



Ganglionic nervous cells and telocytes in the pancreas of *Octodon degus* Extra and intrapancreatic ganglionic cells and telocytes in the degus

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ABSTRACT

This study shows for the first time the presence of intra and extrapancreatic ganglionic neurons and telocytes in *Octodon degus* such as those described in human and guinea pig pancreas. Pancreatic ganglionic neurons were identified by their histological characteristics as well as their positive immunostaining with mouse anti-human neuron specific enolase (NSE) antibody. Somatostatin secreting delta cells (D cells) in the islets of Langerhans were identified by positive immunostaining with rabbit antihuman polyclonal somatostatin antibody. Electron microscopy evidenced the presence of some unmyelinated axons in the interlobular spaces or septa, usually located adjacent to blood vessels and the exocrine epithelial ducts. The presence of telocytes with at least 2 telopodes was observed in the interlobular space, frequently in close spatial relationship with blood vessels and nerve endings. Telocytes were often observed in the vicinity or even in close proximity with both secretory acini and exocrine epithelial ducts and regulatory nerves and blood vessel apparatuses. A possible framework has been put forward within which such structures might contribute to elicit physiological responses in the pancreas. Further studies of synaptic interactions within and between pancreatic neuron cells are needed to help clarify the morphological results reported here. A broad overview of the field of neurogastroenterology with focus on the pancreas of *O. degus* related to the enteric nervous system (ENS) is provided in order to help design future studies on the connections of specific neurons forming pancreatic pathways, their neurotransmission processes and how disruption of these pathways may contribute to pancreatic disease.

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1. Introduction

Octodon degus (degus) is a small diurnal caviomorph rodent native to Chile. The gestation period lasts 90 days and the average litter size is five pups. This animal adapts easily to animal facility conditions and has been used as an experimental model in a variety of studies regarding subjects such as placenta (Bosco, 1997; Bosco et al., 2007; Kertschanska et al., 1997; King, 1992), toxicology (Bosco, 2005; Bosco et al., 1997), diabetic eye cataract development (Nishi and Steiner, 1990), circadian rhythms (Lee, 2004), Alzheimer's disease (Inestrosa et al., 2005) and visual organization (Jacobs et al., 2003).

The degus has ordinary and high circulating glucose levels (Opazo et al., 2004), and its endocrine pancreas has unique alpha-cell crystals, a herpes-like virus, and islet amyloidosis (Spear et al., 1984). The molecular biochemistry of pancreatic hormones in degus (Hellman et al., 1990) and guinea pig (Iturriza et al., 1995) related to beta and alpha cells has been widely analyzed. Clear analogies, such as failure to stain alpha-cells using

antisera against the C-terminal portions of the glucagon molecule, have been described for these two caviomorph species. Additionally, some studies have also demonstrated a number of morphological and structural similarities between other organs of these species, especially regarding the placenta (Bosco, 1997; Bosco et al., 2007; Mess et al., 2007; Valdés et al., 2008).

The morphology, neurochemistry and electrical properties of guinea pig pancreatic neurons have been described by Liu and Kirchgessner (1997). Although their role in the physiology of exocrine and endocrine secretion is still under study, according to these authors pancreatic ganglia should not be regarded as a simple relay ganglia interposed between the vagus nerve and the effector organs. Indeed, the pancreatic ganglia are much more complex, and it is thought that because of this complexity, the pancreas displays a degree of independence when cut off from the brain, spinal cord, or gut (Stagner and Samols, 1985). Furthermore, the observation of spontaneous activity within connected pancreatic ganglia gives support to the idea of an endogenous neural network regulating pancreatic function (Liu and Kirchgessner, 1997).

The aim of this study was to acquire information regarding the morphology of ganglionic neurons in the degus pancreas in order to compare them to those described in the guinea pig (Kirchgessner and Pintar, 1991; Liu et al., 1996), to further our understanding of the function of this organ under normal and pathological conditions.

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2. Materials and Methods

A colony of 10 adult male *O. degus*, weighing 199 ± 15 g, bred in the animal facility at the Department of Anatomy and Developmental Biology, was used in this study. The animals received food and water ad libitum. The handling of the degus was carried out according to internationally accepted ethical standards, after approval of the Animal Care Committee of the Faculty of Medicine, University of Chile. The animals were slightly anesthetized with ether (Merck, Darmstadt, Germany) and subsequently sacrificed by overdose of sodium pentobarbital (80 mg/kg i.p.). For optical microscopy studies, the pancreas of each animal was dissected and fixed for 24 h by immersion in 4% formaldehyde in 0.1 M phosphate buffer (pH 7.3), embedded in paraffin wax, and cut into 5 μ m sections. Routine histological analysis was performed using the hematoxylin–eosin (H/E) technique.

