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Morphological Evidence of Telocytes in Canine Inferior Vena Cava

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Abstract

Telocytes (TCs) are a distinctive population of stromal cells extending special long prolongations with thin segments (podomers) and dilations (podoms). They have been identified in various organs and tissues of multi-species organisms. TCs have been identified in large arteries. The present study aimed to explore whether TCs also exists in large veins by Transmission Electron Microscope (TEM). The results indicated that TCs indeed exist in inferior vena cava, which are a newly recognized compartment distinct from other interstitial cells in large veins. The TCs in inferior vena cava are mainly located in subendothelium and apparently different from the TCs in large artery, which exist in the tunica adventitia and adjacent to the outer elastic lamina. The characteristic morphological features of Tps in inferior vena cava were identified: the presence of secondary lysosomes and endoplasmic reticulum.

Keywords: Telocyte; Telopode; Inferior vena cava; TEM

Introduction

Lately, increasing evidences have come to light about Telocytes (TCs) as peculiar stromal cells, which were previously named as ICLC (interstitial Cajal-like cells) [1,2]. TC, a particular identified type of stromal cell, has been identified morphologically by a small cell body and specific long prolongations called Telopodes (Tp) alternating thin segments (podomers) with dilations (podoms) [3]. TCs have been described in various organs and tissues, such as spleen [4], skin [5], esophagus [6], parotid gland [7], salivary glands [8], endocardium [9], bone marrow [10], pleura [11], vasculature [12], lung [13], duodenum [14], liver [15], eye [16], cardiac valves [17], uterus [18], et al. Although TCs were also identified in large arteries [19], whether TCs exist in large veins was not yet reported. Here, the ultrastructural features of TCs in inferior vena cava were, for the first time, clarified under transmission electron microscope (TEM). The TCs in inferior vena cava are located in subendothelium and apparently different from the TCs distribution in large artery, which exist in tunica adventitia and adjacent to the outer elastic lamina. The characteristic morphological features of Tps in renal vein were identified: the presence of secondary lysosomes and endoplasmic reticulum.

Materials and Methods

Three male beagles, aged 3 months, with the weight between 23 kg and 26 kg, were anesthetized with diazepam (Laboratory Animal Center, Shanghai Medical College, Fudan University) and ketamine hydrochloride (Fujian Gutian Pharmaceutical Company) by intramuscular injection. The anaesthetized animals were fixed in the supine position with their necks extended and thoracic cavities were opened, through a puncture in the left ventricle; 2500 ml of heparin physiological saline and 1000 ml 4% formaldehyde solution each animal were perfused at physiological pressure respectively. After the perfusion, inferior vena cava was removed. TEM was performed on small tissue fragments, processed according to routine Epon-embedding procedure. And the processed specimen were observed under FEI TECAI SPIRITTEM (Eindhoven, The Netherlands), as previously described by Gherghiceanu [20]. Digital TEM images were processed using Adobe Photoshop CS5 in order to highlight TCs. This study was approved by the Ethic Committee for Animal Care and Use of Fudan University, according to the generally accepted international standards.

Results and Discussion

A newly type of interstitial cell with typical ultrastructural features defined as TC was observed in the inferior vena cava under TEM. TCs in inferior vena cava with high nuclear/cytoplasmic ratio had relatively small cell bodies (range from 4.49 μm to 7.44 μm in length, from 1.12 μm to 1.78 μm in width) (Figures 1-3). Their thin and long Tps (range from 5.71 μm to 31.75 μm) were projecting from the cell body (Figures 1-3).

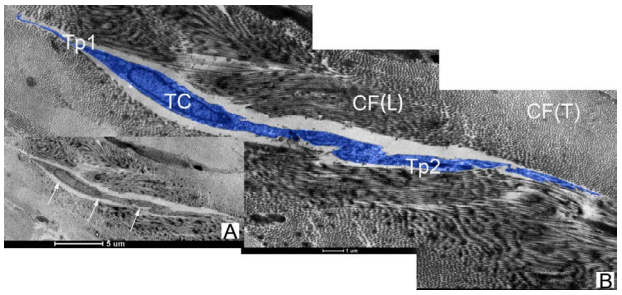

Figure 1: Transmission electron microscope (TEM) images of canine inferior vena cava. (A) One characteristic telocyte (TC) in inferior vena cava is seen (indicated by white arrows); bar=5 μm. (B) It is the image of magnification of figure A. The TC with small spindly cell body extends specially long and thin telopodes (Tp1 and Tp2). The TC body size is 6.71 μm in length and 1.29 μm in the average width. And the measured length of Tp1 and Tp2 is 5.71 μm and 19.71 μm respectively. CF(L): collagen fiber (longitudinal section), CF(T): collagen fiber (transverse section); bar=1μm.

