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Mucous non-goblet cells in the small intestine of guinea pigs (*Cavia porcellus*): a histological and histochemical study

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Background: *The covering and glandular epithelium of the small intestine in guinea pigs (Cavia porcellus) include some mucus-secreting cells. Goblet cells are specific cells for mucus secretion with a distinctive cup-like appearance due to the accumulation of mucin in the apical pole. The deep crypt secretory (DCS) cells were identified in a limited array of species and only recently were noticed in the large intestine in mice, guinea pigs, humans, monkeys, and pigs. Our study focuses on the microscopical and histochemical features of the DCS cells in the small intestine of guinea pigs.*

Materials and methods: *The samples from the small intestine were collected from five fully grown guinea pigs that were presented to the Hospital of the Faculty of Veterinary Medicine Cluj-Napoca (Romania) with severe lesions resulted from domestic activities. The collected tissue samples underwent fixation in 10% buffered formalin and were later processed by standard paraffin technique. Mucous substances were detected using the Periodic Acid-Schiff and Alcian-Blue histochemical stain methods.*

Results: *The intestinal samples of the guinea pigs assessed had a standard microanatomical structure. As regards the mucous-secreting cells from the small intestine, two cell types were identified, i.e. the goblet cells and DCS cells. DCS cells were only detected in the deep parts of the Lieberkühn glands from the jejunum and ileum, and were different morphologically and histochemically from the regular goblet cells.*

Conclusions: *Our study managed to describe for the first time in guinea pigs, the existence of DCS cells in the jejunum and ileum of the small intestine, but not in the duodenum.* (Folia Morphol 2023; 82, 3: 624–632)

Key words: guinea pig, Lieberkühn glands, mucin, deep crypt secretory cells, goblet cells

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INTRODUCTION

The epithelium of the intestinal villi, along with the lining epithelium of the Lieberkühn glands, is made predominantly of columnar cells. According to the classical histological sources, the cells of the glandular epithelium include the enterocytes, goblet cells, undifferentiated cells, enteroendocrine cells, and Paneth cells [5, 39]. The goblet cells are secreting mucin, a substance that reaches the surface of the intestinal epithelium to be laid as a well-represented layer [6]. This gel-like mucous coating consists mainly of heterogeneous glycoproteins [32]. The mucous layer of the gastrointestinal tract is responsible for lubrication facilitating the food passage, protection of the underlying surface epithelium from commensal microorganisms as well as the creation of a physical barrier against invading pathogens, toxins, and other environmental irritants [25]. Additionally, the mucous coat influences several cell signalling pathways that can modulate inflammatory responses, facilitate cell-cell interactions, together with the adjustment of cell proliferation, differentiation, and apoptosis [13, 38, 41].

The intestinal mucus is mainly made of a subset of glycoproteins called mucins, which play a central role in the physical protection and regulate the passage and concentration of ions, water, and other immune mediators (e.g. antimicrobial peptides or AMPs and immunoglobulin-A) [25]. So far, more than 20 genes responsible for mucin production were identified [9]. Based on their structural and functional features, mucins can be classified into gel-forming or transmembrane types. The secreted gel-forming mucins include MUC2, MUC5AC, MUC5B, and MUC6, which are the principal components of the mucus layer and are responsible for viscoelastic properties [19]. MUC2 is the dominant gel-forming mucin in the intestine that contributes to the development of the mucus barrier. MUC5AC is usually present in the stomach, but can also be upregulated in the intestines during enteric infection [16]. MUC5B is usually expressed in low levels in the colon whereas MUC6 is typically expressed in the stomach and duodenum [42]. MUC7 is a secreted mucin detected in saliva and within the oral cavity [28]. Transmembrane mucins (e.g. MUC1, MUC3, MUC4, MUC13, and MUC17) are expressed on the apical poles of epithelial cells and induce the formation of the glycocalyx that acts as a defending coat between the elaborated mucins and the epithelial cells situated below [40]. However, the stomach and colon have a dual-layer of mucus that is made of polymeric sheets of highly glycosylated mucins, which can be classified into (a) the dense internal layer that is anchored to the subjacent epithelium and impermeable to bacteria, and (b) the external layer that is lightly attached to the dense underlying layer and can be penetrated by bacteria. As a comparison, the small intestine has only one layer of mucus with a loose appearance, which is penetrable by bacteria [13, 15].

