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care se bazează pe:

A. **Nota de constatare şi confirmare a indiciilor de plagiat** prin fişa suspiciunii inclusă în decizie.

Fişa suspiciunii de plagiat / Sheet of plagiarism's suspicion

Opera suspicionată (OS) Suspicious work	Opera autentică (OA) Authentic work

OS	DĂNĂILĂ Leon.*The cordocyte.* Proc.Rom.Acad. Series B. **16**(2). 2014. p.83-102
OA	PĂIŞ Viorel; DĂNĂILĂ, Leon and PĂIŞ Emil. From pluripotent stem cells to multi-functional cordocytic phenotypes in the human brain:an ultrastructural study. *Ultra-structural Pathology.* **36**(4). 2012. p.252-259

Incidenţa minimă a suspiciunii / Minimum incidence of suspicion	
p.83:07 - p.83:11	p.252:02-06
p.84:23d - p.85:05s	p.252:11s-19s
p.85:31s – p.85:45s	p.252:14d-p.253:04
p.86:04s - p.86:18s	p.253:07-p.253:08; p.253:12s-p.253:04d
p.86:34s - p.86:08d	p.253:16d-p.254:15s
p.90:Fig.5	p.253:Fig.1(a)
p.91:Fig.7	p.253:Fig.3
p.92:Fig.8	p.254:Fig.4
p.92:Fig.9	p.254:Fig.5
p.101:18s-48s	p.258:26s - p.258:35s; p.258:42s-p.258:53s; p.258:03d – p.258:10d; p.258:14d – p.258:17d
p.101:25d – p.101:27d	p.258:39d – p.258:41d
p.101:34d – p.101:36d	p.258:47d – p.258:49d

Fişa întocmită pentru includerea suspiciunii în Indexul Operelor Plagiate în România de la
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Notă: Prin „p.72:00" se înţelege paragraful care se termină la finele pag.72. Notaţia „p.00:00" semnifică până la ultima pagină a capitolului curent, în întregime de la punctul iniţial al preluării.

Note: By „p.72:00" one understands the text ending with the end of the page 72. By „p.00:00" one understands the taking over from the initial point till the last page of the current chapter, entirely.

B. **Fişa de argumentare a calificării** de plagiat alăturată, fişă care la rândul său este parte a deciziei.

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Fişa de argumentare a calificării

Nr. crt.	Descrierea situaţiei care este încadrată drept plagiat	Se confirmă
1.	Preluarea identică a unor pasaje (piese de creaţie de tip text) dintr-o operă autentică publicată, fără precizarea întinderii şi menţionarea provenienţei şi însuşirea acestora într-o lucrare ulterioară celei autentice.	✓
2.	Preluarea a unor pasaje (piese de creaţie de tip text) dintr-o operă autentică publicată, care sunt rezumate ale unor opere anterioare operei autentice, fără precizarea întinderii şi menţionarea provenienţei şi însuşirea acestora într-o lucrare ulterioară celei autentice.	
3.	Preluarea identică a unor figuri (piese de creaţie de tip grafic) dintr-o operă autentică publicată, fără menţionarea provenienţei şi însuşirea acestora într-o lucrare ulterioară celei autentice.	✓
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12.	Preluarea identică de pasaje (piese de creaţie de tip text) ale unui cuvânt înainte sau ale unei prefeţe care se referă la două opere, diferite, publicate în două momente diferite de timp.	

Notă:

a) Prin „provenienţă" se înţelege informaţia din care se pot identifica cel puţin numele autorului / autorilor, titlul operei, anul apariţiei.

b) Plagiatul este definit prin textul legii[1].

> *„ …plagiatul – expunerea într-o operă scrisă sau o comunicare orală, inclusiv în format electronic, a unor texte, idei, demonstraţii, date, ipoteze, teorii, rezultate ori metode ştiinţifice extrase din opere scrise, inclusiv în format electronic, ale altor autori, fără a menţiona acest lucru şi fără a face trimitere la operele originale…".*

Tehnic, plagiatul are la bază conceptul de **piesă de creaţie** care[2]:

> *„…este un element de comunicare prezentat în formă scrisă, ca text, imagine sau combinat, care posedă un subiect, o organizare sau o construcţie logică şi de argumentare care presupune nişte premise, un raţionament şi o concluzie. Piesa de creaţie presupune în mod necesar o formă de exprimare specifică unei persoane. Piesa de creaţie se poate asocia cu întreaga operă autentică sau cu o parte a acesteia…"*

cu care se poate face identificarea operei plagiate sau suspicionate de plagiat[3]:

> *„…O operă de creaţie se găseşte în poziţia de operă plagiată sau operă suspicionată de plagiat în raport cu o altă operă considerată autentică dacă:*
> *i) Cele două opere tratează acelaşi subiect sau subiecte înrudite.*
> *ii) Opera autentică a fost făcută publică anterior operei suspicionate.*
> *iii) Cele două opere conţin piese de creaţie identificabile comune care posedă, fiecare în parte, un subiect şi o formă de prezentare bine definită.*
> *iv) Pentru piesele de creaţie comune, adică prezente în opera autentică şi în opera suspicionată, nu există o menţionare explicită a provenienţei. Menţionarea provenienţei se face printr-o citare care permite identificarea piesei de creaţie preluate din opera autentică.*
> *v) Simpla menţionare a titlului unei opere autentice într-un capitol de bibliografie sau similar acestuia fără delimitarea întinderii preluării nu este de natură să evite punerea în discuţie a suspiciunii de plagiat.*
> *vi) Piesele de creaţie preluate din opera autentică se utilizează la construcţii realizate prin juxtapunere fără ca acestea să fie tratate de autorul operei suspicionate prin poziţia sa explicită.*
> *vii) In opera suspicionată se identifică un fir sau mai multe fire logice de argumentare şi tratare care leagă aceleaşi premise cu aceleaşi concluzii ca în opera autentică…"*

[1] Legea nr. 206/2004 privind buna conduită în cercetarea ştiinţifică, dezvoltarea tehnologică şi inovare, publicată în Monitorul Oficial al României, Partea I, nr. 505 din 4 iunie 2004
[2] ISOC, D. *Ghid de acţiune împotriva plagiatului: bună-conduită, prevenire, combatere*. Cluj-Napoca: Ecou Transilvan, 2012.
[3] ISOC, D. *Prevenitor de plagiat*. Cluj-Napoca: Ecou Transilvan, 2014.

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MEDICINE
Research article

THE CORDOCYTE

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My research work, which led us to discover this cerebral cell (Cordocyte) has started in the 2000 years, when I have highlighted it for the first time, during a study upon clarification of some undiscovered aspects of cerebral atherosclerosis. In 2005, I have initiated the publishing our results in two atlases and at Cape Town congress in 2006. This work is based on data analysis by light and transmission electron microscopy of the surgical cases operated by me in the last 13 years. We examined cortical arteries and veins, perivascular areas with old hematic masses, vasculogenetic foci, broken large vessels, moyamoya disease, thromboses, tumors and cerebrovascular malformations, to identify and characterize different phenotypes belonging to a new interstitial cell recently described ultrastructurally in the brain and here, named cordocyte. Also, we attempted to identify and characterize precursor/stem cells for cordocytic lineage in the perivascular areas, within perivascular nerves, choroid plexus and pia mater (now considered a cordocytic-vascular tissue). This cytohistopathological study illustrates and explains some facets of cordocytes-stem cells cooperation around on the fundamental role of cordocytes in response to vascular injuries.

Key words: human brain, vessels, cordocytes, stem cells ultrastructure.

INTRODUCTION

History

My research is based on the well-known fact according to which, the brain is devoid of lymphatic tissue and lymphatic circulation.

Considering this phenomenon, I asked myself if it is possible that its functions are taken over by other elements of the central nervous system (CNS) which had not been known until today.

As a neurosurgeon, I had studied day by day, with great patience and attention, with the help of the optical microscope and of the electron microscopy, all the expansive processes and the cerebral biopsies harvested from the patients I had operated on.

In this way, beginning with 2000, I had observed the existence within the brain of a thin and elongated interstitial cell with a protective and defensive role against the various internal and external aggressions, of the most noble and most complex structure in the universe – the brain (Danaila *et al.*, 2000; Danaila *et al.*, 2002 a, b; Danaila *et al.*, 2003 a, b; Danaila *et al.*, 2004 a, b; Danaila and Pais, 2004; Danaila *et al.*, 2005).

The referred to observation, which I had initially considered to be insufficient, did not allow me to make public this new morpho-functional cerebral cytological entity.

It wasn't until the year 2005 when, following the positive rendering evident of the most important morphological (Figure 1) and physiological features, about which I did not have any doubts anymore, I had made public and I had described in two atlases the new cerebral cell I had discovered (Danaila *et al.*, 2005; Danaila and Pais, 2005).

I had postponed the official announcement of my discovery because the analized cell was very thin and thus below the resolution of the optical microscope.