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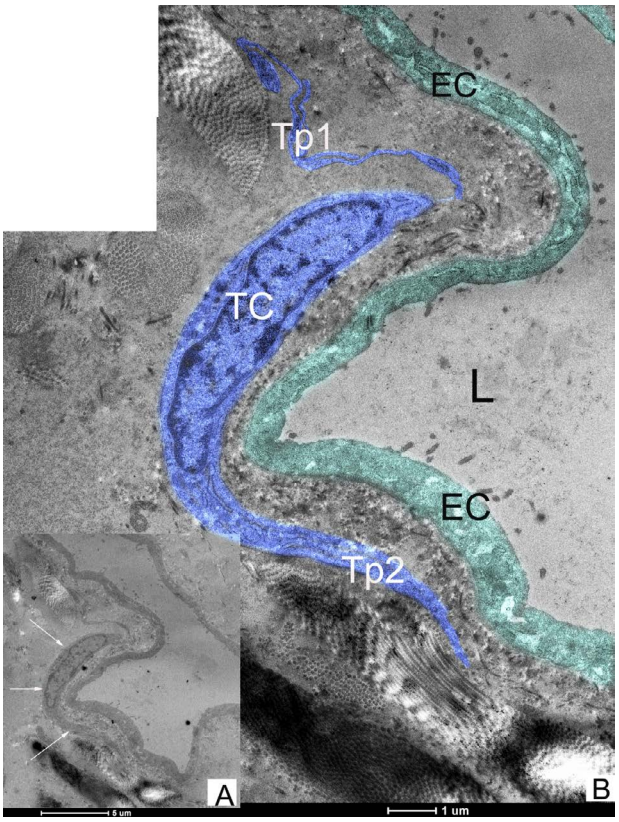

Figure 2: TEM image shows the topographic localization of the TC. (A) The strategic position of TC in subendothelium is visible (indicated by white arrows); bar=5 μm. (B) The higher magnification of Figure 2A shows that the TC, surrounded by collagen fibers in the inferior vena cava, is located in subendothelium. EC-endothelial cell (the nuclear of endothelial cell is not shown); L: lumen of inferior vena cava; bar=1 μm.

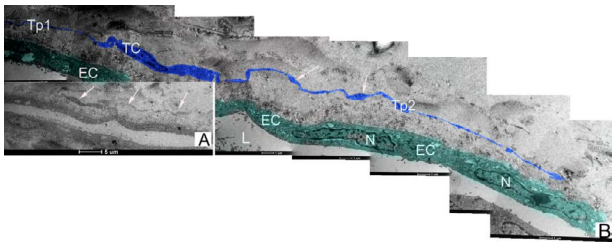

Figure 3: TEM image shows the localization of the TC within inferior vena cava wall. (A) The TC exists in subendothelial layer with a very long telopode (indicated by white arrows). bar=5 μm. (B) The thin segments (podomers) and dilations (podoms, white arrows) of one TC are shown. Tp2, a characteristic cellular prolongation, is special long (about 31.75 μm) and moniliform forms. The inferior vena cava TC is in the subendothelium. EC-endothelial cell; L: lumen of inferior vena cava; N: nuclear of endothelial cell. bar=1 μm.

The morphological features of TPs were identified: very long and thin cellular prolongations, with uneven calibre (moniliform aspect) (Figure 1). TCs were generally distributed in the subendothelial layer of inferior vena cava and surrounded by a great deal of collagen fibers (Figure 2). It was displayed that the typical morphology of cells with very long, thin and moniliform Tps in Figure 3. TCs were morphologically consistent with those previously reported in other tissues and organs (Figures 4-6). The characteristic morphological features of Tps were identified: the presence of secondary lysosomes and endoplasmic reticulum (Figures 4 and 5).