Along with the goblet cells, that are present in all species, some authors mention the existence of another type of mucin-secretory cells in case of a limited range of species (e.g. humans, rabbits, rats, mice), located in the deep glandular area of the colon. Due to a vacuolated mucus-filled aspect of the cytoplasm in these cells, they were named "vacuolar cells" and considered precursors of the goblet cells [26, 27]. Accordingly, since "vacuolar cells" were noted in the bottom third of the glands in the ascending colon of rats, they were named "deep crypt secretory" (DCS) cells. A high number of DCS cells was noted at the level of the large intestine in mice and guinea pigs (*Cavia porcellus*), while in humans, monkeys, and pigs their number is significantly lower [1, 33].

Nowadays there is not a clear consensus on the terminology to be used on these cells. Currently, the terms "vacuolated cells", "non-goblet cells", "DCS cells" are used, but none of these seems to cover all features associated with these cells [23]. The most frequently used term, i.e. DCS cells, seems to prevail in the most recent literature [34].

The presence of such peculiar cells, i.e. DCS cells [34], was hinted for most of the species [2], but their limited number made them not clearly detectable. Some authors claim that these cells might be young goblet cells, but electron-microscopy studies on the nucleus, nucleolus, and cell organelles have demonstrated that DCS cells are different from goblet cells [2]. Furthermore, similar results were provided by histochemical reactions. Regarding the turnover rate, the literature mentions around 14 to 21 days in rats and mice [1, 2]. However, some recent reports sustain the equivalence of DCS cells to the Paneth cells from the mouse [34].

Paneth cells are secretory cells exclusively situated in the small intestine. They are situated at the base of intestinal crypts of Lieberkuhn and include numerous secretory granules that contain microbicidal proteins, such as alpha-defensins, lysozyme, C-type lectins, and

phospholipase A2. Practically, after recognition of microbial signals, Paneth cells discharge their granule contents in the intestinal lumen. Additionally, these cells play a fundamental role in the renewal of the epithelium of the small intestine. Paneth cells are located in crypts along with the multipotent stem cells, and by secreting some specific factors that sustain the proliferation of epithelial stem cells (e.g. EGF, WNt3, and the Notch ligand Dll4), they sustain the epithelial renewal [8, 18]. However, the DCS cells are positioned at bottom regions of colonic crypts and in the caecum [34]. They have a multivacuolated appearance of the cytoplasm with basally located oval nuclei [11]. According to Sasaki et al. (2016) [34], DCS cells support colonic stem cells by adjusting cellular differentiation and apoptosis along with stem cell localization. Basically, DCS cells represent the equivalents of Paneth cells in the colon crypts [34].

In the light of limited available data referring to DCS cells, our study focuses on the microscopical and histochemical features of the DCS cells in the small intestine of guinea pigs (*Cavia porcellus*).

MATERIALS AND METHODS

Biological material originates from 5 fully grown guinea pigs (*Cavia porcellus*), males, originating from the Hospital of the Faculty of Veterinary Medicine Cluj-Napoca (Romania). The biological material was harvested on a 10-month period of time (September 2018–June 2019) from casualties presented at the aforementioned Hospital, from individuals with severe lesions resulted from domestic activities (house accidents). In all utilized individuals, euthanasia was recommended as a humane method for relieving pain or distress that cannot be controlled by other means as recommended by American Veterinary Medical Association (AMVA) [4, 29].