The enormous amount of the material which required analyzing had made me to take on as collaborator the biologist Viorel Pais who, although

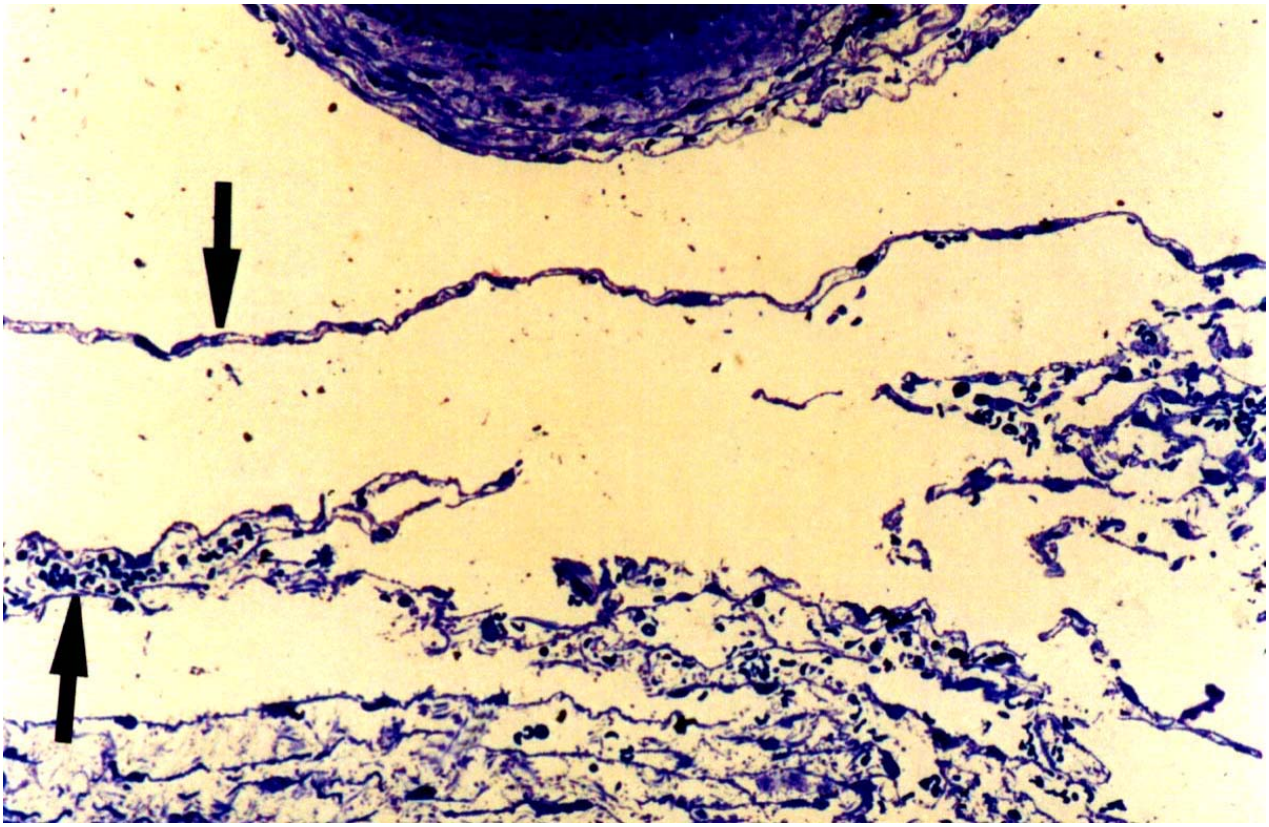

Figure 1. An arteriovenous malformation containing multiple long cordocytes arranged in parallel (arrows).

he had never worked in the Neurosurgery Department of the National Institute of Neurovascular Diseases in Bucharest, had sufficient experience in this field.

After several years, he had been pensioned off from the Ultrastructural Pathology Department of "Victor Babes" National Institute of Research Development in the Pathology Domain and Biomedical Sciences in Bucharest, and he had died on the 2nd of July 2014.

Anyhow, by having enough time at his disposal, he had been a real help for me in the selection of the figures, in their arranging into the atlases and in their drawing up, as well as in the carrying into effect of several scientific papers related to this problem, as it follows.

In 2006, we had presented the results of our research at the World Congress on Stroke in Cape Town (Danaila and Pais, 2006), and in 2008, at the 6th World Stroke Congress in Vienna (Danaila and Pais, 2008).

The first synthesis paper with reference to the morphology and the physiology of the cordocyte (already known at that time) had been published in 2011 (Danaila and Pais, 2011).

