate classification based on the underlying molecular defect, rather than solely clinical phenotype, is critical for selecting the most appropriate and effective immunotherapeutic strategy

Gene Therapy: Correcting the Root Cause

Gene therapy has rapidly progressed from experimental treatment to a transformative therapeutic option for select primary immunodeficiency disorders (PIDs) [16]. Unlike traditional therapies that manage symptoms or mitigate complications, gene therapy directly targets the underlying genetic defect**,** offering the possibility of long-term or even permanent correction of immune dysfunction [17]. Among the most well-established modalities is lentiviral vector-based gene therapy, which has shown success in treating conditions such as X-linked Severe Combined Immunodeficiency (SCID-X1)**,** Adenosine Deaminase Deficiency (ADA-SCID), and Wiskott-Aldrich Syndrome [18]. Lentiviral vectors enable stable gene insertion into the genome of hematopoietic stem cells (HSCs), allowing for durable reconstitution of the immune system [19]. Unlike early retroviral vectors, lentiviral platforms reduce the risk of insertional oncogenesis, although continuous long-term monitoring remains essential [20].

Emerging technologies such as CRISPR/Cas9 gene editing are revolutionizing the field by allowing precise, site-specific correction of pathogenic mutations without the need for random vector integration [21]. CRISPR-based approaches are currently being evaluated in preclinical studies and early-phase clinical trials for diseases including SCID and Chronic Granulomatous Disease (CGD) [22]. While promising, challenges related to off-target effects and delivery efficiency must be carefully addressed. Newer approaches like base editing **and** prime editing further enhance the precision and safety of gene correction. These techniques allow for targeted nucleotide conversions or small DNA insertions without inducing double-strand breaks, thereby minimizing genomic instability [23,24]**.** Though largely in the experimental stage, they hold significant potential for expanding the treatable spectrum of PIDs. Despite these advances, gene therapy carries risks that warrant ongoing research. Concerns include immune responses to viral vectors**,** inflammatory reactions, and the durability of gene expression [25]**.** Regulatory oversight and standardized long-term follow-up protocols are vital to ensure safety, particularly in pediatric patients.

Precision Hematopoietic Stem Cell Transplantation (HSCT)

Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) remains the cornerstone of curative treatment for many congenital immune defects, particularly for severe combined immunodeficiencies and other life-threatening PIDs [26]. Recent innovations have transformed HSCT into a more personalized and accessible therapy, even in the absence of fully matched donors [27]. HLA-matched sibling donors remain the ideal source; however, advancements in haploidentical transplantation with T-cell receptor (TCR) αβ depletion have significantly improved outcomes in patients lacking matched donors [29]. This approach reduces the risk of graft-versus-host disease (GVHD) while maintaining robust immune reconstitution. Reduced-intensity conditioning (RIC) regimens have become standard for many pediatric and high-risk patients [30]. Tailoring conditioning intensity to the patient's

age, genetic background, and comorbid conditions has improved tolerability and survival, especially in infants and those with pre-existing organ damage [30]. The use of gene-modified autologous HSCT is an emerging alternative that combines gene therapy with stem cell transplantation [27]. This approach eliminates the need for an external donor and reduces complications such as GVHD and graft rejection [31]. Additionally, pre-transplant immune profiling, including chimerism assessment and cytokine profiling, and post-transplant monitoring have enabled real-time evaluation of immune reconstitution [32]. These tools support individualized transplant planning, optimize engraftment, and guide early interventions for complications [33]. Together, these precision strategies are reshaping HSCT into a safer, more effective, and patient-centered modality for immune reconstitution in congenital immune defects.

Cell-Based Immunotherapy

Cell-based immunotherapy is emerging as a powerful adjunct or alternative to traditional treatments for congenital immune defects. These approaches leverage the functional properties of specific immune cells to restore or regulate immune function, often with greater specificity and reduced systemic toxicity compared to broader therapies [34].