After the anatomical identification of segments, fragments of duodenum, jejunum, and ileum were collected. Following necropsy examination, no pathological changes were identified in the digestive tract. For the histological investigation, several fragments from the small intestine were harvested (approximately 0.5 cm in length). The collected fragments underwent fixation in 10% buffered formalin for 3 days, followed by a progressive dehydration procedure (ethylic alcohol of 70%, 96%, and 100%) for 1 hour each stage. The clarification was made on 3 successive 1 hour-long 1-butanol baths and subsequentially embedded in the paraffin. For histological evaluation, 5 μm tissue sections were achieved using a Leica rotary microtome (RM2125, Germany) and stained later by Goldner's trichrome method [10].

The detection of mucous substances in the three regions of the small intestine was realized using the Periodic Acid-Schiff (PAS) and Alcian-Blue histochemical stain methods. Accordingly, the presence of neutral mucins was highlighted by the PAS method, whereas the acidic mucins were identified by Alcian-Blue stain, pH-2.5 [3, 24]. The histochemical reaction intensity was measured by grading from 0 (negative reaction) to two pluses (i.e. + faintly positive; ++ intensely positive).

The slides evaluation was performed with the aid of an Olympus BX-41 microscope (Olympus, Japan) attached to the Olympus E330 camera (Olympus, Japan).

The morphometric evaluation of the cells (DCS and Goblet cells) was performed using AmScope Version 4.8 software. The surface of the DCS cells was measured (μm^2) from the ileal and jejunal segments, while for the Goblet cells, their surface was assessed from all the three intestinal segments. The statistical analysis of the obtained results was performed with GraphPad Prism 8 and Microsoft Excel. An unpaired *t*-test, with $p < 0.05$ was used to compare the surfaces of the DCS cells between jejunal and ileal segments. ANOVA One-Way and Tukey's multiple comparisons tests were used for the assessment of Goblet cells surfaces from all the three analysed segments (duodenum, ileum, and jejunum).

RESULTS

Microscopically, typical goblet cells were clearly identified at the level of the surface and glandular epithelium of the Lieberkühn glands, in all segments of the small intestine (duodenum, jejunum, and ileum) collected from the guinea pig (*Cavia porcellus*) individuals (Fig. 1A). The identified goblet cells are similar in shape and size, and they exhibit some specific histological features, e.g. a large mucous droplet located mainly in the apical pole of the cell that induces cell distention in this region, and the placement of the nucleus towards the basal pole of the cells (cup-like appearance), region that is much narrower than the apical pole. The nucleus of the goblet cells is oval-shaped and located in the basal pole of the cell, and as compared to the basal membrane it has a perpendicular orientation. However, apart from the previously described goblet cells, morphologically different

