



ANNALES

UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA

SECTIO DDD

PHARMACIA

3



VOL. XXIII, N 3

LUBLIN

2010

UNIwersytet Marii Curie-Skłodowskiej
UNIwersytet Medyczny
ISSN 0867-0609

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ISSN 0867-0609

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ANNALES

UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA

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ANNA KULINICH, ANNA MASLAK, IRYNA PISMENETSKAYA,
OLEKSANDER MINCHENKO, OLGA SHEVCHENKO, ALLA SHEVTSOVA

*Investigation of fibronectin expression by white blood cells
in diffuse liver disease of viral etiology*

Badania nad ekspresją fibronektyny przez krwinki białe w rozlanych chorobach miększu
wątroby o etiologii wirusowej

INTRODUCTION

Problems of liver chronic damages are major and complex in modern medicine. Chronic hepatitis B and C are serious diseases that often lead to cirrhosis due to significant disruptions in the liver. An accompanying parameter of their clinical course is endotoxycosis in inhibition of which a multifunctional glycoprotein fibronectin (FN) is directly involved as an opsonin [3].

FN is presented in plasma, extracellular matrix, and basement membranes of the cells of many tissues, such as hepatocytes, fibroblasts of connective tissue, etc. It can be associated with membranes of different blood cells. Investigation of surface-associated FN has been intensified in connection with FN participation in non-specific host defense and regulation of T-lymphocyte proliferation.

However, little is known about FN distribution inside the cells. Studies of FN synthesis activation inside the cells involved directly in immune responses and connections of this process with different pathologies can be of great use.

The objectives of this paper were to investigate surface-associated and intracellular FN expression by white blood cells in diffuse liver disease of viral etiology.

MATERIAL AND METHODS

Analysis of FN level was carried out in blood plasma of healthy donors (n=7), patients with chronic hepatitis B or/and C in acute phase (n=7) and cirrhosis in active phase (n=7) by immunodot using polyclonal antibodies to plasma fibronectin (received in our laboratory). Expression of FN was examined by flow cytometry using monoclonal antibodies to fibronectin (AbD Serotec, UK).

RESULTS

The FN level in plasma of patients with chronic hepatitis was not changed (368.81 mkg/ml); it was reliably decreased in plasma of patients with liver cirrhosis (253.2 mkg/ml, $p>0.05$). Analysis of FN expression by blood cells showed that the most significant changes occurred in lymphocytes. In chronic hepatitis the amount of lymphocytes with surface-associated and intracellular FN increased by 36% and 55%, respectively, in comparison with normal blood cells. In cirrhosis of liver the amount of lymphocytes expressing intracellular FN increased by 59% (Table 1).

Table 1. Fibronectin expression by white blood cells in liver diseases

Cells	Chronic hepatitis B or/and C		Cirrhosis of liver		Control	
	On the surface, %	Inside the cell, %	On the surface %	Inside the cell, %	On the surface %	Inside the cell, %
Lymphocyte	136.04±7.77*	154.50±25.19*	114.67±21.53	158.99±25.8**	100±5.97	100±3.56
Monocyte	100.98±0.91	95.54±10.31	100.2±0.68	103.37±0.3	100±0.50	100±2.09
Granulocyte	100.94±0.11	104.44±0.09	100.32±0.76	103.57±0.09	100±1.00	100±3.87

* level of reliability during $p>0.05$; ** $p>0.01$

DISCUSSION

Fibronectin can be associated with membranes of T-lymphocytes, polymorphonuclear neutrophils and monocytes [4, 5]. Our experiments showed an increasing level of fibronectin inside the fraction of lymphocytes in chronic hepatitis and liver cirrhosis.

It has been revealed that fibronectin may be present inside T-lymphocytes [2]. According to Blum et al. endogenous FN interacts through its ED-A and ED-B domains with ganglioside sites on the cell membrane. Functions of this endogenous fibronectin are still unclear [1].

In liver diseases increased expression of FN is a result of increasing lymphocyte populations with intracellular and surface-associated FN which can be synthesized by these cells or captured by cell receptors from blood stream. This can be connected with the functional roles of FN in the diseases.

Further investigation of fibronectin expression by white blood cells can be useful for studying molecular mechanisms of immune processes and their dysfunctions in liver diseases and for searching molecular targets of new medications.

CONCLUSIONS

The level of plasma fibronectin was not changed in chronic hepatitis and it was decreased in liver cirrhosis.

Fibronectin expression by lymphocytes is increased considerably both in chronic hepatitis and liver cirrhosis.