2.1. Immunohistochemical procedures

Standard immunoperoxidase procedure was used to evidence the ganglionic neurons in the pancreas, as well as the distribution of somatostatin positive cells in the islets of Langerhans. Briefly, mouse anti-human neuron specific enolase (NSE) monoclonal antibody (M0873 DAKO, USA), diluted 1:100 (v/v) was applied to the tissue sections for 30 min at 37 °C. In order to obtain optimal staining, microwave heat-induced antigen retrieval in citrate buffer, pH 6.0, was performed. In many of the pancreas samples the same transversal duodenum section appears allowing us to identify the neurons of the submucosal neural plexus and the myenteric plexus of the muscular layer using immunohistochemistry Rabbit anti-human polyclonal somatostatin (M0762 DAKO, USA), diluted 1:200 (v/v) was applied individually to each section for 30 min at 37 °C. Antibodies were omitted in negative controls for NSE and somatostatin. Immunostaining was revealed using the horseradish peroxidase-labelled streptavidin biotin kit (DAKO, USA), according to the manufacturer's directions, using 3, 3'-diaminobenzidine (DAB) as chromogen. All sections were counterstained with Mayer's hematoxylin (DAKO, USA), mounted using Entellan (Merck) and examined by light microscopy (Zeiss Axioplan 2, Germany).

2.2. Electron microscopy procedures

The samples were fixed in 3.5% glutaraldehyde in 0.1 M sodium cacodylate buffer (pH, 7.3) at 4 °C for 3 h and subsequently postfixed for 1 h in 2% osmium tetroxide, prepared in the same buffer. The fixed samples were then dehydrated in ascending grades of ethanol, cleared in propylene oxide and embedded in Epon 812 (EMS, USA). Sections were cut in an OM-U2 ultramicrotome (Richert, Germany) and were stained with uranyl acetate and lead citrate prior to examination under an electron microscope (EM 109; Zeiss; Göttingen, Germany). For orientation purposes, semi-thin sections were stained with 1% toluidine blue in 1% sodium tetraborate and were examined by light microscopy.

3. Results

The pancreas of the degus is enveloped by a thin capsule of connective tissue from which septa extend into the organ, thus separating the pancreatic lobules. As in all animals, this organ is a mixed of exocrine and endocrine glands, constituted by acini and islets of Langerhans (Fig. 1A). The acinar cells display the characteristic serous type of a protein-synthesizing cell: round nuclei located in the basal third (see inset in Fig. 1A). The secretory granules accumulated in the supranuclear region are strongly stained with H/E (Fig. 1A and C). The average size of the islets of Langerhans is 79 ± 15 μ m in diameter. Some groups of pancreatic ganglionic neurons (GN) were observed at optical microscopy level using H/E (Fig. 1C and D) and confirmed by positive NSE immunostaining (Fig. 2C, D and E). The pancreatic GN showed a spherical, large

and faintly stained nucleus displaying a prominent nucleolus. As specified by the manufacturing company, NSE also recognizes neuroendocrine cells of the islets of Langerhans (Fig. 2C and D). Each pancreatic GN is surrounded by satellite glial cells, smaller than the neurones and displaying a chromatinic nucleus (see Fig. 1D). We have included in this study a photomicrograph of degus diabetic islets of Langerhans (Fig. 1B) and of the duodenal enteric nervous system (Fig. 2A and B) to emphasize the differences and similarities observed between these structures and the pancreatic GN.

Somatostatin secreting delta cells (D cells) in the islets of Langerhans were identified by positive cytoplasmic immunostaining with rabbit anti human polyclonal somatostatin antibody (see Fig. 3A, B and D). This antibody rendered negative immunostaining in pancreatic GN (Fig. 3A, C and D).

Electron microscopy evidenced the presence of some unmyelinated axons in the interlobular spaces or septas, usually located adjacent to blood vessels and the pancreatic exocrine epithelial ducts and in proximity to lymphatic capillaries (Fig. 4), in agreement with a previous report (O'Morchoe, 1997). In the interlobular space it was possible to observe the presence of telocytes with at least two telopodes, frequently establishing a close spatial relationship with blood vessels (Fig. 4) and nerve endings (Fig. 5). Telocyte location seemed to follow a pattern, being often observed in the vicinity or in close contact with both secretory (acini and exocrine epithelia ducts) and regulatory apparatuses (nerves and blood vessels) (see Figs. 4 and 5), as it has been recently described (Nicolescu and Popescu, 2012).

