Translation Research in Molecular Disease Diagnosis: Bridging Gap from Laboratory to Practice

Sir,

In the era following accomplishment of the "Human Genome Project," molecular diagnostics has been steadily expanding. The driving force behind this rapid expansion could be the need for specific and rapid identification, a first-ranking priority for the treatment and eradication of infectious diseases. Availability of a wide range of modern molecular diagnostic tools, including genomic, proteomic and cytomic technologies, has made clinicians emphasize evidence-based diagnostics. Molecular diagnostics has been extremely successful in the area of infectious diseases, where nucleic acid identification and bacterial and viral genotyping have made rapid progress. Though presently in an embryonic stage, molecular diagnostics has confirmed its usefulness and is likely to provide further major breakthroughs into clinical practice of infectious biology.

We examined 1,739 samples, referred to our center during the period January 2004 to March 2010, through quantitative polymerase chain reaction (PCR). A total of 688 samples were screened for hepatitis B virus (HBV); 325 samples, for hepatitis C virus (HCV) RNA; and 726 subjects, for the presence of *Mycobacterium tuberculosis* complex (MTBC). A higher prevalence of sero-negative pattern, but positive for HBV-DNA, HCV-RNA and reactive MTBC-DNA in gastrointestinal tuberculosis by quantitative PCR was observed, indicating occurrence of occult infections among the subjects [Table 1]. This prompted us to undertake in-depth immunological and molecular characterization of these cases to rule out any false-positive apprehensions.

Exploring information from the complex interaction of host cellular DNA damage response machinery with viral infection, accumulation of phospho-H2AX foci in peripheral lymphocytes as an early biomarker for characterization of occult viral hepatitis has been proposed.[1] Besides, by applying a novel probe technology based on fluorescence resonance energy transfer (FRET) hybridization, we could characterize the host immune response to HCV genotypes and at the same time delineate the role of occult HCV infection in liver biopsies of patients with cryptogenic cirrhosis who are at increased risk of developing hepatocellular carcinoma.[2,3] Given the insidious course of, and clinical impediments in treating, gastrointestinal tuberculosis (GITB), we developed a novel combinatorial diagnostic approach for rapid detection and characterization of GITB that not only illustrates increased diagnostic accuracy but also signifies the importance of these molecular assays for better disease management and patient survival.[4,5] However, to pave the way for successful translation of our findings from bench to bedside, a larger sample size is a requisite.

Table 1: Results of quantitative polymerase chain reaction

Test performed	Total samples screened	Positive [n (%)]	Stage diagnosed
Hepatitis B virus	688	86 (12.5)	Acute
		324 (47.09)	Chronic
		30 (4.3)	Occult
Hepatitis C virus	325	13 (4.0)	Acute
		74 (22.7)	Chronic
		03 (0.92)	Occult
Mycobacterium tuberculosis	726	108 (14.8)	Pulmonary
		140 (19.2)	Extra-pulmonary

Laboratory research has always provided new technologies and will continue to be the foundation for advances in molecular diagnostics. With time, molecular diagnostics will continue to evolve; not all methods and markers will survive, but those that do will complement rapidly proliferating menu of molecular diagnostic services focused on improving health care and quality of human lives. Clinical utility may not necessarily correspond directly to the quantum of tests performed or the category of the diagnostic services provided. Emphasis on translational research will transform scientific discoveries arising from laboratory into clinical application; however, to flourish, it will require a knowledge-driven ecosystem to provide a continuous feedback loop to accelerate the translation of data into clinical utility.

Pradyumna K Mishra[1,2], Gorantla V Raghuram[1,2], Arpit Bhargava[1,2], Neelam Pathak[1]

[1]Bhopal Memorial Hospital and Research Centre, Bhopal, [2]Division of Translational Research, Tata Memorial Centre, ACTREC, Navi Mumbai, India

Address for correspondence:
Dr. Pradyumna Kumar Mishra, E-mail: pkm_8bh@yahoo.co.uk

REFERENCES

1. Bhargava A, Khan S, Panwar H, Pathak N, Varshney S, Mishra PK, *et al.* Occult Hepatitis B virus infection with low viremia induces DNA damage, apoptosis, oxidative stress and inflammation in peripheral blood lymphocytes. Virus Res 2010;153:143-50.
2. Bhargava A, Punde RP, Varshney S, Pathak N, Mishra PK. A novel FRET probe-based approach for identification, quantification and characterisation of occult HCV infections in patients with cryptogenic liver cirrhosis. Indian J Pathol Microbiol 2011; [In press].
3. Mishra PK, Bhargava A, Khan S, Pathak N, Punde RP, Varshney S. Prevalence of hepatitis C virus genotypes and impact of T helper cytokines in achieving sustained virological response during combination therapy: A study from Central India. Indian J Med Microbiol 2010;28:358-62.
4. Mishra PK, Bhargava A, Punde RP, Pathak N, Desikan P, Jain A, *et al.* Diagnosis of gastrointestinal tuberculosis: Combining cytomorphology, microbiology, immunology and molecular techniques - a study from Central India. Ind J Clin Biochem 2010;25:68-73.
5. Mishra PK, Gorantla VR, Bhargava A, Varshney S, Vashistha, Maudar KK. Molecular detection of *Mycobacterium tuberculosis* in formalin-fixed, paraffin-embedded tissues and biopsies of gastrointestinal specimens using real-time polymerase chain reaction system. Turk J Gastroenterol 2010;21:129-34.

Access this article online	
Quick Response Code:	Website: www.jgid.org
	DOI: 10.4103/0974-777X.81705