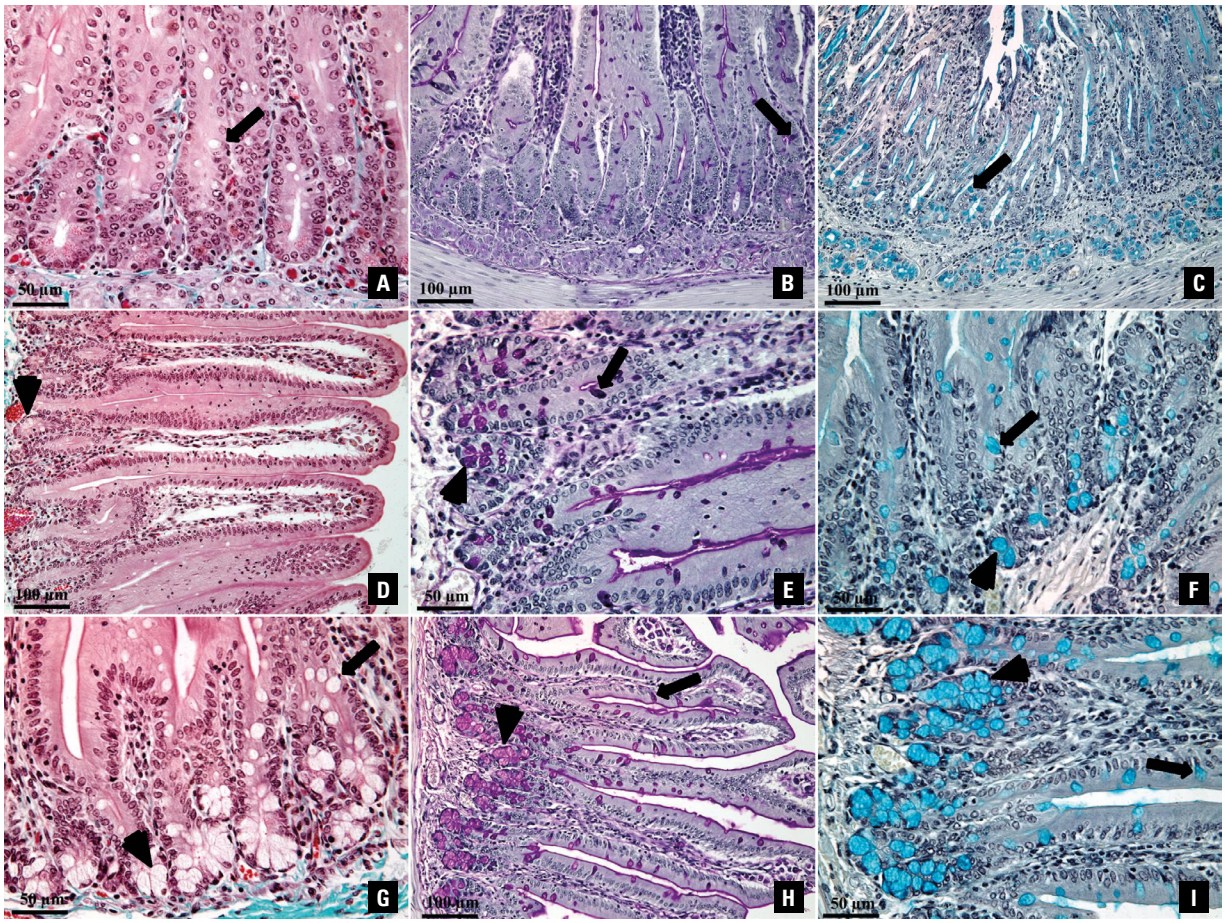

Figure 1. A. Duodenum (Goldner's trichrome stain): the only mucus-secreting cells in Lieberkühn glands are goblet cells with the specific cup-like appearance (black arrow); **B.** Duodenum (Periodic Acid-Schiff [PAS] stain): intensely PAS-positive (++) goblet cells (black arrow); **C.** Duodenum (Alcian-Blue stain): intensely Alcian-Blue-positive (++) goblet cells (black arrow); **D.** Jejunum (Goldner's trichrome stain): the presence of goblet cells and of non-goblet or deep crypt secretory (DCS) cells that have a multivacuolated or foamy cytoplasm (arrowhead), cells that are located in the deep part of the Lieberkühn glands; **E.** Jejunum (PAS stain): DCS cells (arrowhead) displaying a mild PAS-positive reaction (+) as compared to intensely PAS-positive (++) goblet cells (black arrow); **F.** Jejunum (Alcian-Blue stain): intensely Alcian-Blue--positive stain (++) for the both goblet (black arrow) and DCS cells (arrowhead); **G.** Ileum (Goldner's trichrome stain): the presence of the both goblet cells (black arrow) and DCS cells (arrowhead), the last ones in a higher number comparing to jejunum; **H.** Ileum (PAS stain): similar histochemical features as in the jejunum, i.e. mildly PAS-positive stain (+) for DCS cells (arrowhead) and a strong PAS reaction (++) of the goblet cells (black arrow); **I.** Ileum (Alcian-Blue stain): similarly with the jejunum, the both mucus secreting cells displayed a strong Alcian-Blue stain (black arrow — goblet cells, arrowhead — DCS cells).

mucus-secreting cells were identified but only in the jejunum and ileal segments of the small intestine. The so-called non-goblet cells were identified in groups in the bottom part of the Lieberkühn glands from the jejunum and ileum. Microanatomically, these cells are slightly different from goblet cells by their pyramidal shape, but significantly wider in the apical pole as compared to the goblet cells. Due to the presence of several uneven mucous droplets, the cytoplasm of non-goblet cells is multivacuolated, which confer a foamy aspect to the cytoplasm. In the non-goblet cells, the oval nucleus is pushed to the basal pole of the cell with a somehow parallel alignment with the subjacent basal membrane (Fig. 1D, G).