Subsequently, in 2012 and in 2013, Pais Viorel, Danaila Leon and Pais Emil had also published another two scientific papers on this topic in the "Ultrastructural Pathology" medical journal (Pais V, Danaila L and Pais E, 2012; 2013).

Emil Pais, who appears as the third and the last author of several recent scientific papers, but not of the atlases in which it is stored our entire research work relating to the cordocyte, the cellular death, the angiogenesis, etc., did not have any contribution to the research conducted by Leon Danaila and Viorel Pais.

He had been added as the third author by his father, in order to become employed by a medical institution in the United States of America, where he had emigrated immediately after graduating the University of Medicine and Pharmacy in Bucharest.

In 2014 we had published an optical and electron microscopy atlas which comprises new and innovative data with reference to the morphology and the physiology of the cordocytes in the human brain (Danaila Leon and Pais Viorel, 2014).

We had undertaken this study because this interstitial cell, which is similar, but not identical to the interstitial cell of Cajal, has a wide cerebral distribution and multiple functions which had not been reported in the literature by any other author.

We consider it to be a genuine maestro in health and diseases because of its biological potential within the cerebral parenchyma, in the areas surrounding the blood vessels, in the choroid plexuses, in the pia mater, etc.

MATERIAL AND METHODS

This work is based on the data analysis by light scanning and transmission electron microscopy of the surgical cases operated by Danaila during the last 13 years.

The ages of the patients from whom there had been harvesteed the cerebral bioptic material had been between 4 and 90 years old.

The analyzed pathological processes had included thromboses of the carotid system, cerebro-vascular malformations, aneurysms, primary hematomas, Moyamoya disease, perivascular hemorrhages, infarctions, traumatic brain injuries, metastatic brain tumors, tuberculomas, cysts, tumors (tumors of the normal choroid plexus, pineocytomas, germinomas, medulloblastomas, glioblastomas, astrocytomas, schwannomas, meningiomas, hemangiopericytomas, lymphoma craniopharyngioma, hypophyseal tumors, chordomas), abscesses, cysticercosis, hydatidosis, etc.

The normal cerebral cortex and the white matter had been harvested from the patients which had been operated for unbroken cerebral aneurysms (Danaila and Pascu, 2001; Danaila *et al.*, 2002; Danaila *et al.*, 2006; Danaila and Ştefănescu, 2007; Danaila *et al.*, 2008; 2009; 2010 a, b, c; Danaila, 2012; Danaila *et al.*, 2012 a, b, c; Danaila, 2013 a, b, c; Danaila *et al.*, 2013; Danaila and Rădoi, 2013; Danaila and Pascu, 2013).

The samples which had been studied under an optical microscope had been fixed with 2.5% buffered glutaraldehyde and post-fixed with 1% buffered osmium tetroxide, dehydrated in alcohols and embedded in resin epoxy (Epon 812). There had been cut sections with a thickness of 4-6µ using an ultramicrotome which had been then mounted on glass slides, stained with 1% toluidine blue, and examined using optical microscopy. There had also been cut with the ultramicrotome multiple ultrathin sections, with a thickness of 70 nm, which had been then treated with 2% uranyl acetate, as well as with Reynolds lead citrate solution. The specimens were then examined using the JEM 1200 EX (JEOL) transmission electron microscope.

The electron micrographs had been processed on a computer and then converted into images.

Ultrastructurally, there had been identified, characterized and compared both undifferentiated cells and well-differentiated cordocytes found in different locations, from the outer cerebral cortex to the choroid plexus, and in areas with old hematic masses, vasculogenetic foci, heterotopic neural tissue, encapsulation, broken arteries and abnormal proliferations, such as microtumors.

We had demonstrated the existence of phenotypical changes of the cells, and our findings had especially shed light on the roles of these cells which might facilitate the beneficial actions and delay the pathological processes, they being involved in the fundamental processes of the development of the central nervous system.

RESULTS

Several new histopathological features

The protective role of the pia mater cordocytes

The cordocytes, which form the pia mater together with the with blood vessels, are involved postnatally in the normal corticogenesis (which had been demonstrated in the cerebral ectocortex), in the maintenance of the appropriate pericortical microenvironment, in the vasculogenesis, vasomotion and vascular repair / remodeling, in the inhibition of the hematic invasion into the brain parenchyma as physical barriers, especially in the hypertensive human individuals, in the inhibition of the microtumoral growth and of any aberrant cellular migration towards the cerebral cortex, etc. (Figure 2).