Adoptive T-cell therapy has proven particularly beneficial in the post-transplant setting, where reactivation of latent viruses such as cytomegalovirus (CMV), Epstein-Barr virus (EBV), and adenovirus can cause severe complications [35]. Infusion of virus-specific T cells (VSTs), generated from either the patient, donor, or third-party sources, has demonstrated efficacy in controlling infections without the toxicities of antiviral drugs [36].

Regulatory T-cell (Treg) therapy is under investigation for congenital syndromes characterized by immune dysregulation, such as IPEX (Immune dysregulation, Polyendocrinopathy, Enteropathy, X-linked) syndrome [37]. Tregs play a central role in maintaining immune tolerance, and ex vivo expanded Tregs or genetically modified Tregs may help prevent or mitigate autoimmune manifestations in these patients [38].

Chimeric Antigen Receptor (CAR) T-cell therapy, though primarily associated with oncology, is now being explored in primary immunodeficiencies with lymphoproliferative or autoimmune complications [39]. The potential to reprogram autologous T cells with engineered receptors that target specific immune cells or antigens could provide new therapeutic avenues in otherwise treatment-refractory cases. These cell-based therapies are increasingly being incorporated into personalized treatment algorithms, informed by immunophenotyping, genetic diagnosis, and disease severity [40]. As manufacturing processes improve and safety profiles are optimized, cell therapy is likely to become a cornerstone of individualized care in congenital immune defects.

Targeted Biologics and Immune Modulators

In patients for whom gene or cell therapies are not immediately accessible or appropriate, targeted biologics and immune modulators offer effective interim or long-term disease control. These therapies focus on specific molecular pathways involved in immune activation, regulation, or inflammation [41]. mTOR inhibitors (e.g., sirolimus) and JAK inhibitors (e.g., ruxolitinib) have shown promise in managing immune dysregulation, lymphoproliferation, and autoimmunity in several PIDs [42]. Similarly, cytokine-blocking agents, such as anti-IL-6 (tocilizumab) and anti-IFN-γ (emapalumab), can attenuate hyperinflammatory states, including hemophagocytic lymphohistiocytosis (HLH)-like presentations [43]. Checkpoint inhibitors are being evaluated in patients with PID-associated malignancies, especially those with DNA repair defects or cancer predisposition syndromes [43]. For many antibody deficiencies, immunoglobulin replacement therapy (IRT) remains the mainstay of treatment [45]. Administered intravenously or subcutaneously, IRT reduces infection frequency and severity while supporting overall immune function. Increasingly, the selection and dosing of these agents are informed by immune pathway analysis, genetic mutations, and cytokine profiling, enabling a precision medicine approach to pharmacologic immunomodulation [46]. These targeted strategies offer flexibility, especially in complex cases awaiting curative therapy or requiring long-term management

Diagnostic Innovations Driving Personalization

The foundation of personalized immunotherapy lies in accurate and timely diagnosis. Recent advances in diagnostic technology have dramatically enhanced our ability to characterize congenital immune defects at the molecular and cellular levels, facilitating individualized treatment strategies. Next-generation sequencing (NGS) has become a standard tool in the diagnostic workup of suspected primary immunodeficiencies [47]. Whole-exome and targeted gene panel sequencing allow for the rapid identification of pathogenic mutations, which not only confirm the diagnosis but also directly inform therapy selection—such as eligibility for gene therapy, specific transplant protocols, or biologic therapies [48]. Beyond genomics, single-cell RNA sequencing (scRNA-seq) and high-throughput proteomics provide detailed profiles of immune cell populations and their functional states [49]. These technologies can uncover unique immune signatures predictive of disease progression, treatment responsiveness, and post-intervention outcomes. This level of cellular resolution is particularly useful in heterogeneous or atypical presentations. Machine learning and artificial intelligence (AI) tools are increasingly being applied to integrate

genetic, immunological, and clinical datasets [50]. These algorithms enable risk stratification, prediction of adverse events, and decision support for personalized care plans [51]. The integration of dynamic immune monitoring and computational modeling is driving a shift from generalized protocols toward precision immune care tailored to each patient's evolving immunological landscape.

