

This Week's Citation Classic®

Tatarinov Yu S. Obnaruzhenie embriospetsificheskogo α -globulina v syvorotke krovi bolnogo pervichnym rakom pecheni (Detection of embryo-specific α -globulin in the blood serum of a patient with primary cancer of the liver). *Vop. Med. Khim. SSSR* 10:90-1, 1964.
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The discovery of alpha-fetoprotein in hepatocellular carcinoma demonstrates that embryo-specific proteins may be synthesized in other malignant tissues. This is a very important phenomenon for understanding the relationship between molecular mechanisms of embryogenesis and carcinogenesis. [The *SCI*® indicates that this paper has been cited in over 255 publications, making it the most-cited paper from this journal.]

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In 1963 embryo-specific alpha-globulin (alpha-fetoprotein or AFP) was discovered for the first time in the blood serum of two patients with hepatocellular carcinoma, but it was not found in other oncological situations.¹ Two years later I published another article on this topic in a Russian journal,² which in 1966 was translated and published in the *Federation Proceedings*.³ I believe that the translation of the article from Russian into English focused the attention of different scientists on the phenomenon associated with the gene expression of embryonic proteins in human malignant tissues.

From 1967 to 1969 the International Agency for Research of Cancer (IARC) in Lyon, France, carried out a collaborative study of a serologic test for primary cancer of the liver.⁴ Be-

cause the sera were collected at five African centers (Nairobi, Kampala, Kinshasa, Ibadan, and Dakar) and two non-African centers (Singapore and Kingston) and because our results on AFP testing in cancer were of high specificity, we obtained good results supporting the introduction of AFP testing in cancer all over the world. After the collaborative study by IARC, many companies started producing an AFP test for clinical application both in malignancies and in pathological pregnancy (in other words, *spina bifida*).

In 1972 my laboratory was moved by the Soviet government from Astrakhan to the Second Moscow Medical Institute so that I might continue my investigations in research on new embryonic proteins in cancer. Currently, my research activity is focused on new embryonic and placental proteins as markers in cancer, although my general position as head of the Department of Biochemistry is associated with the training of medical students. As for my research activity, it is at least my hobby.

It seems to me that my paper has been cited often for several reasons. The test for AFP has proven to be highly specific for hepatocellular carcinoma and may be used with advantage in the differential diagnosis of this disease and in epidemiologic studies. Also, AFP may be used as a marker for the study of hepatoblast differentiation *in vitro*. Antibodies to AFP are applied for immunotherapy of AFP-producing tumors, particularly with radiotherapy and drug therapy in combination (monoclonal antibodies can also be used in both immunotherapy and immunohistochemical studies). Finally, the finding of AFP synthesis in embryogenesis and carcinogenesis "marked the beginning of the era of modern oncodevelopmental biology."⁵ At present, three embryonic proteins (AFP, CEA, and PAP) are used in diagnostic screening and monitoring for cancer.⁶ For a recent review citing this paper see reference 7.

1. Tatarinov Yu S. The discovery of fetal globulin in blood serum in primary cancer of the liver. (Abstract.) *Proceedings of the First All-Union Biochemical Congress of the USSR*. Moscow-Leningrad: Academy of Sciences, 1963. Vol. 2, p. 274.
2. ———. Content of embryo-specific alpha-globulin in the blood serum of human foetus, newborn and adult man in primary cancer of the liver. *Vop. Med. Khim. SSSR* 11:20-4, 1965. (Cited 125 times.)
3. ———. Content of embryo-specific α -globulin in fetal and neonatal sera and sera from adult humans with primary carcinoma of the liver. *Fed. Proc.* 25:344-6, 1966. (Cited 55 times.)
4. O'Connor G T, Tatarinov Yu S, Abelev G I & Uriel J. A collaborative study for the evaluation of a serologic test for primary liver cancer. *Cancer* 25:1091-8, 1970. (Cited 195 times.)
5. Fishman W H & Hiral H. *Oncodev. Biol. Med.* 1:1-5, 1980.
6. Tatarinov Yu S. α -fetoprotein in the laboratory testing for cancer. *GANN—Jpn. J. Cancer Res.* 70:133-9, 1979.
7. Bergstrand C G. Alpha-fetoprotein in paediatrics. *Acta Paediat. Scand.* 75:1-9, 1986.