4. Discussion

As early as 1869, Langerhans observed that pancreatic islets were innervated. Since then, neural elements in the various compartments of the mammalian pancreas have been extensively studied at anatomical, neurochemical and functional levels Wang et al. (1999b). To our knowledge, this is the first time that the presence of neuronal cells is described in the pancreas of the *O. degus*.

Neurogastroenterology is defined as neurology of the gastrointestinal tract, liver, gallbladder and pancreas and it encompasses control of the digestive process through the enteric nervous system (ENS) (Kiba, 2004), the central nervous system (CNS) and integrative centers in sympathetic ganglia. Neurons in the ENS pathways are related to a wide range of chemical messengers that signal through an even wider range of receptors, which may provide potential targets, playing some role in the modification of digestive functions such as motility, secretion and blood flow (Furness, 2012; Roberts et al., 2010).

ENS was a concept introduced in order to characterize the peculiarity of the neuronal elements observed within the gut wall (Langley, 1900). ENS is a component of the neural control system of the digestive tract, working in concert with the CNS integrative pathways that pass through sympathetic ganglia and the gastroenteropancreatic endocrine system (Furness, 2012). Many functions of the digestive system as well as some functions related to digestion, such as satiety, involve both enteric innervation and the endocrine system of the digestive tract or gastroenteropancreatic endocrine system. In fact, most aspects of gastrointestinal control involve both neurons and endocrine cells. We postulate that the degus' pancreatic neuronal cells probably belong to the ENS and may share the same or similar characteristics to those reported in the pancreas of the guinea pig (Liu and Kirchgessner, 1997), where its influence upon the activity of the organ has been thoroughly described.

Studies in the pancreatic ganglia of the guinea pig have shown that the organ is innervated by neurons originated from neural precursor cells located in the wall of the gut, that migrate into the pancreas from the bowel (Kirchgessner et al., 1994). Hence, it has been concluded that the innervation of the pancreas may be considered as an extension of the ENS. Furthermore, the vagal neural crest is considered to be the embryological origin of most of the neurons and glial cells that constitute the ENS (Burns et al., 2000; Kirchgessner et al., 1994; Young and