Ethical and Societal Considerations

The advent of personalized immunotherapy brings with it significant ethical and societal implications that must be addressed proactively to ensure just and responsible implementation.

A major concern is equitable access to high-cost therapies such as gene editing and cell-based interventions [52]. Many patients, particularly in low- and middle-income countries, may be excluded from these innovations due to financial, infrastructural, or logistical barriers. Bridging this gap requires global collaboration, innovative funding mechanisms, and capacity-building in resource-limited settings. Long-term safety of gene editing, particularly in pediatric patients, is another critical issue [53]. While genome editing technologies like CRISPR offer curative potential, the risks of off-target effects, insertional mutagenesis, or unknown late-onset complications necessitate robust preclinical testing and lifelong surveillance. Informed consent is complex in the pediatric context, especially for experimental therapies. Parents or guardians must be adequately informed about risks, benefits, and uncertainties, while also considering the child's future autonomy and right to an open future [54]. Ethical oversight, stakeholder engagement, and policy development are essential to address these challenges and promote safe, transparent, and equitable deployment of personalized immunotherapy [55].

Future Directions

The future of personalized immunotherapy is poised to benefit from ongoing technological and conceptual breakthroughs. In vivo gene editing direct correction of mutations within the patient may eliminate the need for ex vivo cell manipulation, reducing cost and complexity.

Organoid and organ-on-chip technologies offer promising platforms to model patient-specific immune responses and test interventions in a controlled, physiologically relevant setting. Artificial intelligence (AI) will play an increasingly central role in designing adaptive treatment algorithms, integrating real-time immune monitoring data to guide clinical decisions dynamically. Collectively, these innovations aim to achieve durable, safe, and individualized immune reconstitution for each patient, with minimal toxicity and maximal long-term benefit.

CONCLUSION

Personalized immunotherapy represents a paradigm shift in the treatment of congenital immune defects. By correcting the root genetic causes and tailoring interventions to the individual's molecular and clinical profile, these approaches offer hope for durable immune reconstitution, improved quality of life, and long-term survival. As the field advances, it is imperative to ensure that scientific innovation is matched by ethical responsibility, equitable access, and global collaboration. A multidisciplinary, patient-centered, and precision-based framework will be key to realizing the full potential of personalized immunotherapy in congenital immunodeficiency care.

REFERENCES

1. McCusker C, Upton J, Warrington R. Primary immunodeficiency. Allergy Asthma and Clinical Immunology. 2018;14(S2). doi:10.1186/s13223-018-0290-5
2. McCusker C, Upton J, Warrington R. Primary immunodeficiency. Allergy Asthma and Clinical Immunology. 2018;14(S2). doi:10.1186/s13223-018-0290-5
3. Bucciol G, Meyts I. Recent advances in primary immunodeficiency: from molecular diagnosis to treatment. F1000Research. 2020;9:194. doi:10.12688/f1000research.21553.1
4. Satam H, Joshi K, Mangrolia U, Waghoo S, Zaidi G, Rawool S, et al. Next-Generation Sequencing Technology: Current trends and advancements. Biology. 2023;12(7):997. doi:10.3390/biology12070997
5. Chai KL, Wood EM, Estcourt LJ, Csenar M, Iannizzi C, Monsef I, et al. Immunoglobulin replacement to prevent infections in people with haematological malignancies and haematopoietic stem cell transplantation. Cochrane Library. 2024;2024(3). doi:10.1002/14651858.cd015719
6. Raanani P, Gafter-Gvili A, Paul M, Ben-Bassat I, Leibovici L, Shpilberg O. Immunoglobulin prophylaxis in Hematopoietic Stem cell Transplantation: Systematic Review and Meta-Analysis. Journal of Clinical Oncology. 2008;27(5):770–81. doi:10.1200/jco.2008.16.8450
7. Su J, Yang L, Sun Z, Zhan X. Personalized Drug therapy: innovative concept guided with proteoformics. Molecular & Cellular Proteomics. 2024;23(3):100737. doi:10.1016/j.mcpro.2024.100737
8. Yazdani R, Tavakol M, Motlagh AV, Shafiei A, Darougar S, Chavoshzadeh Z, et al. Combined immunodeficiencies with associated or syndromic features. In: Elsevier eBooks. 2021. p. 41–91. doi:10.1016/b978-0-12-821028-4.00008-7

