Biomarkers for parasitic infections: advances and prospects.

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Parasitic infections remain a significant global health challenge, necessitating improved diagnostic and prognostic tools. Biomarkers—measurable indicators of biological states—offer promising avenues for early detection, disease monitoring, and therapeutic targeting in parasitic diseases. Recent research highlights diverse classes of biomarkers derived from both parasites and hosts, enhancing our understanding and management of these infections [1, 2, 3, 4].

Parasite-Derived Biomarkers

MicroRNAs (miRNAs): Parasite-derived circulating miRNAs have emerged as potential diagnostic biomarkers for various parasitic infections, including helminths and protozoa. These small non-coding RNAs are secreted into host biological fluids like serum and plasma, making them accessible for non-invasive diagnosis. Their stability and specificity to parasite species underpin their utility, although clinical guidelines for their application are still in development.

Extracellular Vesicles (EVs): Parasites release EVs containing proteins and nucleic acids detectable in host plasma. Studies on filarial parasites and Plasmodium species show that parasite proteins within EVs can serve as reliable biomarkers, aiding in early and specific diagnosis of infections such as malaria and filariasis [5, 6, 7].

Circulating Antigens and Metabolites: Detection of parasite proteins such as circulating anodic and cathodic antigens (CAA and CCA) has shown promise, particularly in schistosomiasis diagnosis. Metabolomic approaches have identified trans-genus biomarkers like vitamin D derivatives and other metabolites that reflect early infection and disease progression across multiple Schistosoma species [8, 9, 10].

Host-Derived Biomarkers

Immune and Endothelial Activation Markers: In malaria, host biomarkers indicative of immune response and endothelial dysfunction—such as Angiopoietin-2 (Angpt-2), soluble Tie-2 receptor (sTie-2), and inflammatory cytokines—correlate with disease severity and parasite biomass. These markers, alongside parasite antigens like HRP-2, hold potential for risk stratification and guiding therapy in severe pediatric malaria.

Macrophage Response Signatures: In leishmaniasis, macrophages are central both as host cells harboring parasites and as modulators of immune response. Transcriptomic and proteomic analyses have identified specific gene and protein

expression profiles in infected macrophages that could serve as indirect biomarkers of infection and disease outcome, facilitating early diagnosis and therapeutic monitoring.

Advantages and Challenges

Biomarkers offer rapid, sensitive, and less invasive alternatives to conventional parasitological methods, enabling earlier diagnosis and better disease management. They also facilitate smaller, more efficient clinical trials and could accelerate regulatory approval of treatments. However, challenges remain, including variability in biomarker expression, lack of standardized clinical guidelines, and the need for validation across diverse populations and parasite species.

Future Directions

Ongoing research aims to integrate parasite-derived and host-derived biomarkers into multiplex diagnostic platforms, enhancing specificity and sensitivity. The development of point-of-care tests incorporating these biomarkers could revolutionize parasitic disease control, especially in resource-limited settings. Further studies are needed to understand biomarker dynamics during infection, their relation to disease severity, and their potential as therapeutic targets.

Conclusion

Biomarker research is advancing the frontier of parasitic infection diagnosis and management. By harnessing molecular signatures from both parasites and hosts, these tools promise to improve early detection, monitor disease progression, and guide effective interventions against parasitic diseases worldwide.

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