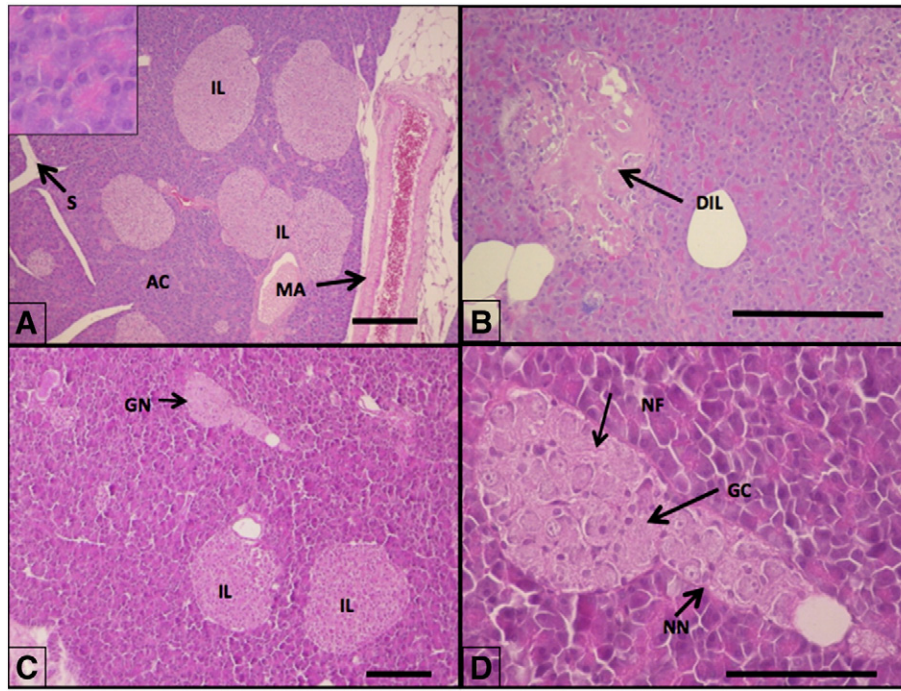


Fig. 1. Optical microscopic photomicrograph of degus pancreas. A) Panoramic view showing the connective tissue septa (S) separating the pancreatic lobules, the exocrine acinar cells (AC) and endocrine islets of Langerhans (IL). The inset depicts a higher magnification of acinar cells. A muscular artery (MA) is observed in the connective tissue of the lobule. B) Islet of Langerhans of a diabetic animal (DIL) showing the characteristic amyloid deposits of age-associated forms of diabetes in this specie. C) Normal pancreas showing the presence of a structure different to islets of Langerhans normal or diabetic, surrounded by acini and two IL. D) Higher magnification of the structure depicted in panel C, evidencing histological characteristics of an intrapancreatic nerve ganglion. Neuronal cell bodies with a large, spherical and pale nucleus, displaying a prominent nucleolus (NN) are clearly observed. These neurons are surrounded by some satellite glial cells (GC), smaller than the neurones, with a more chromatinic nucleus than those observed in neurones. Note the presence of nerve fibers (NF) in the upper zone of the GN. H/E staining. Calibration bars: A) 61 μm ; B) 41 μm ; C) 61 μm ; and D) 46 μm .

Newgreen, 2001). It has also been suggested that pancreatic ganglia appear to be interconnected, in a similar way that enteric ganglia are (Burns et al., 2000; Kirchgessner et al., 1994). Although both the exocrine and endocrine portions of the pancreas are influenced by the ENS, it seems that the activity of neither is predominantly influenced by enteric nerves that terminate directly onto acinar or islet cells. Instead, the

primary target of the entero-pancreatic innervation appears to be the pancreatic ganglia (as suggested in Fig. 1C), which transmits the signal to the effectors. A detailed study in the guinea pig pancreas has revealed that these ganglia are more abundant in the head and body regions of the organ, compared to the tail (Tay et al., 1994). Also, most of these ganglia were observed in interlobular spaces, usually adjacent to blood vessels

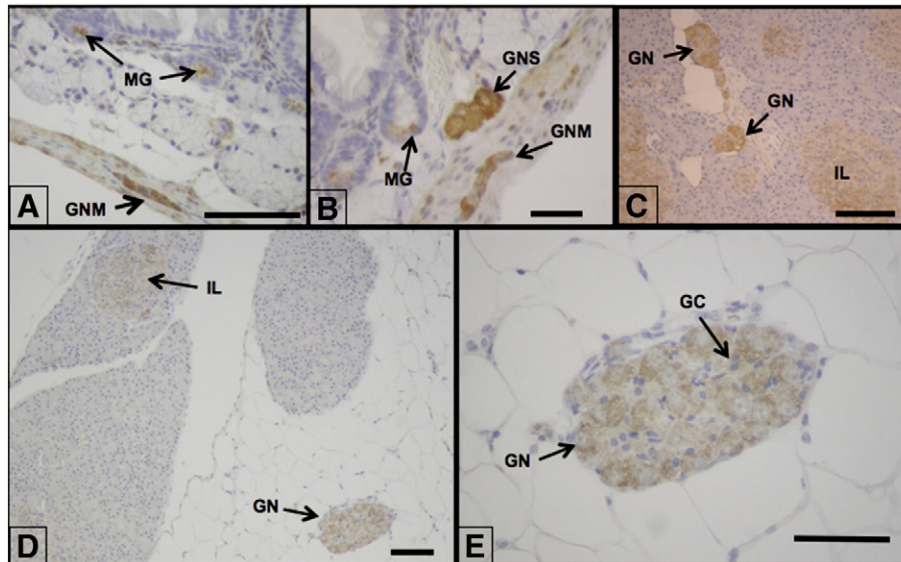


Fig. 2. Immunohistochemical expression of NSE antibody in degus duodenum and pancreas. A) Immunohistochemical expression of NSE antibody in ganglionic neurons of the duodenal myenteric plexus (GNM). Note that this antibody also recognizes neuroendocrine cells in the end of the mucosal glands (MG). B) NSE immunorexpression in the myenteric (GNS) and submucosa (GNM) plexus as well as in the neuroendocrine cells at the end of the mucosal glands (MG). C) NSE positive intrapancreatic ganglionic neurons (GN) of a ganglion located in connective tissue septa. The neuroendocrine cells of the IL are also positive to this antibody. D) NSE positive expression in neurons from an intrapancreatic ganglion (GN) located in septa of adipose tissue. Satellite glial cells (GC). E) Higher magnification of the ganglion depicted in panel D. Note that immunorexpression in these cells is as strong as that expressed in the neurons of the duodenal plexus (compare with panels A and B). A, B, C, D, E: NSE immunorexpression. Calibration bars: A) 79 μm ; B) 30 μm ; C) 10.5 μm ; D) 24 μm ; E) 55 μm .