9. Justiz-Vaillant AA, Gopaul D, Akpaka PE, Soodeen S, Fundora RA. Severe Combined Immunodeficiency—Classification, Microbiology association and Treatment. Microorganisms. 2023;11(6):1589. doi:10.3390/microorganisms11061589
10. Lackey AE, Ahmad F. X-Linked agammaglobulinemia. StatPearls - NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549865/
11. Ruschel M a. P, Vaqar S. Common variable immunodeficiency. StatPearls - NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549787/
12. Lent-Schochet D, Jialal I. Chronic granulomatous disease. StatPearls - NCBI Bookshelf. 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493171/
13. Mollah F, Tam S. Complement deficiency. StatPearls - NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557581/
14. Gambineri E, Torgerson TR, Ochs HD. Immune dysregulation, polyendocrinopathy, enteropathy, and X-linked inheritance (IPEX), a syndrome of systemic autoimmunity caused by mutations of FOXP3, a critical regulator of T-cell homeostasis. Current Opinion in Rheumatology. 2003;15(4):430–5. doi:10.1097/00002281-200307000-00010
15. Tan QK g, Louie RJ, Sleasman JW. IPEX Syndrome. GeneReviews® - NCBI Bookshelf. 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1118/
16. Houghton BC, Booth C. Gene therapy for primary immunodeficiency. HemaSphere. 2020;5(1):e509. doi:10.1097/hs9.0000000000000509
17. Gonçalves GAR, De Melo Alves Paiva R. Gene therapy: advances, challenges and perspectives. Einstein (São Paulo). 2017;15(3):369–75. doi:10.1590/s1679-45082017rb4024
18. Fischer A, Hacein-Bey-Abina S. Gene therapy for severe combined immunodeficiencies and beyond. The Journal of Experimental Medicine. 2019;217(2). doi:10.1084/jem.20190607
19. Mátrai J, Chuah MK, VandenDriessche T. Recent advances in lentiviral vector development and applications. Molecular Therapy. 2010;18(3):477–90. doi:10.1038/mt.2009.319
20. Milone MC, O'Doherty U. Clinical use of lentiviral vectors. Leukemia. 2018;32(7):1529–41. doi:10.1038/s41375-018-0106-0
21. Ugwu OPC, Anyanwu CN, Alum EU, Okon MB, Egba SI, Uti DE and Awafung EA. (2024). CRISPR-Cas9 Mediated Gene Editing for Targeted Cancer Therapy: Mechanisms, Challenges, and Clinical Applications. Newport International Journal Of Biological And Applied Sciences,5(1):97-102. https://doi.org/10.59298/NIJBAS/2024/5.1.9297102
22. Laurent M, Geoffroy M, Pavani G, Guiraud S. CRISPR-Based gene Therapies: From preclinical to clinical treatments. Cells. 2024;13(10):800. doi:10.3390/cells1310080
23. Alum EU, Ikpozu EN, Offor CE, et al. RNA-based diagnostic innovations: A new frontier in diabetes diagnosis and management. Diabetes & Vascular Disease Research. 2025;22(2). doi:10.1177/14791641251334726
24. Rees HA, Liu DR. Base editing: precision chemistry on the genome and transcriptome of living cells. Nature Reviews Genetics. 2018;19(12):770–88. doi:10.1038/s41576-018-0059-1
25. Shirley JL, De Jong YP, Terhorst C, Herzog RW. Immune responses to viral gene therapy vectors. Molecular Therapy. 2020;28(3):709–22. doi:10.1016/j.ymthe.2020.01.001
26. Marçais A, Mahlaoui N, Neven B, Lanternier F, Catherinot É, Salvator H, et al. Curative allogeneic hematopoietic stem cell transplantation following reduced toxicity conditioning in adults with primary immunodeficiency. Bone Marrow Transplantation. 2022;57(10):1520–30. doi:10.1038/s41409-022-01739-x
27. Ashorobi D, Naha K, Bhatt R. Hematopoietic stem cell transplantation in sickle cell disease. StatPearls - NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538515/
28. Spellman SR. Hematology 2022—what is complete HLA match in 2022? Hematology. 2022;2022(1):83–9. doi:10.1182/hematology.2022000326
29. Gaziev J, Isgrò A, Sodani P, Paciaroni K, De Angelis G, Marziali M, et al. Haploidentical HSCT for hemoglobinopathies: improved outcomes with TCRαβ+/CD19+-depleted grafts. Blood Advances. 2018;2(3):263–70. doi:10.1182/bloodadvances.2017012005
30. Verneris MR, Eapen M, Duerst R, Carpenter PA, Burke MJ, Afanasyev BV, et al. Reduced-Intensity Conditioning Regimens for Allogeneic Transplantation in Children with Acute Lymphoblastic Leukemia. Biology of Blood and Marrow Transplantation. 2010;16(9):1237–44. doi:10.1016/j.bbmt.2010.03.009
31. Morgan RA, Gray D, Lomova A, Kohn DB. Hematopoietic stem cell gene therapy: progress and lessons learned. Cell Stem Cell. 2017;21(5):574–90. doi:10.1016/j.stem.2017.10.010
32. Singh M, D'Silva SZ, Saxena A. Assessment of immune reconstitution following hematopoietic stem cell transplantation. In: IntechOpen eBooks. 2019. doi:10.5772/intechopen.89198

