Title
Structure, development and evolution of the digestive system

Journal
Cell and Tissue Research, 377(3)

ISSN
0302-766X

Authors
Hartenstein, V
Martinez, P

Publication Date
2019-09-01

DOI
10.1007/s00441-019-03102-x

Peer reviewed

HHS Public Access

Author manuscript

Cell Tissue Res. Author manuscript; available in PMC 2020 September 01.

Published in final edited form as:

Cell Tissue Res. 2019 September ; 377(3): 289–292. doi:10.1007/s00441-019-03102-x.

Structure, Development and Evolution of the Digestive System

V. Hartenstein[1,*], **P. Martinez**[2,3]

[1]Department of Biology, University of California, Los Angeles (UCLA)

[2]Departament de Genètica, Microbiologia i Estadística, Universitat de Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain

[3]ICREA (Institut Català de Recerca i Estudis Avancats), Passeig Lluís Companys 23, 08010 Barcelona, Spain

Summary

Living cells depend on a constant supply of energy-rich organic molecules from the environment. Small molecules pass into the interior of the cell via simple diffusion or active transport carried out by membrane bound transporters; macromolecules, or entire cells, are taken up by endocytosis/phagocytosis, and are degraded intracellularly in specialized membrane bound compartments (lysosomes). Whereas all cells are capable of transporting molecules through the membrane, the efficient procurement, digestion and uptake of nutrients have become the function of specialized cell types and organs, forming the digestive system in multicellular animals. In mammals, for example, the digestive system is comprised of glandular organs with classes of cells specialized in the secretion of enzymes for the extracellular digestion of food particles (e.g., exocrine cells of the salivary gland, pancreas), as well as other organs with absorptive function (e.g., small intestine). Numerous other cell types, such as smooth muscle cells, neurons and enteroendocrine cells, are associated with glandular cells and intestinal cells to promote the digestive process.

The complex mammalian digestive system is a highly derived character among animals. It is well known that animals belonging to more early diversified clades, such as Porifera or Cnidaria, ingest food mainly in the form of single cells (e.g., bacteria, microalgae, protists) that are taken up phagocytotically and degraded subsequently by intracellular digestion (Lunger 1963; Afzelius and Rosen 1965; Weissenfels 1976; Imsiecke 1993). Historically, the widespread occurrence of phagocytosis and intracellular digestion among invertebrates was clearly recognized by pioneers of cell biology, such as Eli Metschnikoff (1884). More recently, the push to analyze physiological processes, like digestion, at a cellular and molecular level has restricted our focus towards a few experimentally tractable model systems, which include vertebrates, as well as a few invertebrates (the insect *Drosophila melanogaster* or the nematode *Caenorhabditis elegans*, where food assimilation also occurs mainly by extracellular digestion (see Holthof et al. 2019 and Dimov and Maduro, 2019, this issue). As a result, the pervasive role of phagocytosis and intracellular digestion in animal

*Corresponding authors: volkerh@mcdb.ucla.edu.

digestion has remained less investigated, and this includes both the cellular organization and the essential molecular players. For most phyla the mechanisms controlling digestion are scarcely known, leaving us with a very fragmentary view of the evolution of digestive systems. With new technologies having been made available in recent years, and phylogenetic relationships between different taxa becoming clearer, it is now possible to address cellular and molecular details of food digestion and uptake in the context of evolution. For the first time we are able to follow the evolution of cell types, specification genes and digestive system's architectures in many animal groups. OMIC approaches, including singe cell molecular profiles are telling us some of the evolutionary paths that digestion and its constitutive components have followed over evolutionary time. The present special issue of Cell and Tissue Research presents a series of reviews that look at the current state of knowledge in this area, addressing some of the relevant issues concerning (1) regionalization and development of the gut; (2) the role of extracellular digestion and phagocytosis in food assimilation; (3) structure, development and evolution of the gut endocrine system; (4) functional and evolutionary relationship between the digestive and immune system.

Conserved genetic mechanism specify diverse guts

In all animals excepting the basal clade of Placozoa, digestion is the function of epithelial cells lining an inner lumen (gut cavity). The general pattern of the gut and the way to regionalize it seem to depend on many shared genes, which points to the fact that the general organization of the gut is, most probably, evolutionarily ancient, dating back to the cnidarian-bilaterian (the "old" Planulozoa) ancestor. Molecular-genetic have revealed important themes in gut development, and several reviews of the special issue summarize the current knowledge in this area [Annunziata et al. (2019), for echinoderms; Nakayama et al. (2019), for protochordates; Dimov and Maduro (2019) for nematodes; Steinmetz (2019) for cnidarians]. Contrasting with a strongly conserved repertoire of genetic mechanisms acting in gut development is the evident diversity of the architectures and cellular compositions of the digestive systems, which results from the need to adapt to the different types of food that animals consume. Examples of gut diversity surveyed in detail in this special issue include the sponges (Godefroy et al. 2019), acoels (Gavilan et al. 2019) and molluscs (Lobo-da-Cunha 2019).

