REVIEW

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

PV-1 expression could distinguish the subset of caveolae-presenting telocytes that are endothelial progenitors

ALEXANDRA DIANA VRAPCIU[1)], MUGUREL CONSTANTIN RUSU[1,2)]

[1)]*Division of Anatomy, Department 1, Faculty of Dental Medicine, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

[2)]*MEDCENTER, Center of Excellence in Laboratory Medicine and Pathology, Bucharest, Romania*

Abstract

Telocytes (TCs) are stromal cells with characteristic long, thin and moniliform prolongations termed telopodes. They were formerly termed interstitial Cajal-like cells. A characteristic set of markers to identify TCs in light microscopy has not been established until now. Transmission electron microscopy (TEM) is a better tool for identifying TCs. Telocytes display caveolae and can express caveolin-1. On the other hand, endothelial cells (ECs) as well as endothelial progenitor cells (EPCs) have caveolae. Recent evidence suggests that a subset of TCs are in fact EPCs. The distinction of this progenitor subset of TCs can be easily made by a specific set of ultrastructure markers, as follows. Caveolae of endothelial cells present stomatal diaphragms (SDs). The plasmalemma vesicle-associated protein-1 (PV-1), which is identical with the Pathologische Anatomie Leiden endothelium (PAL-E), is specifically identifying the ECs SDs of caveolae. We therefore raise the reasonable hypothesis that the EPCs subset of caveolae-presenting TCs could be accurately identified, without exploration in TEM, by the positive expression of PV-1 or PAL-E in the SDs.

Keywords: EPCs, endothelial cells, PAL-E, stomatal diaphragms, telopodes.

Introduction

Telocytes (TCs) are a peculiar type of stromal (interstitial) cells, which were renamed from "Interstitial Cajal-like Cells (ICLCs)" in an Editorial (Review-Article) published by Popescu & Faussone-Pellegrini in 2010 [1]. At that time, an ultrastructural standard of identification of TCs was indicated, and it included the (sub)plasmalemmal caveolae [1]. Telocytes' peculiarity consists in their long, thin and moniliform prolongations termed telopodes (Tps), which consist of thin segments named podomers, and dilations named podoms [2–5]. This determined Popescu to simply define TCs as "*cells with telopodes*" [6]. It was repeatedly stated that the key tool for identifying TCs is the transmission electron microscopy (TEM) [1, 7–10], which raises doubts on different methods of TEM which were used to identify TCs. One should note here that different attempts of identifying a specific molecular phenotype of TC indicated CD34 as a suitable marker, although it is equally an endothelial, as well a mesenchymal one [11–20].

However, although numerous studies were published on TCs, their functional roles within stromal compartments are still blurred. Several studies indicate the CD34-expressing telocytes as cells with progenitor capacity [13–15, 17, 21], which is in agreement with a previous assumption, that ICLCs "*might represent stromal progenitor cells*" [22]. Some other research groups claim that TCs "*nurse*" stem and progenitor cells within niches [23, 24]. Different molecular phenotypes, which were assigned to TCs, indicated their stemness capacity [3, 19]. The origin of TCs from circulating precursors was also suggested [20, 25]. It was critically reviewed that most of the functions assumed for TCs are purely hypothetic, and it was observed that there is no reference about TCs in the internationally accepted *Terminologia Histologica* [26].

Caveolae, with and without stomatal diaphragms

Caveolae, the 50–100 nm flask-shaped plasmalemmal organelles, were discovered in early 1950s and can be encountered in a variety of cells, such as endothelial cells, adipocytes, pneumocytes, fibroblasts, striated and smooth muscle cells (a detailed review on caveolae was published by Cohen *et al.* in 2004 and can be consulted) [27]. In striated muscle, caveolae, as well as *t*-tubules, express common markers, such as is the dihydropiridine receptor (DHPR) [28, 29].

Endothelial cells (ECs) are provided with caveolae at blood and tissue fronts, these being plasmalemmal vesicles of 65–75 nm bound by typical unit membranes [30].

Stomata of endothelial plasmalemmal caveolae (or vesicles), but not of caveolae of any other cell types, are subtended by specialized structures called stomatal diaphragms (SDs) (Figure 1) [31–38]. Palade & Bruns (1968) described these structures as consisting of one or more dense layers, presenting a central thickening or knob [30, 39], and being anchored by fibrillar elements to the rim of the caveolar openings [40].