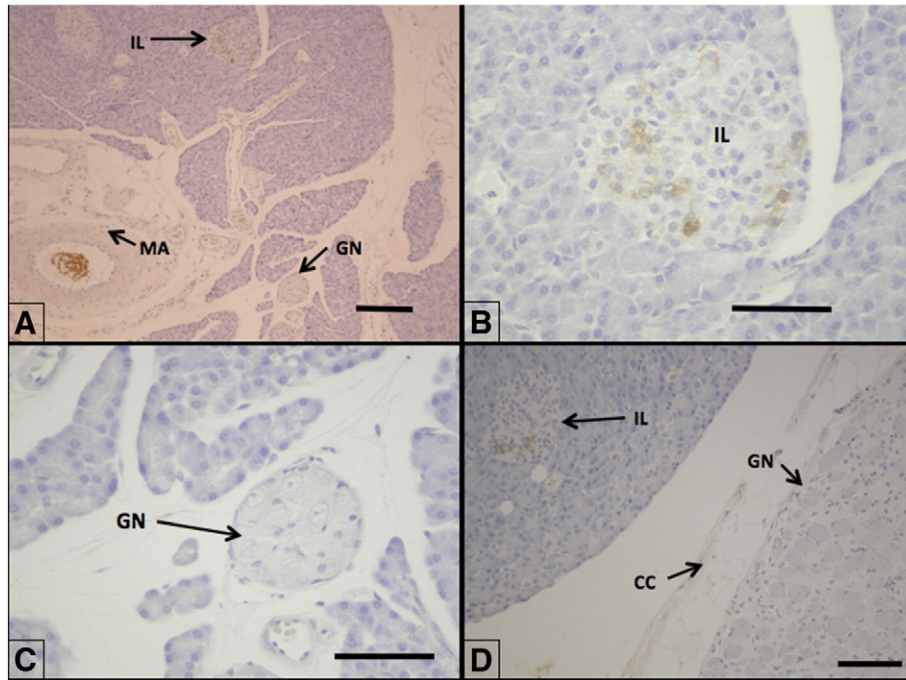


Fig. 3. Somatostatin immunohistochemistry in degus pancreas. A) Somatostatin positive cells from islet of Langerhans (IL) and negative expression in ganglionic neurons (GN). A muscular artery (MA) can be observed in the connective septa. B) Higher magnification of the IL depicted in panel A to emphasize the somatostatin immune expression. C) Higher magnification of the GN depicted in panel A to emphasize the lack of immunoreactivity in these ganglionic neurons. D) Extrapancreatic ganglion (GN) located out of the connective tissue capsule (CC). A somatostatin positive IL is also observed. Calibration bars: A and D) 34 μm ; B and C) 61 μm .

and pancreatic exocrine epithelial ducts and ductules. The results reported here are in close concordance with previous work (Tay et al., 1994), as can be observed in Figs. 1C and 2C of the present study. Furthermore, we provide evidence that the ganglionic pancreatic neurons described in our study are enveloped by satellite glial cells, which have been proposed to be specialized glial cells termed as ‘enteric glia’ (Hanani, 2010). They are clearly separated from adjacent neurons,

which enables them to control the neuronal microenvironment (see Fig. 1D), in agreement with similar descriptions in the autonomic nervous system (Pannese, 2010).

It is well known that the mammalian pancreas receives abundant innervation from both the parasympathetic and sympathetic autonomic nervous systems (King et al., 1989; Larsson, 1979). Preganglionic parasympathetic nerve fibers run alongside the vagus nerve and make synaptic contact with small pancreatic ganglia that lie in the interlobular connective tissue. These authors also showed that postganglionic parasympathetic neurones innervate pancreatic acini and ducts as well as