Cellular mechanisms of extracellular and intracellular digestion

When considering the evolutionary origins of the digestive system, the ventral epithelial cells of Placozoa that phagocytose microorganisms trapped in the cleft between the animal and the substrate, may present an anatomical scenario from which more complex digestive systems evolved (Smith and Mayorova 2019, this issue). In all other animals phagocytotic cells carrying out the digestive process are associated with internal chambers. In sponges, these cells are represented by choanocytes, which, together with mesenchymal archaeocytes, are responsible for the uptake, intracellular digestion, and distribution of nutrients (Imsiecke 1993; Godefroy et al. 2019, this issue). In ctenophores, cnidarians and bilaterians, phagocytes form a gastrodermal (or intestinal) epithelium, which also contains other cell types, notably secretory (glandular) cells and endocrine cells (Chapman 1978; Van-Praet

1985; Steinmetz, 2019, this issue; Hartenstein and Martinez, 2019, this issue). Enzymes produced by secretory cells break down nutrients, and in some clades (e.g., vertebrates, most insects) extracellular digestion followed by absorption of small molecules have superseded phagocytosis and intracellular digestion as the main mechanism of food assimilation (Holthof et al. 2019, this issue). However, in most clades, including protochordates, which are the closest relatives of vertebrates, phagocytosis combined with intracellular digestion is the predominant method of operation of the digestive system (He et al. 2018; Nakayama et al. 2019, this issue; Satake et al. 2019, this issue). Cellular and molecular details of these processes are not known in detail. Studies that do exist mainly include descriptions of the ultrastructure of cells involved in digestion, and these are reviewed in this special issue for several specific clades by Smith and Dimov (2019; Placozoa), Godefroy et al. (2019; Porifera), Gavilan et al. (2019; Xenacoelomorpha), Lobo-da-Cunha (2019; Mollusca), Štrus et al. (2019; Crustacea) and Caccia et al. (2019; Hexapoda) and for prebilaterian and bilaterian clades in more general, by Steinmetz (2019) and Hartenstein and Martinez (2019), respectively.

The gut endocrine system

An interesting issue raised by some recent studies is the control of digestive functions by different neuropeptides. The recent flurry of papers dealing with the sequencing of animal genomes has provided us with detailed catalogues of putative neuropeptides in many clades, some of which might be involved in the control of intestinal functions. This is the case of some echinoderms (Garcia Arraras et al. 2019, this issue) that express neuropeptides in the enteroendocrine cells. Whether these cells contact/respond to the nervous system is a matter of current investigation. In other chordate systems, such as the lancelet *Branchiostoma floridae*, neuropeptides seem to be also expressed in the alimentary canal (Nakayama et al. 2019, this issue). Moreover in the urochordate model *Ciona intestinalis* (described by Satake et al. 2019) many peptides/receptors have been detected in the alimentary canal (including some clade-specific peptides). Annunziata et al. (2019, this issue) report the presence of insulin-like producing cells located in a particular domain of the gut in what they assume to be endocrine cells.

Other authors that mention the presence of specific neuropeptides in the gut, without going into details, are (Strus et al.; Holtof et al. and Tettamanti et al; both dealing with the Arthropoda) or even in the old placozoan lineage (in gland cells), which shares neuropeptides with other bilaterian clades (Smith et al.) though, at present, are still poorly characterized. Poriferans do not seem to have secretory peptides in their genomes and the ctenophores use a completely different set of peptides unrelated to those of any other metazoan phyla (Moroz et al. 2014). Though the capacity to generate peptides seems to be a premetazoan invention, the use for regulation of digestive roles seems to be associated to the emergence of the Planulozoa (Bilateria + Cnidaria; depending of the phylogenetic position accepted for the Placozoa).

