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Opinion Article

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Alpha-Fetoprotein as a Biomarker and its Diagnostic Significance across Medical Conditions

Cardaso Rolfes*

Department of Gastroenterology, Centro Hospitalar Universitário de São João, Porto, Portugal

Corresponding Author: Cardaso Rolfes, Department of Gastroenterology, Centro Hospitalar Universitário de São João, Porto, Portugal; E-mail: rolfescard@gmail.com

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Description

Alpha-Fetoprotein (AFP) is a glycoprotein predominantly synthesized by the fetal liver and yolk sac during embryogenesis. While its physiological function in adults remains incompletely understood, AFP has garnered significant attention as a biomarker with diagnostic and prognostic utility in various pathological conditions. AFP is a single-chain polypeptide comprising approximately 591 amino acids, with a molecular weight of approximately 70 kilodaltons. Structurally, AFP belongs to the albuminoid superfamily and shares homology with serum albumin and vitamin D-binding protein. It contains three distinct domains: A serum albumin-like domain, an alpha-1-fetoprotein domain, and a carboxyterminal domain. AFP exhibits remarkable heterogeneity in its glycosylation patterns, contributing to its diverse isoforms and molecular forms. Glycosylation plays a crucial role in modulating AFP's stability, solubility, and biological activity, with alterations in glycan structures implicated in various pathological conditions. During fetal development, AFP serves essential functions in embryogenesis and fetal homeostasis.

It acts as a carrier protein for various ligands, including steroids, fatty acids, and metal ions, facilitating their transport across the placental barrier. Moreover, AFP exhibits immunomodulatory properties, suppressing maternal immune responses to fetal antigens and contributing to immune tolerance. In adults, AFP expression is markedly reduced following birth, with circulating levels typically declining to negligible concentrations by the first year of life. While the physiological role of AFP in adults remains elusive, emerging evidence suggests potential involvement in tissue repair, immune regulation, and oncogenesis. AFP has emerged as a valuable biomarker in the diagnosis, surveillance, and prognostication of various pathological conditions, most notably Hepatocellular Carcinoma (HCC) and certain fetal abnormalities. In HCC, AFP serves as a sensitive tumor marker, with elevated serum levels observed in the majority of patients with HCC, particularly in advanced stages.

AFP's diagnostic performance in HCC is further enhanced when used in conjunction with imaging modalities such as ultrasound and computed tomography, enabling early detection and monitoring of tumor progression. Additionally, AFP kinetics, including the rate of change in serum levels over time, provide valuable prognostic information and guide therapeutic decision-making. Beyond HCC, AFP is also implicated in other malignancies, including germ cell tumors, yolk sac tumors, and hepatoblastoma, where elevated AFP levels serve as a diagnostic hallmark and correlate with tumor burden and treatment response. Furthermore, AFP screening is routinely performed during pregnancy to assess for fetal neural tube defects and chromosomal abnormalities, such as Down syndrome. The clinical applications of AFP extend beyond diagnostic biomarker utility to therapeutic targeting and disease monitoring.

In HCC management, AFP-guided surveillance strategies facilitate early detection of recurrence following curative-intent therapies, including surgical resection, liver transplantation, and locoregional therapies. Moreover, AFP-directed therapies, such as AFP-targeted immunotherapy and molecularly targeted agents, hold promise as novel treatment modalities for HCC, offering the potential for personalized and precision medicine approaches. Furthermore, AFP dynamics serve as surrogate endpoints in clinical trials evaluating novel therapeutic interventions, enabling rapid assessment of treatment efficacy and informing drug development strategies.

Conclusion

Alpha-fetoprotein represents a multifaceted biomarker with diverse clinical applications in health and disease. Through its diagnostic, prognostic, and therapeutic roles, AFP plays a pivotal role in the management of hepatocellular carcinoma, fetal abnormalities, and other malignancies. Continued study and efforts aimed at elucidating AFP's molecular mechanisms, refining diagnostic algorithms, and exploring therapeutic targets hold the promise of further enhancing its clinical utility and improving patient outcomes.

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