Srp Arh Celok Lek. 2015 Jan-Feb;143(1-2):100-104
ИСТОРИЈА МЕДИЦИНЕ / HISTORY OF MEDICINE
DOI: 10.2298/SARH1502100N
UDC: 616-006.6-074:577.112"1963/2013"

Fifty Years of Discovery of Alpha-Fetoprotein as the First Tumor Marker

Dina Nikulina[1], Alexander Terentyev[2], Khalil Galimzyanov[1], Vladimir Jurišić[3]

[1]State Medical Academy, Astrakhan, Russia;
[2]N. I. Pirogov Russian National Research Medical University, Moscow, Russia;
[3]University of Kragujevac, Faculty of Medical Sciences, Kragujevac, Serbia

SUMMARY
Alpha-fetoprotein represents the most prominent oncobiomarker, widely used in the diagnosis of hepatocellular carcinoma for monitoring of tumor progression, presence of metastasis, assessment of cancer prognosis and successful antitumor therapeutic measures. Yuri Semenovich Tatarinov is a Russian scientist who first published antigen specific for human hepatocellular carcinoma in 1963. To commemorate the 50th anniversary of the discovery of alpha-fetoprotein, 9th International Scientific-Practical Conference entitled "Achievements of fundamental science and translational medicine capabilities in solving actual problems of practical public health", was held from May 6–8th, 2013 in Astrakhan, Russia. The conference was held in memory of historical scientific work of Yuri Semenovich Tatarinov.
Keywords: alpha fetoprotein; first tumor marker; history of medicine; Yuri Semenovich Tatarinov

INTRODUCTION

Alpha-fetoprotein (AFP) is a 591 amino acid-gycoprotein (69000 Da) containing 4% carbohydrates, structurally very similar to albumin, with difference in N terminal sequence. Synthesis of AFP starts early in the fetus [1, 2, 3] and a high concentration of AFP can be also found in neonates [3, 4, 5]. During pregnancy the concentration of AFP is usually very high, with values 25-30 times above the reference values in human adults. It has been found that the gene for AFP is localized on the chromosome 4 [6]. AFP is an embryo-specific and tumor-associated protein that is additionally present in small quantities in adults in normal physiological conditions [2-7].

Modern medicine is constantly searching for new molecules that could be used as tumor markers. However, those identified so far have proven not to be perfect [8, 9, 10]. AFP is one of many tumor markers used in the clinical diagnosis [5, 7]. In combination with other proteins AFP has been also proposed to be biomarkers for the detection of human hepatocellular carcinoma (HCC) [5, 7, 11]. Although serum AFP level is obviously raised in most patients with HCC at the time of diagnosis, unexpectedly low or even normal AFP values are reported in about 10–15% of cases. Moderate increase of AFP is also detected in 15% of gastrointestinal cancer, mainly gastric especially associated with worse prognosis. The most common cause of AFP false positivity are acute or chronic liver disorders including cirrhosis, as well as hepatitis and toxic liver diseases occurring mainly after the use of paracetamol and anesthetic. In these cases the increase of AFP is usually moderate and generally under 100 ng/mL in serum. Clinical data indicates that total AFP may be an indicator of tumor mass in liver cancer. Based on this, AFP is considered as a "golden standard" among tumor-specific molecular biomarkers for HCC since the 1970s [12, 13].

Over the past decades, literature data have shown that total AFP is a collection of heterogeneous glycoproteins consisting of three different glycoforms [12, 13]. The total AFP can be separated into three fractions, AFP-L1 to AFP-L3, based on its reactivity to Lens culinaris agglutinin (LCA) on affinity electrophoresis. The AFP-L1 fraction is mostly present in chronic hepatitis and liver cirrhosis, and constitutes a majority fraction of total AFP in the non-malignant liver diseases. AFP-L3 fraction appears to be produced only by cancer cells, indicating their measurements most sensitive for tumor diagnosis [11-14].

HISTORY OF THE DISCOVERY OF ALPHA FETOPROTEIN

The history of Russian science is filled with important milestones, which determined the development of the worldwide biological and medical science. One of them is connected with the names of Harry I. Abelian and Yuri S. Tatarinov.

Scientific Tatarinov's intuition led him to cooperation with a group of scientists from the Institute of Epidemiology and Microbiology of N.F. Gamaleja Academy of Medical Sciences of the USSR (Moscow), which studied tumor tissue in the early 60's of the last century.

Harry Abelev and colleagues have identified new protein in blood of mice with experimen-

Correspondence to:
Vladimir JURIŠIĆ
Faculty of Medical Sciences
University of Kragujevac
P.O. box 124, 34000 Kragujevac
Serbia
vdvd@mailcity.com