Histochemically, the goblet cells appear intensely PAS-positive (++) (Fig. 1B, E, H) and strongly Alcian-Blue positive (++) (Fig. 1C, F, I) in all intestinal segments (duodenum, ileum, jejunum). As a comparison, the non-goblet deep-crypt mucin-secreting cells from the jejunum and ileum displayed a mild PAS-positive reaction (+) and a strong reaction to Alcian-Blue (++) stain (Fig. 1B, C, E, F, H, I).

A total number of 60 glands (20 glands per intestinal segment) were analysed. In terms of cell counts, it can be observed that the proportion of goblet cells from the total number of cells is higher in ileal segments (13.13%) compared to the jejunum (8.13%) and duodenum (11.33%). Regarding DCS cells, their

Table 1. Descriptive statistics for cell count analysis

Segment		Descriptive statistics for cell count analysis						
		All cells	DCS cell count	Goblet cell count	Other type of cells	DCS cells [%]	Goblet cells [%]	Other type of cells [%]
Duodenum	Mean	51.15	0	5.6	45.55	**0.00%**	**11.33%**	88.67%
	SD	12.62	0	2.84	12.50			
	Min	32	0	3	27	0.00%	4.11%	75.00%
	Max	73	0	14	70	0.00%	25.00%	95.89%
	Range	41	0	11	43	0	0.208904	0.208904
Jejunum	Mean	33.63	3.74	2.89	27	**11.00%**	**8.13%**	80.87%
	SD	13.61	2.58	1.73	11.25			
	Min	11	0	0	10	0.00%	0.00%	65.63%
	Max	55	8	6	49	33.33%	13.04%	94.44%
	Range	44	8	6	39	0.33	0.13	0.29
Ileum	Mean	36.72	8.67	5.11	22.94	**24.93%**	**13.13%**	61.93%
	SD	8.66	2.30	2.72	6.42			
	Min	13	3	0	7	9.68%	0.00%	47.37%
	Max	49	13	10	33	46.15%	25.81%	78.57%
	Range	36	10	10	26	0.36	0.26	0.31

DCS — deep crypt secretory; SD — standard deviation; Min — minimal value; Max — maximal value

absence in the duodenal segment can be noted, while for the other two segments, their proportion is higher in the ileum (24.93%) as compared to the jejunal region (11.00%; Table 1).

Regarding the analysed surface of the cells in the three intestinal segments, it can be observed that the surface of the goblet cells is higher in the ileum (1162 ± 368.8 μm^2) as compared to the jejunum (932 ± 366.5 μm^2). The surface of goblet cells from the duodenum showed the smallest values compared to the other two analysed segments (825.7 ± 410.3 μm^2). The DCS cells surfaces follow the same pattern, having a bigger surface in the ileal segment (1829 ± 657.9 μm^2) vs. jejunal segment (936 ± 337.6 μm^2; Table 2). According to the obtained results, the differences between the surfaces of DCS cells in the ileum and jejunum are highly significant ($p < 0.0001$; Table 3, Fig. 2). The surface differences of goblet cells varied among the three segments, with a highly significant difference of the duodenal vs. ileal segments ($p < 0.0001$), significant differences of the jejunal vs. ileal segments ($p < 0.001$), and insignificant differences of the duodenal vs. jejunal segments (Fig. 3, Tables 4, 5).