Caveolins in caveolae-presenting cells

Caveolins are integral membrane proteins specifically expressed in caveolae; three mammalian caveolins are known, caveolin-1, -2 and -3 [41]. Endothelial cells express, but not exclusively, only caveolin-1 and caveolin-2, while caveolin-3 is predominantly expressed in muscle cells [31, 41].

Caveolin-1 and -3 play a key-role in the caveolae formation [42, 43]. Caveolin-1 is specific for caveolar coat ridges [44]. Caveolin-1 and caveolin-2 are co-expressed in the vast majority of cells or tissues [45]. Confined initially to muscular cells [46], caveolin-3 is expressed in different cellular types [47]. A short guide of caveolin-1 and caveolin-3 specific expressions is presented in Table 1.

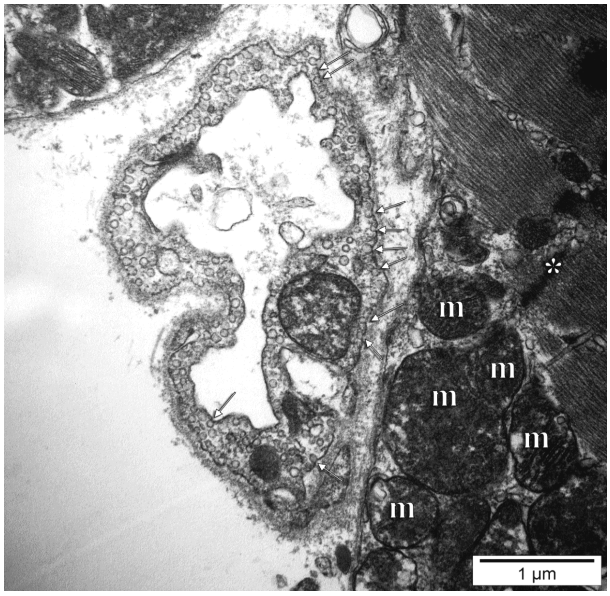

Figure 1 – ***Transmission electron microscopy. Masseter muscle, rabbit. There are indicated stomatal diaphragms of endothelial caveolae (arrows) of an endomysial microvessel. m: Mitochondria; *: Z-disk of a striated muscular fiber.***

Table 1 – ***Caveolin-1 and -3 specific expressions***

Caveolin	Expression	Reference
Caveolin-1	Endothelial cells	[48, 49]
	Adipocytes	[50, 51]
	Type I alveolar pneumocytes	[52]
	Smooth muscle cells	[43, 53]
	Osteoblasts	[54]
	Leydig cells	[55]
	Airway epithelium	[56]
Caveolin-3	Skeletal muscle	[57]
	Myocardium	[58–60]
	Smooth muscle cells	[46]
	Astrocytes	[47]
	Sinus endothelial cells	[61]

PV-1 is PAL-E, as well as FELS, in endothelial cells

A caveolae purification procedure was developed on luminal plasmalemmal patches from rat pulmonary vessels; caveolae were isolated by immunoabsorption on caveolin-coated microspheres and the only protein found to strictly colocalize with caveolin on the immunoisolated endothelial caveolae (ECav) was PV-1 [plasmalemma vesicle(-associated) protein], formerly known as gp68 [36]. gp68 was initially isolated as a glycoprotein expressed in the developing mouse brain [62]. PV-1 (PV1) is a single-span, 60-kDa, type II membrane N-glycosylated glycoprotein with a short intracellular tail and a long extracellular domain [36]. PV-1 is so endothelium specific, and is specifically associated with the SDs of caveolae and transendothelial channels (TECs) and fenestral diaphragms (FDs) of ECs [37, 63].

To discriminate between vascular and lymphatic endothelia, several vascular endothelial specific markers were used in various studies, including CD105 (endoglin), CD34, von Willebrand factor (vWF) and Pathologische Anatomie Leiden endothelium (PAL-E, the anti-endothelium antibody) [64]. It was recently confirmed that the anti-PAL-E antibody recognizes the PV-1 molecule, as does the PV-1 antibody [64]. Probably, the first found function of PV-1 is the leukocyte transendothelial migration, the transcellulary migrating lymphocytes being surrounded by rings which contain PV-1 and caveolin-1 [65]. Although PAL-E is identical with PV-1, as well as with the fenestrated endothelial-linked structure protein (FELS), it is however not identical with vimentin [66], although it is physically associated with this intermediate filament protein [65].