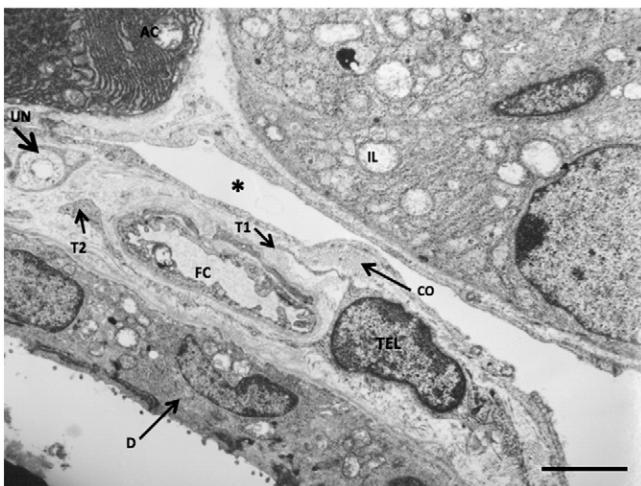


Fig. 4. Electron micrograph of degus pancreas showing a fenestrated capillary (FC) located in the septa, surrounded by two telopodes (T1 and T2) of a telocyte (TEL). The presence of a lymphatic capillary (asterisks) characterized by a very thin endothelial wall and the presence of anchoring collagen fibrils (CO) is observed in the vicinity of the TEL (note the absence of a clearly defined basal membrane). To the left of the FC it is possible to observe the presence of an unmyelinated nerve fiber (UN). Below this capillary, an exocrine epithelial duct (D) with microvilli to the apical zone can also be observed. In the upper part an acinar (AC) and an islet cell (IL) are also observed. Calibration bar: 2.4 μm .

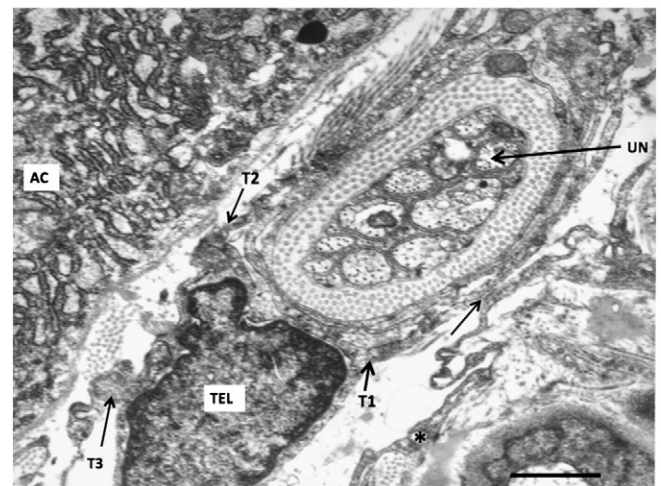


Fig. 5. Electron micrograph of degus pancreas showing an unmyelinated nerve fiber (UN) surrounded by two telopodes (T1 and T2) emerging from the body of a telocyte (TEL) such as T3. A large telopode from another telocyte (*) seems to contact T1 (arrow). Towards the left of the nerve, an acinar cell (AC) is also observed. Calibration bar: 0.645 μm .

the islets of Langerhans. On the other hand, preganglionic sympathetic nerves run alongside the splanchnic nerve and make synaptic contact with neurons of the celiac ganglion, which in turn innervate blood vessels, pancreatic epithelial exocrine ducts, islets of Langerhans and the pancreatic ganglia, in a similar way as we are describing in the degus pancreas (Figs. 4 and 5). King et al. (1989) concluded that the innervation of the pancreas reveals a ganglionated nerve plexus, lying in the interlobular connective tissue. The existence of pancreatic neurons would suggest that pancreatic ganglia are not simple unidirectional relays of information from the CNS to the endocrine and exocrine cells of the pancreas. Rather, they may also participate in local control of pancreatic function through local circuits formed with other pancreatic ganglia or through peripheral reflexes involving the peripheral processes of central sensory neurones (King et al., 1989).

The morphological results described in the present study are in agreement with a number of studies in the pancreas of mouse (Ekblad et al., 1994), rat (Liu et al., 1994, 1996), chicken (Shimosegawa et al., 1992), guinea pig (Tay et al., 1994) and human (Ekblad et al., 1994). In all these studies it has been reported that most of the neuronal cell bodies in the ganglia are located in the interlobular and interacinar connective tissues (Figs. 1C and 2C). Furthermore, Larsson (1979) demonstrates that the cat pancreas receives abundant innervation from both the parasympathetic and sympathetic autonomic nervous systems.