DISCUSSION

Goblet cells are specific structures for the production and secretion of mucus. They received their name due to a distinctive goblet or cup-like appearance induced by the granular mucin that accumulates in the apical pole of the cell. Even if there is still incomplete information on the cell biology of goblet cells, it is evident that there are a number of types that function in diverse ways. The goblet cell from the small intestine (i.e. the ones adjacent to enterocytes) supply the bicarbonate for appropriate mucin unfolding [14]. In the large intestine, the goblet cell supplies bicarbonate by its own bestrophin-2 bicarbonate transporter [43]. The surface goblet cells from the inter-crypt region of the colon discharge the mucus continuously, whereas the goblet cells from the upper part of the colonic crypts secrete by fast compound exocytosis [20]. As observed, the goblet cells are more dissimilar and capable than have been earlier anticipated [6].

The intestinal samples of the guinea pigs (*Cavia porcellus*) assessed had a standard microanatomical structure, that includes mucosa, submucosa, muscularis externa, and serosa. As regards the mucous-secreting cells from the small intestine in guinea pigs (*Cavia porcellus*), two cell types were identified, i.e. the goblet cells and DCS cells. The goblet cells were identified in all the segments of the small intestine both in the covering the glandular epithelium, whereas DCS cells were only detected in the deep parts of the Lieberkühn glands from the jejunum and il-

Table 2. Descriptive statistics of measured cell surfaces

Intestinal segment	Descriptive statistics	Cell type	
		Goblet cells	DCS cells
		Cell surface [μm^2]	
Duodenum	Number of values	63	NA
	Minimum	263.8	NA
	Maximum	2039	NA
	Range	1775	NA
	Mean	825.7	NA
	SD	410.3	NA
	SEM	51.69	NA
	CV%	49.70%	NA
Jejunum	Number of values	64	71
	Minimum	326.4	253.7
	Maximum	1754	1630
	Range	1428	1376
	Mean	932	936
	SD	366.5	337.6
	SEM	45.81	40.06
	CV%	39.32%	36.06%
Ileum	Number of values	83	133
	Minimum	491.6	755.4
	Maximum	2093	4009
	Range	1601	3254
	Mean	1162	1829
	SD	368.8	657.9
	SEM	40.48	57.05
	CV%	31.73%	35.97%

DCS — deep crypt secretory; NA — not available; SD — standard deviation; CV% — coefficient of variation; SEM —standard error of the mean

Table 3. Comparison of deep crypt secretory cell surfaces from the jejunum and ileum, using two-tailed *t*-test

Unpaired *t*-test	
P value	< 0.0001
P value summary	≤ 0.0001
Significantly different ($p < 0.05$)?	Yes
One- or two-tailed p-value?	Two-tailed
t, df	$t = 10.70$, $df = 202$

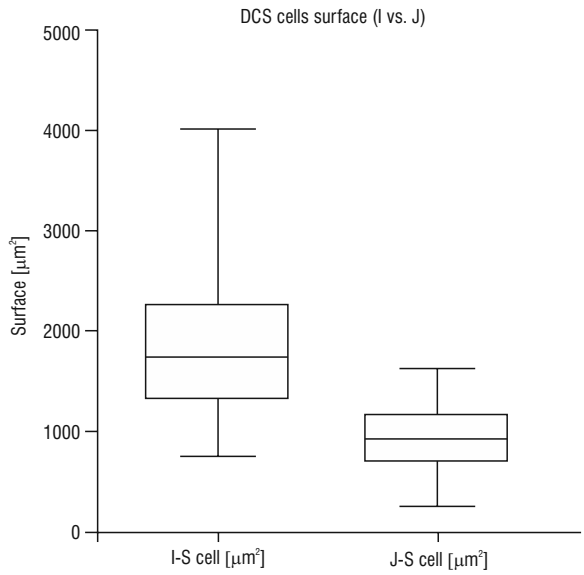

Figure 2. Comparison of the surface of deep crypt secretory (DCS) cells between jejunal and ileal segments; I — ileum; J — jejunum; J-S cell — surface of the DCS cells from the jejunal segment; I-S cell — surface of the DCS cells from the ileal segment.