Thus, the pia mater is composed of cordocytes. This assembly of cordocytes as the ultimate and active defender of the cerebral cortex and of the cortical vessels is a very dynamic structure, it undergoing numerous phenotypical modulation changes and accompanying various events, both in healthy individuals and during pathological processes, as a barrier within the immune surveillance.

The cordocytes and the blood-brain-barrier (BBB)

The blood-brain-barrier concept is based on the fact according to which the vital dyestuffs introduced into the blood flow do not color the brain.

Therefore, the blood-brain-barrier is the morphofunctional system which selectively regulates the access and the exit of the biological substances and of the cells, in order to control and to preserve the normal microenvironment, the morphology and the physiology of the brain.

To that effect, we had ascertained that not only the close interendothelial junctions have such a role, but the entire wall of the capillaries, of the arteries and of the veins are overprotected on the outside by well defined layers of cordocytes. (Figures 3 and 4).

The cordocytes prevent the access into the brain especially of the red blood cells, whose degradation products have a nocuous effect not only on the cerebral parenchyma, but also on the blood vessels, in which they have a spasmodic effect.

Its consequences, which can sometimes be even fatal, can be found in the patients with subarachnoid hemorrhage.

The cordocytes block the uncontrolled spreading within the brain of the red blood cells

which cross the intercellular junctional complexes which tightly connect the endothelial cells among themselves.

Our microscopic observations had been focused on the periarterial areas.

In this way, we had observed that the extravasated red blood cells are detained by the cordocytes either through adhesion or through catching. Finally, the red blood cells which had been loaded on the cordocytes are hemolyzed.

Whenever the protective cordocytic network is overwhelmed by the large quantity of red blood cells, or when these die, there are generated self-signals which concentrates numerous perivascular stem cells in the injured area (Figure 5).

In such situations, in the respective area there can be found unidentified cells, transitional forms and well defined cells.

Generally, most of our body is constantly renewed. The adult neurogenesis is the production of new functional neurons in the adult brain (Figure 6, adapted from Altman and Dass, 1965).

The cordocyte and its antitumoral role

The defensive means of the human body against cancers are equally numerous as their causes.

Therefore, during his or her lifetime, an individual can suffer and can be cured of cancer several times.

Actually, the human body can sometimes survive even the most terrible diseases.

Among the multiple defensive possibilities of the brain against the abnormally proliferating cells we can also find the cordocyte.

In such circumstances, every single cell which usually surrounds an artery can be activated, and they will position themselves in front of the abnormal cellular mass, with the nuclear long axis perpendicular to the advancing cell mass (Figure 7).

This peculiar inhibitory role of the abnormal cell proliferations is demonstrated by this cell type in the genuine tumoral cases, when large perivascular formations are closely surrounded by cordocytes, which inhibit and delay both the cell growth and their movement (Figure 8). This property to impede / delay both the cell growth and any motion is easily observable in the cases with arteriovenous malformations, where the cordocytes seem to have an efficient role in controlling the development of the neural tissue, closely surrounding all the neuroepithelial cells, and extending their filopodia towards the target cells. Moreover, overlapping cordocytes form a thick barrier between the neuroepithelial and the lymphocytic population, with the lymphocytes being separated from the neural cells (Figure 9).

In the analysis performed by Pais, Danaila and Pais (2013) there had been observed certain important aspects which we shall present as follows.

Thus, we had ascertained the interesting fact that the tumor formation is often surrounded by a thin basement membrane consisting of fibrils. The referred to thin fibrils surround each one of the tumoral cells, but not the immune cells infiltrated within the tumor mass.

The presence of the long and thin protrusions of the cordocytes around the microtumor suggests their role of antitumoral barrier.

Nevertheless, this barrier is missing here and there, while in other areas, where it is degenerated, there are found numerous peripheral thin connective fibrils.

In the zone surrounding the microtumoral mass, with areas of autophagy, the white matter is degenerated, the axons are caricatured, the oligodendrocytes are in an apoptotic phase, while the microglial cells are loaded with autophagosomes, secondary lysosomes and vascular cytoplasmic areas.

At the analysis of the transmission electron microscopy images of another tumoral node located within the white matter, in a female patient with a traumatic brain injury, we had observed an increased density of cells which appeared to be derived from the perivascular cells and the modified endothelial cells of the staghorn-shaped vessels.

These proliferated polygonal cells which surround the endothelial cells in the so-called staghorn pattern are characteristic for a hemangiopericytoma, which can metamorphose later into a true intraparenchymal tumor.

The traumatic injury could have been an etiological factor for the tumor.

In conclusion, in some tumors, the cause can be represented by the traumatic brain injury.