Immunopathological markers in organ transplant rejection: Advances in diagnosis and monitoring.

David B. Foster*

Clinical Pathology Unit, Columbia University Irving Medical Center, New York, NY, USA.

Introduction

Organ transplantation is a life-saving treatment for patients with end-stage organ failure. However, transplant rejection, driven by immune-mediated damage to the graft, remains a major obstacle to long-term success. Rejection can be classified into hyperacute, acute, and chronic forms, each with distinct immunopathological features. Identifying immunopathological markers is crucial for the early diagnosis, classification, and monitoring of rejection, enabling timely intervention and improved graft survival.

Transplant rejection is primarily mediated by T and B cell responses against donor antigens, particularly human leukocyte antigens (HLAs). These immune reactions lead to direct cytotoxicity, inflammation, and vascular injury within the graft. Traditionally, diagnosis has relied on clinical indicators and histopathological evaluation of graft biopsies. While valuable, these methods can be invasive, nonspecific, and may detect rejection only after significant damage has occurred [1-5].

Advances in immunopathology and molecular diagnostics have led to the identification of **biomarkers** that offer earlier, more specific, and less invasive ways to detect and monitor rejection. Among these, **donor-specific antibodies (DSAs)** play a central role. DSAs are antibodies produced by the recipient's immune system against donor HLAs and are associated with antibody-mediated rejection (AMR), a major cause of graft loss. Detection of DSAs using highly sensitive assays such as Luminex single-antigen bead technology has become standard practice in transplant monitoring.

Complement split product C4d is another important immunopathological marker. C4d deposition in peritubular capillaries, especially in kidney allografts, is a hallmark of AMR. It reflects activation of the classical complement pathway by DSAs and is included in the Banff classification system for diagnosing renal allograft rejection. While highly specific, C4d may not be present in all cases of AMR, prompting the search for additional markers.

Cell-free donor-derived DNA (dd-cfDNA) has emerged as a promising non-invasive biomarker for detecting allograft injury. Released into the recipient's bloodstream during graft cell injury or rejection, elevated levels of dd-cfDNA can signal acute rejection before clinical or histological changes appear. This tool is particularly useful in kidney, heart, and lung transplantation and offers a valuable means of surveillance without requiring biopsy.

Gene expression profiling is another advancing field. For instance, the AlloMap test, used in heart transplant recipients, assesses the expression of immune-related genes in peripheral blood to detect rejection. Similarly, the molecular microscope diagnostic system (MMDx) uses tissue transcriptomics to complement histopathological findings and improve diagnostic accuracy in kidney transplants [6-10].

Beyond diagnostic applications, immunopathological markers also offer **prognostic value**. Persistent DSAs, especially those with complement-binding ability (e.g., C1q-positive), correlate with worse long-term outcomes. Monitoring these markers can help tailor immunosuppressive therapy, reducing the risk of both rejection and over-immunosuppression.

Conclusion

In conclusion, the integration of immunopathological markers into transplant medicine has significantly advanced the ability to diagnose and monitor rejection. These markers offer greater sensitivity, specificity, and non-invasiveness compared to traditional methods. Ongoing research continues to refine these tools, bringing the field closer to personalized immunosuppression and improved long-term outcomes in organ transplantation.

References

1. McGuigan A, Kelly P, Turkington RC, et al. Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment and outcomes. World J Gastroenterol. 2018;24(43):4846.
2. Egawa S, Toma H, Ohigashi H, et al. Japan pancreatic cancer registry; 30th year anniversary: Japan pancreas society. Pancreas. 2012 Oct 1;41(7):985-92.
3. Asrani SK, Devarbhavi H, Eaton J, et al. Burden of liver diseases in the world. J Hepatol. 2019;70(1):151-71.
4. Makri E, Goulas A, Polyzos SA. Epidemiology, pathogenesis, diagnosis and emerging treatment of nonalcoholic fatty liver disease. Arch Med Res. 2021;52(1):25-37.

***Correspondence to:** David B. Foster, Clinical Pathology Unit, Columbia University Irving Medical Center, New York, NY, USA. E-mail: dbfoster@columbiapath.edu

***Received:** 10-Feb-2025, Manuscript No. AACPLM- 25-164075; **Editor assigned:** 11-Feb-2025, Pre QC No. AACPLM- 25-164075 (PQ); **Reviewed:** 20-Feb-2025, QC No. AACPLM- 25-164075; **Revised:** 22-Feb-2025, Manuscript No. AACPLM- 25-164075 (R); **Published:** 28-Feb-2025, DOI: 10.35841/ aacplm-7.1.255*

***Citation:** Foster DB. Immunopathological markers in organ transplant rejection: Advances in diagnosis and monitoring. J Clin Path Lab Med.2025;(7)1:255*

5. Di Marzo, V. (2018). New approaches and challenges to targeting the endocannabinoid system. Nat Rev Drug Discov. 17(9), 623-639.
6. Gerard JP, Noël P, Mayer M, et al. A topographic approach to breast cancer. The relation of topographic and mammographic findings. Cancer. 1977;40(2):928-30.
7. Cappell MS. Pathophysiology, clinical presentation, and management of colon cancer. Gastroenterol Clin North Am. 2008;37(1):1-24.
8. Labianca R, Beretta GD, Kildani B, et al. Colon cancer. Critic Rev Oncol. 2010;74(2):106-33.
9. Wen J, Min X, Shen M, et al. ACLY facilitates colon cancer cell metastasis by CTNNB1. J Exp Clin Cancer Res. 2019;38(1):1-2.
10. Sánchez-Guillén L, Arroyo A. Immunonutrition in patients with colon cancer. Immunotherapy. 2020;12(1):5-8.

Citation: *Foster DB. Immunopathological markers in organ transplant rejection: Advances in diagnosis and monitoring. J Clin Path Lab Med.2025;(7)1:255*