33. Blouin AG, Ye F, Williams J, Askar M. A practical guide to chimerism analysis: Review of the literature and testing practices worldwide. Human Immunology. 2021;82(11):838–49. doi:10.1016/j.humimm.2021.07.013
34. Wu J. Emerging innate immune cells in cancer immunotherapy: Promises and challenges. BioDrugs. 2024;38(4):499–509. doi:10.1007/s40259-024-00657-2
35. Jalili A, Hajifathali A, Mohammadian M, Sankanian G, Sayahinouri M, Ghorbi MD, et al. Virus-Specific T cells: promising adoptive T cell therapy against infectious diseases following hematopoietic stem cell transplantation. Advanced Pharmaceutical Bulletin. 2022;13(3):469–82. doi:10.34172/apb.2023.046
36. Rubinstein JD, Zhu X, Leemhuis T, Pham G, Ray L, Emberesh S, et al. Virus-specific T cells for adenovirus infection after stem cell transplantation are highly effective and class II HLA restricted. Blood Advances. 2021;5(17):3309–21. doi:10.1182/bloodadvances.2021004456
37. Quirós AB, Sanz EA, Ordiz DB, Adrados JAG. From autoimmune enteropathy to the IPEX (immune dysfunction, polyendocrinopathy, enteropathy, X-linked) syndrome. Allergologia Et Immunopathologia. 2009;37(4):208–15. Available from: https://www.elsevier.es/es-revista-allergologia-et-immunopathologia-105-articulo-from-autoimmune-enteropathy-ipex-immune-S0301054609000238
38. Goswami TK, Singh M, Dhawan M, Mitra S, Emran TB, Rabaan AA, et al. Regulatory T cells (Tregs) and their therapeutic potential against autoimmune disorders – Advances and challenges. Human Vaccines & Immunotherapeutics. 2022;18(1). doi:10.1080/21645515.2022.2035117
39. Zhang C, Durer S, Thandra KC, Kasi A. Chimeric Antigen Receptor T-Cell therapy. StatPearls - NCBI Bookshelf. 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537294/
40. Stolfi F, Brasso C, Raineri D, Landra V, Mazzucca CB, Ghazanfar A, et al. Deep immunophenotyping of circulating immune cells in major depressive disorder patients reveals immune correlates of clinical course and treatment response. Brain Behavior & Immunity - Health. 2024;43:100942. doi:10.1016/j.bbih.2024.100942
41. Sharma Y, Arora M, Bala K. The potential of immunomodulators in shaping the future of healthcare. Deleted Journal. 2024;1(1). doi:10.1007/s44337-024-00029-3
42. Walter JE, Farmer JR, Foldvari Z, Torgerson TR, Cooper MA. Mechanism-Based strategies for the management of autoimmunity and immune dysregulation in primary immunodeficiencies. The Journal of Allergy and Clinical Immunology in Practice. 2016;4(6):1089–100. doi:10.1016/j.jaip.2016.08.004
43. Bazarbachi AH, Mapara MY. Cytokines in hematopoietic cell transplantation and related cellular therapies. Best Practice & Research Clinical Haematology. 2024;37(4):101600. doi:10.1016/j.beha.2025.101600