A subset of telocytes are in fact endothelial progenitor cells

Recently, brought evidence is suggestive for a subset of TCs actually being spindle-shaped endothelial progenitor cells (EPCs) [67]. It is interesting to note here that TCs within the skeletal muscle interstitium were indicated as expressing caveolin-1, c-kit and vascular endothelial growth factor (VEGF) [68]. Telocytes in human term placenta were found expressing CD34, c-kit, vimentin, caveolin-1, VEGF and inducible nitric oxide synthase, but this phenotype was assessed in cultures in which "*cells resembling TC were successfully maintained*" [69]. It should be observed that these markers are also indicative either for a hematopoietic lineage, or for an endothelial progenitor one. Early immature EPCs express hemato-poietic cell markers (c-kit, CD34, CD133) and markers of the myeloid lineage, while in a more differentiated state EPCs lose expression of hematopoietic markers and gain expression of endothelial markers, such as vWF, VE-cadherin, or caveolin-1 [70]. On the other hand, EPCs have a strong expression of angiogenic growth factors, such as VEGF [71]. The fact that different subsets of TCs, regarded as cells with Tps, exist, is also supported by previous evidence of caveolae-presenting TCs [72] and of caveolae-lacking TCs [73], these later being, or not, adequate candidates for the endothelial lineage.

Raising the hypothesis: PV-1 should differentiate without TEM exploration the subset of caveolae-presenting TCs, which belong to the endothelial lineage

We therefore raise the reasonable hypothesis for the EPCs subset of caveolae-presenting spindle-shaped stromal cells/TCs being accurately identified, without exploration in TEM, by the positive expression of PV-1 or PAL-E in the SDs. This specific labeling needs however also an immunoelectron microscopy (IEM) testing, although simple identification of SDs in TEM would be indicative. In this support stands previous evidence of caveolae-presenting TCs undoubtfully being closed by SDs (Figure 5A in [74], Figure 1E in [75], Figure 2A in [76]).

Conflict of interests

The authors declare that they have no conflict of interests.

References

[1] Popescu LM, Faussone-Pellegrini MS. Telocytes – a case of serendipity: the winding way from interstitial cells of Cajal (ICC), *via* interstitial Cajal-like cells (ICLC) to telocytes. J Cell Mol Med, 2010, 14(4):729–740.

[2] Rusu MC. Letter to the Editor. Skin telopodes. Rom J Morphol Embryol, 2014, 55(2 Suppl):723–724.

[3] Grigoriu F, Hostiuc S, Vrapciu AD, Rusu MC. Subsets of telocytes: the progenitor cells in the human endocardial niche. Rom J Morphol Embryol, 2016, 57(2 Suppl):767–774.

[4] Mirancea N. Telocyte – a particular cell phenotype. Infrastructure, relationships and putative functions. Rom J Morphol Embryol, 2016, 57(1):7–21.

[5] Rusu MC, Duţă I, Didilescu AC, Vrapciu AD, Hostiuc S, Anton E. Precursor and interstitial Cajal cells in the human embryo liver. Rom J Morphol Embryol, 2014, 55(2):291–296.

[6] Popescu LM. The tandem: telocytes – stem cells. Int J Biol Biomed Eng, 2011, 5(2):83–92.

[7] Rusu MC, Pop F, Hostiuc S, Dermengiu D, Lală AI, Ion DA, Mănoiu VS, Mirancea N. The human trigeminal ganglion: c-kit positive neurons and interstitial cells. Ann Anat, 2011, 193(5):403–411.

[8] Rusu MC, Pop F, Hostiuc S, Curca GC, Jianu AM, Paduraru D. Telocytes form networks in normal cardiac tissues. Histol Histopathol, 2012, 27(6):807–816.

[9] Rusu MC, Mirancea N, Mănoiu VS, Vâlcu M, Nicolescu MI, Păduraru D. Skin telocytes. Ann Anat, 2012, 194(4):359–367.

[10] Rusu MC, Folescu R, Mănoiu VS, Didilescu AC. Suburothelial interstitial cells. Cells Tissues Organs, 2014, 199(1):59–72.