Ramón y Cajal, the eminent Spanish neuropathologist of the 19th century, discovered, more than 100 years ago, a particular cell type in the gut, which he named 'interstitial neuron'. In the early 1970s, electron microscopy studies corroborated that a special interstitial cell type, corresponding to the cells discovered by Cajal, is indeed located in the gut muscle layer but it became obvious that they were not neurons. Consequently, these cells were renamed 'interstitial cells of Cajal' (ICC). ICC are difficult to identify and they constitute a peculiar cell network. These cells are morphologically characterized by a spindle- or stellate-shaped body with scarce perinuclear cytoplasm, presenting a number of long branching processes, with an oval-shaped nucleus and the presence of one or more nucleoli. Several studies have established ultrastructural criteria for the identification of these previously enigmatic cells (Komuro et al., 1999). The ICC cytoplasm is rich in mitochondria, smooth endoplasmic reticulum and caveolae (Faussonne-Pellegrini and Thuneberg, 1999). ICC have been reported in a wide range of tissues, usually in close proximity to smooth muscle and have been particularly well studied in the gut (Cantarero Carmona et al., 2011), where they form networks within the myenteric plexuses and between the layers of circular muscle of the muscularis externa. It is worth emphasizing that the study of Wallace and Burns (2005) concluded that in the gut intestinal motility patterns result from interactions between enteric neurons, ICC and intrinsic smooth muscle mechanisms. It is now widely accepted that ICC are pacemaker cells in the gut (Wang et al., 2011), and are probable progenitor cells of gastrointestinal stromal tumors (GIST) (Min and Leabu, 2006), and pancreatic extragastrointestinal stromal tumors (pEGIST) (Padhi et al., 2013).

Comparative morphological studies have shown synaptic-like structures between enteric nerve terminals and ICC in mice (Ward et al., 2000), guinea pig Wang et al. (1999a) and dog gastrointestinal tracts (Horiguchi et al., 2003). Like in the gut, ICC are believed to act as pacemaker cells and their dysfunction has been linked to a variety of intestinal motility disorders (Lee et al., 2005).

Given that the pancreas has no smooth muscle layer, we postulate here that the contractions of the epithelial exocrine ducts and the rhythmicity of vessel walls are likely a consequence of a network of interactions between ganglionic neurons, ICC (now called telocytes; Popescu and Faussonne-Pellegrini, 2010) and epithelial exocrine duct cells or pericytes of the capillary vessels (see Fig. 4). Popescu et al. (2005) reported for the first time the presence of ICC in human and rat exocrine pancreas (pICC). They described that most pICC (88%) have 2 or 3 long cytoplasmic processes emerging from the cell body. They also found that these cells represent $3.3 \pm 0.5\%$ of all pancreatic

cells, and seem to establish close spatial relationships with acini, epithelial exocrine ducts, nerves and blood vessels, in agreement with the observations in the degus pancreas reported here (see Figs. 4 and 5). Finally, these authors concluded that the dogma: "ICC only in cavitory organs" is overpassed. Wang et al. (2011) also found ICC around the main pancreatic epithelial exocrine duct (as seen in our Fig. 4) and they proposed that ICC function as pacemaker cells for the previously observed spontaneous rhythmic pancreatic epithelial exocrine duct contractions, and that ICC around the large blood vessels likely affect vessel wall rhythmicity.

In the last 10 years many groups have sought to elucidate whether or not ICC are present outside the gastrointestinal tract, and indeed, peculiar interstitial cells were found in a variety of organs such as upper and lower urinary tracts (McCloskey, 2010), blood vessels (Cantarero et al., 2011), pancreas (Nicolescu and Popescu, 2012), lung (Popescu et al., 2011), placenta (Suciu et al., 2010), gut (Cantarero et al., 2011) and in the heart (Gherghiceanu and Popescu, 2012). Popescu and Faussonne-Pellegrini (2010) defined ICC as telocytes and the processes emerging from the cell body as telopodes. The presence of telocytes in the interstitium of human exocrine pancreas has been recently described at EM level (Nicolescu and Popescu, 2012). Human pancreatic telocytes appear as small cells with prolongations or telopodes similar to those observed in our study (see Figs. 5 and 6). These authors described the following ultrastructural features of telopodes: (a) number: 1 to 3 per cell; (b) length: tens of micrometers; (c) moniliform aspect: with podoms (thicker portions) and podomers (thin segments, with a mean width of 60 nm, undetectable by light microscopy) (d) branching: dichotomous branching forming a network; (e) establish homocellular and heterocellular junctions; and (f) release of microvesicles/multivesicular bodies. In their study, telopodes were observed in the vicinity of blood vessels, nerves and pancreatic acinar cells and ducts, in concordance with our results. These authors postulated that these cells are essential for the development and physiology of the pancreas. Our results are also in concordance with a study, in human parotid gland (Nicolescu and Popescu, 2012), that reported that telocytes clearly form a network, by branching of their long dichotomous telopodes. Elements of this telocyte network interact with each other (homocellular connections) as well as with other cell types (heterocellular connections). These interactions are achieved by direct contact (stromal synapse), or mediated via shed microvesicles/exosomes (Nicolescu and Popescu, 2012). In recent years, it has become apparent that functions of many organs might involve telocytes, for example, i) myocardial telocytes: intercellular signalling, cardiac repair/remodelling and stem cell nursing in cardiac renewal (Kostin, 2010); ii) skin telocytes: skin homeostasis, skin remodelling, skin regeneration and skin repair (Ceafalan et al., 2012).