Immunity and digestion: Functional and evolutionary relationships

Our current knowledge of phagocytosis and lysosomal digestion is mainly informed by studies on macrophages, motile phagocytic cells that ingest invading microorganisms and cellular debris resulting from tissue damage. Macrophages also play important developmental roles, removing apoptotic cells and laying down extracellular matrices. Little is known about the relationship between the the immune system and digestive system. Functionally, both systems have to cooperate, given the immunological challenge caused by the ingestion of particles directly from the environment (a clear case are aquatic animals). In the reviews provided by Buckley and Rast (2019, this issue), Nakayama et al. (2019, this issue) and Satake et al. (2019, this issue) a detailed analysis of the molecular players involved in the interaction of the immune system and the gut epithelia in larval echinoderms and protochordates is presented. Interestingly, some players are shared between this system and vertebrates (i.e. IL-17), which point to some common (ancient) systems of interaction between immune cells and those of the gut epithelium, recognizing the gut as the physical location of interaction between the immune system and the microbiota (beneficial or pathogenic) of the gut lumen".

In regard to ultrastructure, macrophages of the immune system and phagocytes of the digestive system of most invertebrates have many features in common (Hartenstein and Martinez, 2019, this issue), prompting the question of common roots unifying these two cell types. Developmentally, they derive from two different germ layers, the mesoderm and endoderm, respectively. However, it is possible that at the root of the metazoan tree, they formed a common pool of cells. This can still be seen in extant sponges, where phagocytes lining the choanocyte chambers (choanocytes, "enteric phagocytes") can convert into motile archaeocytes ("macrophages") that inhabit the interior space (mesohyl), and vice versa (Nakanishi et al. 2014; Sogabe et al. 2016). For some bilateran clades, in particular annelids (Kermack 1955) and echinoderms (Chia and Koss 1991), motile macrophages (coelomocytes) also become associated with the intestinal epithelium, where they could be involved in immune functions, as well as food uptake. An intriguing evolutionary scenario, based on recent studies in cnidarians, is proposed by Steinmetz (2019; this issue), according to which the phagocytes and other cell types of the endoderm of the cnidarian-bilateran ancestor gave rise to the bilaterian mesoderm; the bilaterian endoderm and its products, including gland cells and endocrine cells, evolved from the ectoderm of the cnidarian-bilateran ancestor. This sequence of events would explain how endodermal phagocytes, initially involved in food uptake in the cnidarian-bilateran ancestor, evolved into macrophages in the bilaterian lineage. On the other hand, one would have to assume that other cell types commonly found in the bilaterian intestinal epithelium, including phagocytes, evolved convergently, which (given the widespread distribution of these cells among different bilaterian clades) appears unlikely. However, one should note that, despite shared structural and functional characters, homology between any of these cell types (e.g., archaeocytes in sponges; enteric phagocytes in cnidarians and various bilaterian taxa) has not been established. Fortunately, currently available tools make it possible to gain detailed insight into the genetic makeup of cells, and we can be hopeful that in the near future we

will have a clearer picture of the evolutionary relationship between phagocytes and other cell types of the gut, as well as macrophages carrying out immune functions.

References

Afzelius BA, Rosén B (1965) Nutritive phagocytosis in animal cells. An electron microscopical study of the gastroderm of the hydroid Clava squamata Müll. Z Zellforsch Mikrosk Anat 67:24–33. [PubMed: 4379911]

Annunziata R, Andrikou C, Perillo M, Cuomo C, and Arnone MI (2019) Development and evolution of gut structures: from molecules to function. Cell Tissue Res. DOI "To be completed"

Buckley KM, and Rast JP (2019) Immune activity at the gut epithelium in the larval sea urchin. Cell Tissue Res. DOI "To be completed"

Caccia S, Casartelli M, and Tettamanti G (2019) The amazing complexity of insect midgut cells: types, peculiarities, and functions. Cell Tissue Res. 10.1007/s00441-019-03076-w

Chapman DM (1978) Microanatomy of the cubopolyp,Tripedalia cystophora (Class Cubozoa). Helgoländer Wissenschaftliche Meeresuntersuchungen 31:128–168. 10.1007/BF02296994

Chia FS, Koss R (1991) Asteroidea In: Harrison FW, Chia TS (eds). Microscopic anatomy of invertebrates, vol 14 John Wiley and Sons, New York, pp 169–246.