[11] Perlea P, Rusu MC, Didilescu AC, Pătroi EF, Leonardi RM, Imre M, Răducanu AM. Phenotype heterogeneity in dental pulp stem niches. Rom J Morphol Embryol, 2016, 57(4): 1187–1193.

[12] Cretoiu SM, Popescu LM. Telocytes revisited. Biomol Concepts, 2014, 5(5):353–369.

[13] Díaz-Flores L, Gutiérrez R, García MP, González M, Sáez FJ, Aparicio F, Díaz-Flores L Jr, Madrid JF. Human resident CD34+ stromal cells/telocytes have progenitor capacity and are a source of *α*SMA+ cells during repair. Histol Histopathol, 2015, 30(5):615–627.

[14] Díaz-Flores L, Gutiérrez R, García MP, Sáez FJ, Aparicio F, Díaz-Flores L Jr, Madrid JF. Uptake and intracytoplasmic storage of pigmented particles by human CD34+ stromal cells/ telocytes: endocytic property of telocytes. J Cell Mol Med, 2014, 18(12):2478–2487.

[15] Díaz-Flores L, Gutiérrez R, García MP, Sáez FJ, Díaz-Flores L Jr, Valladares F, Madrid JF. CD34+ stromal cells/ fibroblasts/fibrocytes/telocytes as a tissue reserve and a principal source of mesenchymal cells. Location, morphology, function and role in pathology. Histol Histopathol, 2014, 29(7): 831–870.

[16] Díaz-Flores L, Gutiérrez R, González-Gómez M, Díaz-Flores L Jr, Valladares F, Rancel N, Sáez FJ, Madrid JF. Telocyte behaviour during inflammation, repair and tumour stroma formation. Adv Exp Med Biol, 2016, 913:177–191.

[17] Díaz-Flores L, Gutiérrez R, Pino García M, González M, Díaz-Flores L, Francisco Madrid J. Telocytes as a source of progenitor cells in regeneration and repair through granulation tissue. Curr Stem Cell Res Ther, 2016, 11(5):395–403.

[18] Díaz-Flores L, Gutiérrez R, Sáez FJ, Díaz-Flores L Jr, Madrid JF. Telocytes in neuromuscular spindles. J Cell Mol Med, 2013, 17(4):457–465.

[19] Rusu MC, Cretoiu D, Vrapciu AD, Hostiuc S, Dermengiu D, Manoiu VS, Cretoiu SM, Mirancea N. Telocytes of the human adult trigeminal ganglion. Cell Biol Toxicol, 2016, 32(3):199–207.

[20] Rusu MC, Loreto C, Mănoiu VS. Network of telocytes in the temporomandibular joint disc of rats. Acta Histochem, 2014, 116(4):663–668.

[21] Petre N, Rusu MC, Pop F, Jianu AM. Telocytes of the mammary gland stroma. Folia Morphol (Warsz), 2016, 75(2): 224–231.

[22] Popescu LM, Gherghiceanu M, Cretoiu D, Radu E. The connective connection: interstitial cells of Cajal (ICC) and ICC-like cells establish synapses with immunoreactive cells. Electron microscope study *in situ*. J Cell Mol Med, 2005, 9(3): 714–730.

[23] Boos AM, Weigand A, Brodbeck R, Beier JP, Arkudas A, Horch RE. The potential role of telocytes in tissue engineering and regenerative medicine. Semin Cell Dev Biol, 2016, 55: 70–78.

[24] Bei Y, Wang F, Yang C, Xiao J. Telocytes in regenerative medicine. J Cell Mol Med, 2015, 19(7):1441–1454.

[25] Vrapciu AD, Rusu MC, Leonardi R, Corbu CG. Stem potentialities of the human iris – an *in situ* immunohistochemical study. Acta Histochem, 2014, 116(8):1509–1513.

[26] Varga I, Urban L, Kajanová M, Polák Š. Functional histology and possible clinical significance of recently discovered telocytes inside the female reproductive system. Arch Gynecol Obstet, 2016, 294(2):417–422.

[27] Cohen AW, Hnasko R, Schubert W, Lisanti MP. Role of caveolae and caveolins in health and disease. Physiol Rev, 2004, 84(4):1341–1379.

[28] Yuan SH, Arnold W, Jorgensen AO. Biogenesis of transverse tubules and triads: immunolocalization of the 1,4-dihydropyridine receptor, TS28, and the ryanodine receptor in rabbit skeletal muscle developing *in situ*. J Cell Biol, 1991, 112(2): 289–301.