Regarding endocrine pancreas, somatostatin is a polypeptide hormone widely distributed outside the brain and exerts various inhibitory actions for endocrine and exocrine secretions. Among the endocrine cells and organs, somatostatin is produced and released from the gastro-enteric-pancreatic endocrine system. In most regions, somatostatin acts as local a hormone conveyed by local circulation or diffusion through the intercellular space in order to regulate neighboring cell functions (Iwanaga et al., 2011). In our study, somatostatin immunoreactivity was in fact observed as intracytoplasmic granules in D cells of the islets of Langerhans (see Fig. 3A, B and D). These observations are in agreement with the study of Pelletier et al. (1975) which describes these granules in rat and dog endocrine pancreas. In degus, these islets D-cells were present in a number of 19 ± 3 cells and it has been suggested that these cells in cat and rat pancreas have local hormone-cell interactions or a paracrine relationship with one or both of the neighboring alpha and beta cell types, that might influence glucagon and/or insulin secretion (Koerker et al., 1974; Orci and Unger, 1975). In addition, Patton et al. (1977) proposed a feedback relationship between alpha and D-cell in which glucagon secretion stimulates the release of somatostatin, which in turn reduces glucagon secretion and perhaps glucagon-mediated insulin secretion.

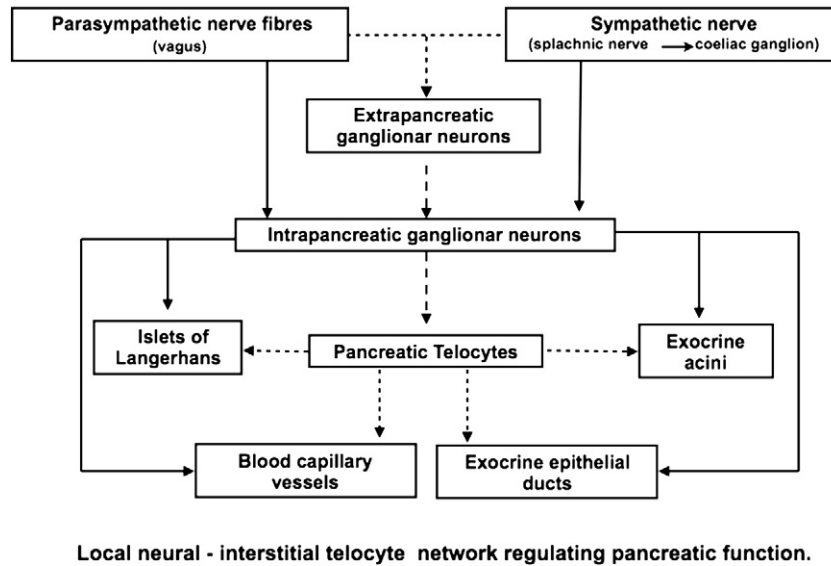


Fig. 6. Schematic representation of the local neural network of interstitial telocytes regulating pancreatic function. Solid lines represent the current idea stated in the literature regarding the internal functioning of the organ. Dotted lines represent our current proposal regarding the regulation of this organ in the degus.

5. Conclusions

The observations reported here raise many questions about telocytes within the pancreas and their physiological role. In our opinion, the presence of telocytes supports the notion of the existence of a network, either by direct cell to cell contact, or indirectly, by secreting paracrine signalling molecules in order to regulate pancreatic function. Further studies of synaptic interactions within and between pancreatic ganglia and telocytes are needed to help clarify the results emerging from this morphological study.

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