Dimov I, and Maduro MF (2019) The C. elegans intestine: organogenesis, digestion, and physiology. Cell Tissue Res. 10.1007/s00441-019-03036-4

García-Arrarás JE, Lefebre-Rivera M, and Qi-Huang S (2019) Enteroendocrine cells in the Echinodermata. Cell Tissue Res. 10.1007/s00441-019-03053-3

Gavilán B, Sprecher SG, Hartenstein V and Martinez P (2019) The digestive system of xenacoelomorphs. Cell Tissue Res. 10.1007/s00441-019-03038-2

Godefroy N, Le Goff E, Martinand-Mari C, Belkhir K, Vacelet J and Baghdiguian S (2019) Sponge digestive system diversity and evolution: filter feeding to carnivory. Cell Tissue Res. 10.1007/s00441-019-03032-8

Hartenstein V and Martinez P (2019) Phagocytosis in Cellular Defense and Nutrition: A Food-Centered Approach to the Evolution of Macrophages. Cell Tissue Res. DOI "To be completed"

He C, Han T, Liao X, Zhou Y, Wang X, Guan R, Tian T, Li Y, Bi C, Lu N, He Z, Hu B, Zhou Q, Hu Y, Lu Z, Chen JY. (2018) Phagocytic intracellular digestion in amphioxus (Branchiostoma). Proc Biol Sci 285:20180438 10.1098/rspb.2018.0438 [PubMed: 29875301]

Holtof M, Lenaerts C, Cullen D, Van den Broeck J (2019) Extracellular nutrient digestion and absorption in the insect gut. Cell Tissue Res. 10.1007/s00441-019-03031-9

Imsiecke (1993) Ingestion, digestion, and egestion in Spongilla lacustris (Porifera, Spongillidae) after pulse feeding with Chlamydomonas reinhardtii (Volvocales). Zoomorphology 113:233–244. 10.1007/BF00403314

Kermack DM (1955) The anatomy and physiology of the gut of the polychaete Arenicola marina (L.). Proc Zool Soc Lond 125:347–381

Lobo-da-Cunha A (2019) Structure and Function of the Digestive System in Molluscs. Cell Tissue Res. DOI "To be completed"

Lunger PD (1963) Fine-structural aspects of digestion in a colonial hydroid. Journal of Ultrastructure Research 9:362–380. 10.1016/S0022-5320(63)80012-X

Metschnikoff E (1884) Memoirs: Researches on the Intracellular Digestion of Invertebrates. J Cell Sci 93: 89–111.

Moroz LL, Kocot KM, Citarella MR, Dosung S, Norekian TP, Povolotskaya IS, Grigorenko AP, Dailey C, Berezikov E, Buckley KM, Ptitsyn A, Reshetov D, Mukherjee K, Moroz TP, Bobkova Y, Yu F, Kapitonov VV, Jurka J, Bobkov YV, Swore JJ, Girardo DO, Fodor A, Gusev F, Sanford R, Bruders R, Kittler E, Mills CE, Rast JP, Derelle R, Solovyev VV, Kondrashov FA, Swalla BJ, Sweedler JV, Rogaev EI, Halanych KM, Kohn AB. (2014) The ctenophore genome and the evolutionary origins of neural systems. Nature. 510(7503):109–14. DOI 10.1038/nature13400. [PubMed: 24847885]

Nakanishi N, Sogabe S, Degnan BM (2014) Evolutionary origin of gastrulation: insights from sponge development. BMC Biology 12:26 10.1186/1741-7007-12-26 [PubMed: 24678663]

Nakayama S, Sekiguchi T, and Ogasawara M(2019) Molecular and evolutionary aspects of the protochordate digestive system. Cell Tissue Res. 10.1007/s00441-019-03035-5

Satake H, Matsubara S, Shiraishi A, Yamamoto T, Osugi T, Sakai1 T, and Kawada T (2019) Peptide receptors and immune-related proteins expressed in the digestive system of a urochordate, Ciona intestinalis. Cell Tissue Res. 10.1007/s00441-019-03024-8

Smith CL, and Mayorova TD (2019) Insights into the evolution of digestive systems from studies of Trichoplax adhaerens. Cell Tissue Res. 10.1007/s00441-019-03057-z

Sogabe S, Nakanishi N, Degnan BM (2016) The ontogeny of choanocyte chambers during metamorphosis in the demosponge Amphimedon queenslandica. Evodevo 7:6 10.1186/s13227-016-0042-x [PubMed: 26958337]

Steinmetz PRH. (2019) A non-bilaterian perspective on the development and evolution of animal digestive systems Cell Tissue Res. 10.1007/s00441-019-03075-x

Štrus J, Žnidaršič N, Mrak P, Bogataj U, and Vogt G (2019) Structure, function and development of the digestive system in malacostracan crustaceans and adaptation to different lifestyles. Cell Tissue Res. 10.1007/s00441-019-03056-0

Van-Praët M (1985) Nutrition of Sea Anemones In: Advances in Marine Biology Volume 22 Elsevier, pp 65–99.

Weissenfels N (1976) Bau und Funktion des Süwasserschwamms Ephydatia fluviatilis L. (Porifera). Zoomorphologie 85:73–88. 10.1007/BF00995405