[29] Pouvreau S, Berthier C, Blaineau S, Amsellem J, Coronado R, Strube C. Membrane cholesterol modulates dihydropyridine receptor function in mice fetal skeletal muscle cells. J Physiol, 2004, 555(Pt 2):365–381.

[30] Bruns RR, Palade GE. Studies on blood capillaries. I. General organization of blood capillaries in muscle. J Cell Biol, 1968, 37(2):244–276.

[31] Stan RV. Structure and function of endothelial caveolae. Microsc Res Tech, 2002, 57(5):350–364.

[32] Rusu MC, Mănoiu VS, Popescu VM, Ciuluvică C. Endothelial progenitor cells populate the stromal stem niche of tympanum. Folia Morphol (Warsz), 2017 May 29, doi: 10.5603/FM.a2017. 0038.

[33] Stan RV. Multiple PV1 dimers reside in the same stomatal or fenestral diaphragm. Am J Physiol Heart Circ Physiol, 2004, 286(4):H1347–H1353.

[34] Stan RV. Structure of caveolae. Biochim Biophys Acta, 2005, 1746(3):334–348.

[35] Stan RV. Endothelial stomatal and fenestral diaphragms in normal vessels and angiogenesis. J Cell Mol Med, 2007, 11(4):621–643.

[36] Stan RV, Ghitescu L, Jacobson BS, Palade GE. Isolation, cloning, and localization of rat PV-1, a novel endothelial caveolar protein. J Cell Biol, 1999, 145(6):1189–1198.

[37] Stan RV, Kubitza M, Palade GE. PV-1 is a component of the fenestral and stomatal diaphragms in fenestrated endothelia. Proc Natl Acad Sci U S A, 1999, 96(23):13203–13207.

[38] Tkachenko E, Tse D, Sideleva O, Deharvengt SJ, Luciano MR, Xu Y, McGarry CL, Chidlow J, Pilch PF, Sessa WC, Toomre DK, Stan RV. Caveolae, fenestrae and transendothelial channels retain PV1 on the surface of endothelial cells. PLoS One, 2012, 7(3):e32655.

[39] Palade GE, Bruns RR. Structural modulations of plasmalemmal vesicles. J Cell Biol, 1968, 37(3):633–649.

[40] Roberts WG, Palade GE. Endothelial fenestrae and fenestral diaphragms. In: Risau W, Rubanyi GM (eds). Morphogenesis of endothelium. Harwood Academic Publishers, Overseas Publishers Association, Amsterdam, The Netherlands, 2000, 23–41.

[41] Parton RG, del Pozo MA. Caveolae as plasma membrane sensors, protectors and organizers. Nat Rev Mol Cell Biol, 2013, 14(2):98–112.

[42] Park DS, Woodman SE, Schubert W, Cohen AW, Frank PG, Chandra M, Shirani J, Razani B, Tang B, Jelicks LA, Factor SM, Weiss LM, Tanowitz HB, Lisanti MP. Caveolin-1/3 double-knockout mice are viable, but lack both muscle and non-muscle caveolae, and develop a severe cardiomyopathic phenotype. Am J Pathol, 2002, 160(6):2207–2217.

[43] Williams TM, Lisanti MP. The caveolin genes: from cell biology to medicine. Ann Med, 2004, 36(8):584–595.

[44] Rothberg KG, Heuser JE, Donzell WC, Ying YS, Glenney JR, Anderson RG. Caveolin, a protein component of caveolae membrane coats. Cell, 1992, 68(4):673–682.