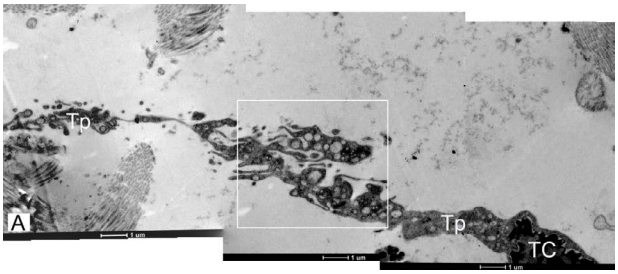

Figure 4: Transmission electron microscope image of TCs from inferior vena cava. (A) It shows a typical TC with one very long Tp; bar=1 μm. (B) there are a lot of secondary lysosomes (black arrowheads) and endoplasmic reticulum (white arrowheads) in the higher magnification of square in Figure 4A. SL: secondary lysosome; ER: endoplasmic reticulum; bar=500 nm.

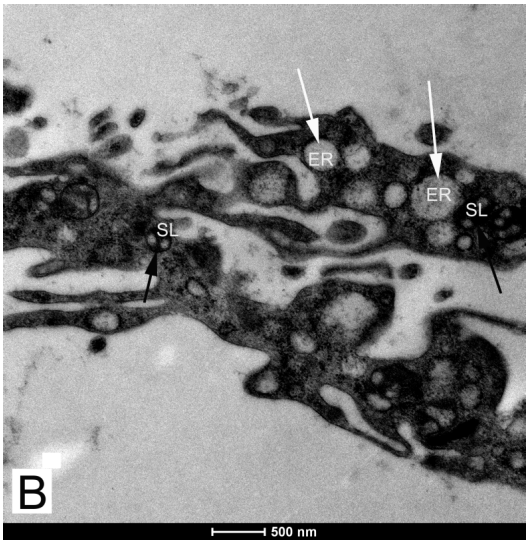

Figure 5: Transmission electron microscope images of inferior vena cava. It is a TC with two long Tps, in which abundantly secondary lysosomes (black arrowheads) and endoplasmic reticulum (white arrowheads) are seen. SL: secondary lysosome; ER: endoplasmic reticulum; bar=1 μm.a

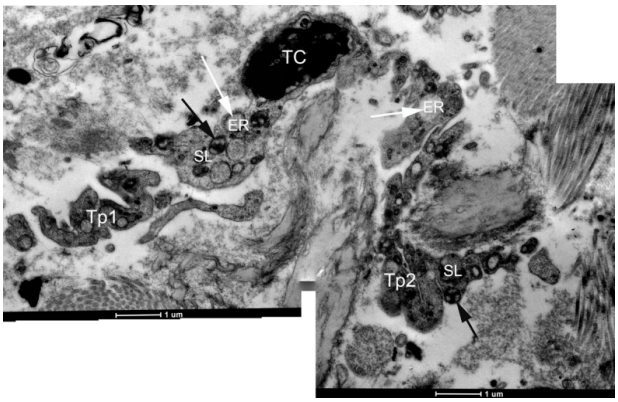

Figure 6: Transmission electron microscope image of TCs from inferior vena cava. The TC with two long Tps owns narrow and long cell body; bar=1 μm.

TCs are a novel type of stromal cells. So far, characteristic ultrastructure under electron microscope remained the most precise identification of TCs. Telocytes have been described to possess different immunophenotype markers, such as CD34/PDGFRa [21]. However, we failed to mark immunofluorescent labeling of CD34/PDGFRa in canine inferior vena cava. Further research about the matter of immunohistochemistry was considered to be done. Conventionally, the inferior vena cava is formed by the joining of the left and right common iliac veins and carries deoxygenated blood from the posterior half of the body to the right atrium. In addition, the anomaly of inferior vena cava in structure and function is closely related with a number of diseases, such as deep vein thrombosis [22,23]. Previous research has testified that the blood vessels could develop vascular remodeling during coronary bypass (for example: greater saphenous vein is grafted into coronary artery). After vein being interposed into the artery, the thickness of the wall gradually increased, due to the change of the hemodynamics (the factors of both blood pressure and shear stress). These remodeling mainly represented the proliferation of vascular smooth muscle cells and the increase of collagen fibers [24]. As we know, endothelial cells and smooth muscle cells are the main cell components of the vascular wall. TCs, as a novel population of inferior vena cava, might play an important role during the process of the remodeling. Also, inferior vena cava TCs, presumed accessory cells for stem cells [20], might play a key part in maintaining the homeostasis including angiogenesis, regeneration and reparation during vascular injury. The possible mechanism of inferior vena cava TCs during the progress needs further to be investigated. Once this mechanism is clarified, there will be potential clinical application prospect.

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Conflicts of Interest

The authors confirm that there are no any conflicts of interest.

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