44. Liu YL, Weigelt B. A tale of two pathways: Review of immune checkpoint inhibitors in DNA mismatch repair-deficient and microsatellite instability-high endometrial cancers. Cancer. 2024;130(10):1733–46. doi:10.1002/cncr.35267
45. Vivarelli E, Matucci A, Bormioli S, Parronchi P, Liotta F, Cosmi L, et al. Effectiveness of low-dose intravenous immunoglobulin therapy in minor primary antibody deficiencies: A 2-year real-life experience. Clinical & Experimental Immunology. 2021;205(3):346–53. doi:10.1111/cei.13629
46. Puccetti M, Pariano M, Schoubben A, Giovagnoli S, Ricci M. Biologics, theranostics, and personalized medicine in drug delivery systems. Pharmacological Research. 2024;201:107086. doi:10.1016/j.phrs.2024.107086
47. Raje N, Soden S, Swanson D, Ciaccio CE, Kingsmore SF, Dinwiddie DL. Utility of next generation sequencing in clinical primary immunodeficiencies. Current Allergy and Asthma Reports. 2014;14(10). doi:10.1007/s11882-014-0468-y
48. Pei XM, Yeung MHY, Wong ANN, Tsang HF, Yu ACS, Yim AKY, et al. Targeted sequencing approach and its clinical applications for the molecular diagnosis of human diseases. Cells. 2023;12(3):493. doi:10.3390/cells12030493
49. Jovic D, Liang X, Zeng H, Lin L, Xu F, Luo Y. Single-cell RNA sequencing technologies and applications: A brief overview. Clinical and Translational Medicine. 2022;12(3). Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8964935/
50. Farzan R. Artificial intelligence in Immuno-genetics. Bioinformation. 2024;20(1):29–35. doi:10.6026/973206300200029
51. Khalifa M, Albadawy M. Artificial intelligence for clinical prediction: Exploring key domains and essential functions. Computer Methods and Programs in Biomedicine Update. 2024;5:100148. doi:10.1016/j.cmpbup.2024.100148
52. Salzman R, Cook F, Hunt T, Malech HL, Reilly P, Foss-Campbell B, et al. Addressing the value of gene therapy and enhancing patient access to transformative treatments. Molecular Therapy. 2018;26(12):2717–26. doi:10.1016/j.ymthe.2018.10.017

53. Rubeis G, Steger F. Risks and benefits of human germline genome editing: An ethical analysis. Asian Bioethics Review. 2018;10(2):133–41. doi:10.1007/s41649-018-0056-x
54. Shah P, Thornton I, Kopitnik NL, Hipskind JE. Informed consent. StatPearls - NCBI Bookshelf. 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430827/
55. Petkovic J, Magwood O, Lytvyn L, Khabsa J, Concannon TW, Welch V, et al. Key issues for stakeholder engagement in the development of health and healthcare guidelines. Research Involvement and Engagement. 2023;9(1). doi:10.1186/s40900-023-00433-6
56.

CITE AS: Kagambira Zimbuga M. (2025). Personalized Immunotherapy for Congenital Immune Defects: Precision Approaches to Immune Reconstitution. Research Output Journal of Engineering and Scientific Research 4(3): 95-101. https://doi.org/10.59298/ROJESR/2025/4.3.95101