[45] Scherer PE, Lewis RY, Volonte D, Engelman JA, Galbiati F, Couet J, Kohtz DS, van Donselaar E, Peters P, Lisanti MP. Cell-type and tissue-specific expression of caveolin-2. Caveolins 1 and 2 co-localize and form a stable hetero-oligomeric complex *in vivo*. J Biol Chem, 1997, 272(46):29337–29346.
[46] Song KS, Scherer PE, Tang Z, Okamoto T, Li S, Chafel M, Chu C, Kohtz DS, Lisanti MP. Expression of caveolin-3 in skeletal, cardiac, and smooth muscle cells. Caveolin-3 is a component of the sarcolemma and co-fractionates with dystrophin and dystrophin-associated glycoproteins. J Biol Chem, 1996, 271(25):15160–15165.
[47] Ikezu T, Ueda H, Trapp BD, Nishiyama K, Sha JF, Volonte D, Galbiati F, Byrd AL, Bassell G, Serizawa H, Lane WS, Lisanti MP, Okamoto T. Affinity-purification and characterization of caveolins from the brain: differential expression of caveolin-1, -2, and -3 in brain endothelial and astroglial cell types. Brain Res, 1998, 804(2):177–192.
[48] Byrne S, Ahenkorah J, Hottor B, Lockwood C, Ockleford CD. Immuno-electron microscopic localisation of caveolin 1 in human placenta. Immunobiology, 2007, 212(1):39–46.
[49] Sawada N, Taketani Y, Amizuka N, Ichikawa M, Ogawa C, Nomoto K, Nashiki K, Sato T, Arai H, Isshiki M, Segawa H, Yamamoto H, Miyamoto K, Takeda E. Caveolin-1 in extracellular matrix vesicles secreted from osteoblasts. Bone, 2007, 41(1):52–58.
[50] Codenotti S, Vezzoli M, Poliani PL, Cominelli M, Bono F, Kabbout H, Faggi F, Chiarelli N, Colombi M, Zanella I, Biasiotto G, Montanelli A, Caimi L, Monti E, Fanzani A. Caveolin-1, caveolin-2 and cavin-1 are strong predictors of adipogenic differentiation in human tumors and cell lines of liposarcoma. Eur J Cell Biol, 2016, 95(8):252–264.
[51] Palacios-Ortega S, Varela-Guruceaga M, Martínez JA, de Miguel C, Milagro FI. Effects of high glucose on caveolin-1 and insulin signaling in 3T3-L1 adipocytes. Adipocyte, 2015, 5(1):65–80.
[52] Newman GR, Campbell L, von Ruhland C, Jasani B, Gumbleton M. Caveolin and its cellular and subcellular immunolocalisation in lung alveolar epithelium: implications for alveolar epithelial type I cell function. Cell Tissue Res, 1999, 295(1):111–120.
[53] Drab M, Verkade P, Elger M, Kasper M, Lohn M, Lauterbach B, Menne J, Lindschau C, Mende F, Luft FC, Schedl A, Haller H, Kurzchalia TV. Loss of caveolae, vascular dysfunction, and pulmonary defects in caveolin-1 gene-disrupted mice. Science, 2001, 293(5539):2449–2452.
[54] Gangadharan V, Nohe A, Caplan J, Czymmek K, Duncan RL. Caveolin-1 regulates P2X7 receptor signaling in osteoblasts. Am J Physiol Cell Physiol, 2015, 308(1):C41–C50.
[55] Casanova MB, Lustig L, Diaz ES, Pellizzari EH, Cigorraga SB, Denduchis B. Expression of caveolin-1 in rat Leydig cells. Biocell, 2006, 30(3):431–438.
[56] Krasteva G, Pfeil U, Drab M, Kummer W, König P. Caveolin-1 and -2 in airway epithelium: expression and *in situ* association as detected by FRET-CLSM. Respir Res, 2006, 7:108.
[57] Galbiati F, Engelman JA, Volonte D, Zhang XL, Minetti C, Li M, Hou H Jr, Kneitz B, Edelmann W, Lisanti MP. Caveolin-3 null mice show a loss of caveolae, changes in the microdomain distribution of the dystrophin-glycoprotein complex, and *t*-tubule abnormalities. J Biol Chem, 2001, 276(24):21425–21433.
[58] Wright PT, Nikolaev VO, O'Hara T, Diakonov I, Bhargava A, Tokar S, Schobesberger S, Shevchuk AI, Sikkel MB, Wilkinson R, Trayanova NA, Lyon AR, Harding SE, Gorelik J. Caveolin-3 regulates compartmentation of cardiomyocyte beta2-adrenergic receptor-mediated cAMP signaling. J Mol Cell Cardiol, 2014, 67:38–48.