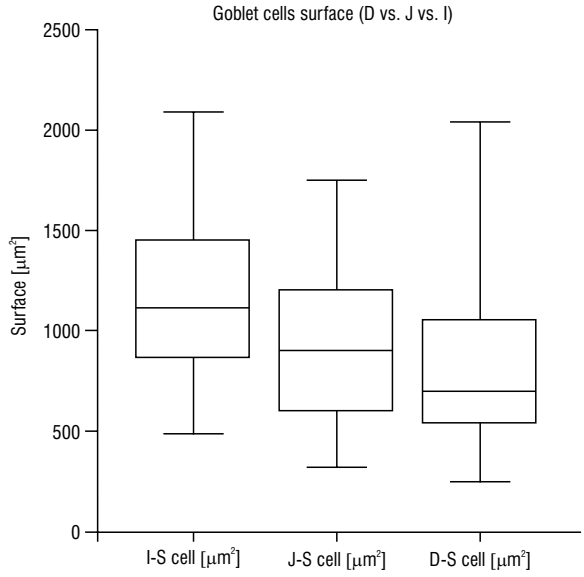

Figure 3. Comparison between the surface of goblet cells between duodenal, jejunal, and ileal segments; D — duodenum; I — ileum; J — jejunum; D-S cell — surface of the goblet cells from the duodenal segment; J-S cell — surface of the goblet cells from the jejunal segment; I-S cell — surface of the goblet cells from the ileal segment.

eum. The DCS cells are different morphologically and histochemically from the regular goblet cells. The non-goblet or DCS cells have higher dimensions than the typical goblet cells, somehow pyramidally shaped with the base against the basal membrane. On regular Goldner's trichrome stain, DCS cells present a vacuolated mucus-filled cytoplasm and a flattened nucleus, placed towards the basal membrane.

Similar cells (as concerns the shape, localization, and dimensions) were reported in some mammals in different regions of the large intestine. Accordingly, one of the first signallings of non-goblet cells

Table 4. Comparison of goblet cell surfaces from duodenal, jejunal, and ileal segments using Tukey's multiple comparison test

Tukey's multiple comparisons test	Mean diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P value	
D-S cell μm^2 vs. J-S cell μm^2	–106.3	–266.0 to 53.30	No	NS	0.2599	A-B
D-S cell μm^2 vs. I-S cell μm^2	–336.5	–486.8 to –186.2	Yes	≤ 0.0001	< 0.0001	A-C
J-S cell μm^2 vs. I-S cell μm^2	–230.2	–379.8 to –80.55	Yes	≤ 0.01	0.001	B-C

CI — confidence interval; D — duodenum; J — jejunum; I — ileum; S — surface of the cell [μm^2]

Table 5. Comparison of goblet cell surfaces from duodenal, jejunal, and ileal segments using ANOVA One-Way

ANOVA summary	
F	15.08
P value	< 0.0001
P value summary	≤ 0.0001
Significant different among means ($p < 0.05$)?	Yes
R square	0.1271

was made in the deep region of the crypts from the rectum in humans, rabbit, mouse and rat, and they were named "vacuolated" cells [37]. Later, similar cells were described as non-goblet or DCS cells by Altmann (1983) [1] in the ascending colon of the rat, cells that were reported also by other more recent study [23]. However, we did not find any report to mention the presence of DCS cells in the small intestine in mammals, so it seems that our study is the first to report their presence in the small intestine in guinea pigs (*Cavia porcellus*).

The histochemical investigations performed in our study showed that the goblet cells displayed an intensely positive reaction to PAS and Alcian-Blue stains in all segments of the small intestine, in both superficial and deep glandular epithelium. This is a clear indicator of the fact the goblet cells are in charge of the synthesis of neutral and acidic mucins. However, the DCS cells identified in the deeper part of the jejunum and ileum in guinea pig (*Cavia porcellus*) displayed a mild PAS-positive reaction and a strong reaction to Alcian-Blue stain, implying the fact that these cells synthesize predominantly acidic mucins, and in a slightly lower amount the neutral mucin.