Investigation of fibronectin expression by white blood cells can be useful for studying molecular mechanisms of immune processes and searching for new medicines.

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SUMMARY

We investigated plasma and cell fibronectin level in 14 patients with chronic liver diseases. The level of plasma fibronectin was not changed in chronic hepatitis and it was decreased in liver cirrhosis. In chronic hepatitis the number of lymphocytes expressed fibronectin on the surface and inside the cells was increased; in cirrhosis only the lymphocyte amount with intracellular FN was increased. Investigation of the expression of fibronectin by blood cells can be useful for studying molecular mechanisms of immune processes and searching for new medicines.

Keywords: fibronectin, chronic hepatitis, expression, white blood cells, cirrhosis

STRESZCZENIE

Oznaczono stężenia osoczowe i komórkowe fibronektyny u 14 pacjentów z przewlekłymi schorzeniami wątroby. Stężenia osoczowe fibronektyny nie ulegały zmianie w przewlekłym zapaleniu wątroby, były natomiast obniżone u pacjentów z marskością wątroby. W przewlekłym zapaleniu wątroby liczba limfocytów z ekspresją fibronektyny na powierzchni i wewnątrz komórki była zwiększona; w marskości wątroby podwyższona była jedynie liczba limfocytów z wewnątrzkomórkową ekspresją FN. Badanie ekspresji fibronektyny na komórkach krwi może być pomocne w badaniach nad molekularnymi mechanizmami procesów immunologicznych oraz w poszukiwaniach nowych leków.

Słowa kluczowe: fibronektyna, przewlekłe zapalenie wątroby, ekspresja, krwinki białe, marskość

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14. MONIKA KARAŚ, ANNA JAKUBCZYK, BARBARA BARANIAK
Antiradical and antihypertensive activity of peptides obtained from proteins
pea sprouts (*Pisum sativum*) by enzymatic hydrolysis
Antyrodnikowa i antynadciśnieniowa aktywność peptydów otrzymanych w wyniku
enzymatycznej hydrolizy białek kielków grochu (*Pisum sativum*) 115
15. JADWIGA BŁONIAK, STANISŁAW ZARĘBA
Evaluation of some macroelement levels in selected dietary supplements supporting
the immune system of the human organism
Ocena zawartości niektórych makroelementów w wybranych suplementach diety
wspomagających system odpornościowy organizmu ludzkiego 123
16. JAROGNIEW J. ŁUSZCZKI, ANNA JASKÓLSKA, WOJCIECH DWORZAŃSKI,
DOROTA ŻÓLKOWSKA
Effect of 7-nitroindazole and NG-nitro-L-arginine on the protective action of
clobazam in the maximal electroshock-induced seizures in mice
Wpływ 7-nitroindazolu i NG-nitro-L-argininy na ochronne działanie klobazamu
w teście maksymalnego wstrząsu elektrycznego u myszy 135
17. JAROGNIEW J. ŁUSZCZKI, ANNA RĘKAS, LECH P. MAZURKIEWICZ,
MICHAŁ GLEŃSK, GRAŻYNA OSSOWSKA
Effect of osthole on the protective activity of carbamazepine and phenobarbital against
maximal electroshock-induced seizures in mice
Wpływ ostolu na ochronne działanie karbamazepiny i fenobarbitalu w teście
maksymalnego wstrząsu elektrycznego u myszy 145
18. ANDRIY SUKHOMLYN, KARINE NEPORADA
Experimental correction of pathological changes in salivary glands by multiprobiotic
Symbiter® *acidofilus* under conditions of hypergastrinemia
Doświadczalna korekcja zmian patologicznych gruczołów ślinowych pod wpływem
multiprobiotyku *Symbiter*® *acidofilus* w warunkach hipergastrynemii 157
19. ANNA KRYSHCHYSHYN, BORYS ZIMENKOVSKY, ROMAN LESYK
Synthesis of novel fused thiopyrano[2,3-d]thiazole derivatives as potential
anticancer agents
Synteza nowych pochodnych tiopirano[2,3-d]tiazolu jako potencjalnych
leków przeciwnowotworowych 163
20. ANNA KULINICH, ANNA MASLAK, IRYNA PISMENETSKAYA,
OLEKSANDER MINCHENKO, OLGA SHEVCHENKO, ALLA SHEVTSOVA
Investigation of fibronectin expression by white blood cells in diffuse
liver disease of viral etiology
Badania nad ekspresją fibronektyny przez krwinki białe w rozlanych
chorobach miąższu wątroby o etiologii wirusowej 169