[59] Xiao Y, Cai X, Atkinson A, Logantha SJ, Boyett M, Dobrzynski H. Expression of connexin 43, ion channels and Ca^{2+}-handling proteins in rat pulmonary vein cardiomyocytes. Exp Ther Med, 2016, 12(5):3233–3241.
[60] Wang Y, Wang X, Jasmin JF, Lau WB, Li R, Yuan Y, Yi W, Chuprun K, Lisanti MP, Koch WJ, Gao E, Ma XL. Essential role of caveolin-3 in adiponectin signalsome formation and adiponectin cardioprotection. Arterioscler Thromb Vasc Biol, 2012, 32(4):934–942.
[61] Uehara K, Miyoshi M. Localization of caveolin-3 in the sinus endothelial cells of the rat spleen. Cell Tissue Res, 2002, 307(3):329–336.
[62] Noguchi S, Ogata S, Sato M, Muramatsu T. Stage-specific polypeptides in the developing mouse brain as demonstrated by two-dimensional gel electrophoresis. J Biochem, 1984, 96(3):881–886.
[63] Stan RV, Tkachenko E, Niesman IR. PV1 is a key structural component for the formation of the stomatal and fenestral diaphragms. Mol Biol Cell, 2004, 15(8):3615–3630.
[64] Keuschnigg J, Tvorogov D, Elima K, Salmi M, Alitalo K, Salminen T, Jalkanen S. PV-1 is recognized by the PAL-E antibody and forms complexes with NRP-1. Blood, 2012, 120(1):232–235.
[65] Keuschnigg J, Henttinen T, Auvinen K, Karikoski M, Salmi M, Jalkanen S. The prototype endothelial marker PAL-E is a leukocyte trafficking molecule. Blood, 2009, 114(2):478–484.
[66] Niemelä H, Elima K, Henttinen T, Irjala H, Salmi M, Jalkanen S. Molecular identification of PAL-E, a widely used endothelial-cell marker. Blood, 2005, 106(10):3405–3409.
[67] Rusu MC, Hostiuc S, Vrapciu AD, Mogoantă L, Mănoiu VS, Grigoriu F. Subsets of telocytes: myocardial telocytes. Ann Anat, 2017, 209:37–44.
[68] Popescu LM, Manole E, Serboiu CS, Manole CG, Suciu LC, Gherghiceanu M, Popescu BO. Identification of telocytes in skeletal muscle interstitium: implication for muscle regeneration. J Cell Mol Med, 2011, 15(6):1379–1392.
[69] Suciu L, Popescu LM, Gherghiceanu M, Regalia T, Nicolescu MI, Hinescu ME, Faussone-Pellegrini MS. Telocytes in human term placenta: morphology and phenotype. Cells Tissues Organs, 2010, 192(5):325–339.
[70] Liew A, Barry F, O'Brien T. Endothelial progenitor cells: diagnostic and therapeutic considerations. Bioessays, 2006, 28(3):261–270.
[71] Urbich C, Aicher A, Heeschen C, Dernbach E, Hofmann WK, Zeiher AM, Dimmeler S. Soluble factors released by endothelial progenitor cells promote migration of endothelial cells and cardiac resident progenitor cells. J Mol Cell Cardiol, 2005, 39(5):733–742.
[72] Gherghiceanu M, Manole CG, Popescu LM. Telocytes in endocardium: electron microscope evidence. J Cell Mol Med, 2010, 14(9):2330–2334.
[73] Rusu MC, Nicolescu MI, Jianu AM, Lighezan R, Mănoiu VS, Păduraru D. Esophageal telocytes and hybrid morphologies. Cell Biol Int, 2012, 36(12):1079–1088.
[74] Luesma MJ, Gherghiceanu M, Popescu LM. Telocytes and stem cells in limbus and uvea of mouse eye. J Cell Mol Med, 2013, 17(8):1016–1024.
[75] Ceafalan L, Gherghiceanu M, Popescu LM, Simionescu O. Telocytes in human skin – are they involved in skin regeneration? J Cell Mol Med, 2012, 16(7):1405–1420.
[76] Nicolescu MI, Popescu LM. Telocytes in the interstitium of human exocrine pancreas: ultrastructural evidence. Pancreas, 2012, 41(6):949–956.

Corresponding author
Mugurel Constantin Rusu, Professor, MD, Dr. Hab., Dr. Med., Dr. Biol., Division of Anatomy, Department 1, Faculty of Dental Medicine, "Carol Davila" University of Medicine and Pharmacy, 8 Eroilor Sanitari Avenue, 050474 Bucharest, Romania; Phone +40722–363 705, e-mail: mugurel.rusu@umcd.ro

Received: October 25, 2016 *Accepted: July 29, 2017*