According to some other reports, in rats, DCS cells seem to be specialized for mucin production and capable to synthesize at least two distinctive mucin patterns [36]. The aforementioned authors stated the fact that the goblet cells located more superficial in the intestinal mucosa are in charge of sulfomucin secretion, whereas the mucus-secreting cells with a deeper location in the epithelium (i.e. DCS cells) are more likely associated with a sialomucin profile. Further histochemical investigations (e.g. PAS, Alcian-Blue stains) led to the conclusion that DCS cells are different from the typical goblet cells [33]. Electron-microscopy studies [30] confirmed the different mucin patterns as well as the fact that the DCS cells show a fine vacuolar material while the goblet cells have a much denser peculiar matrix with discrete secretory vesicles that fill most of the cellular cytoplasm. The presence of the rough endoplasmic reticulum and a developed Golgi apparatus suggests an intense glycoprotein secretory activity [17, 30, 39].

Goblet cells, as enterocytes, enteroendocrine cells, and Paneth cells of the gut mucosa derive from multipotent stem cells located at the base of crypts of Lieberkühn [12]. Due to the influence of the mucous layer on gastrointestinal inflammatory pathologies, the interest regarding gut-associated mucus is increasing in the last period. Frequently such pathological conditions go along with impaired goblet cell function along with dysregulated mucin biosynthesis, which triggers significant qualitative and quantitative changes [7, 25]. Inflammatory bowel disease is a group of disorders influenced by an inappropriate function of goblet cells, including their synthesized mucins. Inflammatory bowel disease is classified into Crohn's disease and ulcerative colitis [13]. These disorders are characterised by chronic inflammatory lesions in the gastrointestinal tract and are associated with obscure causes and poorly efficient therapies [21]. Some other morbid entities that evolve with alterations in gastrointestinal mucin production and function are represented by colorectal cancer and some bacterial and parasitic infections. The last ones are frequently associated with mucin dysfunction and inflammation of the gastrointestinal tract [25]. As regards the role of DCS cells, Sasaki et al (2016) [34] observed that ablation of Reg4+ DCS cells in the murine colon results in loss of stem cells from colonic crypts, a fact that disturbs gut homeostasis and colon organoid growth [34]. It is known that stem cells

fundamentally depend on their intricate microenvironment, otherwise known as niche (i.e. an anatomic place consisting of specialised cells that anchor stem cells and additionally offer physical protection and essential growth/maintenance signals). In the murine small intestine, an important part of the cellular niche for Lgr5+ stem cells is made by Paneth cells, which deliver molecules like Wnt3, EGF, and Notch ligands to preserve intestinal stem cells. Since the murine colon does not contain typical Paneth cells, the Reg4-DCS cells represent the colon equivalent of Paneth cells [34]. Accordingly, DCS cells support the organoid development of single Lgr5+ colon stem cells. As a fact, Reg4+ cells were also detected within colorectal tumoral lesions in humans [22, 31]. A connection between Reg4+ cells and Lgr5+ stem cells in mouse colon adenoma was observed, a fact that may suggest that Reg4+ cells in adenoma play a role as a niche for cancer stem cells [35].

CONCLUSIONS

Mucous cells, including goblet and non-goblet cells, along with their secretory product were underestimated for a long period of time. However, the latest findings changed this and situated these cells at the focal point for the understanding of intestinal mucosa biology and immunology. The intestinal mucosa possesses several types of mucous cells that can be outlined based on their position and microanatomy. Our study managed to describe for the first time in guinea pig (*Cavia porcellus*), the existence of formerly known vacuolated/non-goblet cells, or recently called DCS cells in the jejunum and ileum sections of the small intestine. Finally, the understanding of the full function of the mucous goblet and non-goblet cells will offer a further vision not only about gut homeostasis and organoid growth of the large intestine but some elucidation regarding the inflammatory bowel disease and the intricate biology of the niche for cancer stem cells that may reveal innovative therapeutic protocols for colorectal cancer.

Conflict of interest: None declared

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