Seminars in Cell & Developmental Biology 36 (2014) 186–193

Contents lists available at ScienceDirect

Seminars in Cell & Developmental Biology

journal homepage: www.elsevier.com/locate/semcdb

Review

Molecular organization and function of invertebrate occluding junctions

Yasushi Izumi[a,*], Mikio Furuse[a,b]

[a] Division of Cell Biology, Department of Physiology and Cell Biology, Graduate School of Medicine, Kobe University, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan
[b] Division of Cerebral Structure, National Institute for Physiological Sciences, Okazaki, Aichi 444-8787, Japan

ARTICLE INFO

Article history:
Available online 17 September 2014

Keywords:
Epithelial cell
Permeability barrier
Occluding junction
Septate junction
Tight junction
Drosophila

ABSTRACT

Septate junctions (SJs) are specialized intercellular junctions that function as permeability barriers to restrict the free diffusion of solutes through the paracellular routes in invertebrate epithelia. SJs are subdivided into several morphological types that vary among different animal phyla. In several phyla, different types of SJ have been described in different epithelia within an individual. Arthropods have two types of SJs: pleated SJs (pSJs) and smooth SJs (sSJs), found in ectodermally and endodermally derived epithelia, respectively. Several lines of *Drosophila* research have identified and characterized a large number of pSJ-associated proteins. Two sSJ-specific proteins have been recently reported. Molecular dissection of SJs in *Drosophila* and animals in other phyla will lead to a better understanding of the functional differences among SJ types and of evolutionary aspects of these permeability barriers.

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* Corresponding author. Tel.: +81 78 382 5807; fax: +81 78 382 5806.
E-mail address: yizumi@med.kobe-u.ac.jp (Y. Izumi).

http://dx.doi.org/10.1016/j.semcdb.2014.09.009
1084-9521/

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1. Introduction

Epithelia isolate the body from the outer environment and separate distinct fluid compartments within the body of metazoans. To accomplish these functions, epithelia possess specialized cell–cell junctions, designated as occluding junctions. These form circumferential intercellular contacts between epithelial cells and restrict the leak of solutes through the paracellular pathway. In vertebrates, tight junctions (TJs) act as occluding junctions (Fig. 1). In TJs, claudin family proteins organize their core structures and regulate their barrier and channel properties [1–4]. In contrast to vertebrates, the epithelial cells of most invertebrate species lack TJs, with a few exceptions, such as tunicates (see Section 5) [5,6]. Instead, they possess different kinds of occluding junctions, generally called septate junctions (SJs) [6,7]. SJs typically form circumferential belts around the apicolateral regions of epithelial cells. In cross-section, the transmission electron microscope shows the parallel plasma membranes between adjacent cells with ladder-like septa spanning the intermembrane space (15–20 nm) (Fig. 1) [6]. The genetic and molecular properties of SJs have been extensively analyzed, particularly in *Drosophila*, and more than 20 SJ-related proteins have been identified and characterized. In this review, we summarize the molecular organization of SJs and mechanisms underlying SJ formation in *Drosophila*.

2. Overview of septate junctions in invertebrates

The morphological features of SJs have been defined using transmission electron microscopy combined with freeze-fracture replicas and lanthanum infiltration. The common characteristic of SJs is an electron-dense ladder-like appearance between adjacent cells. The lowest phylum known to possess SJs is the Porifera. In the calcareous sponge *Sycon ciliatum*, SJs are observed between the spicule-secreting sclerocytes [8]. However, it remains unclear whether sponge SJs act as occluding junctions. Other invertebrate groups in which SJs have been described include coelenterates, platyhelminths, nematodes, annelids, arthropods, mollusks, echinoderms and hemichordates [6,9–19], although some exceptions were noted [20]. In vertebrates, SJ-like structures (termed paranodal SJs) are present at the paranodal regions between neurons and myelinated glial cells. They are thought to form a molecular fence that maintains the segregation of nodal and juxtaparanodal domains [19].

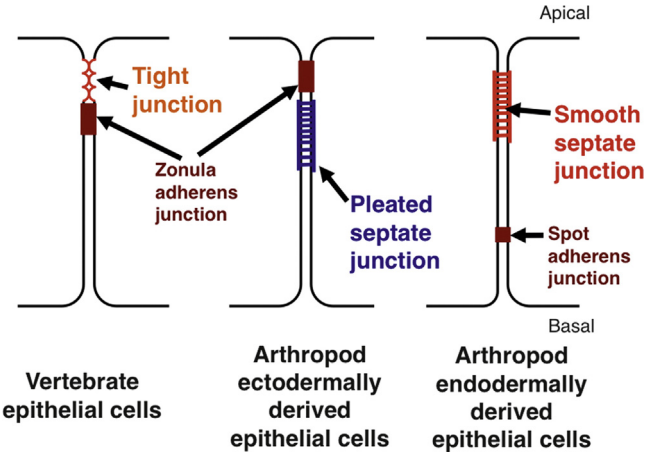

Fig. 1. Schematic drawings of vertebrate TJs and arthropod SJs. TJs are the most apical cell–cell junctions in vertebrate epithelial cells. Pleated SJs are located just basal to the zonula adherens junctions. Smooth SJs are located in the apicolateral membranes. Spot adherens junctions, but not zonula adherens junctions, are formed between adjacent cells in endodermally derived epithelial cells.

Analyses using lanthanum infiltration and freeze-fracture replicas have described a number of morphological variants of SJs among invertebrate species [6], including: straight SJs [21], pleated SJs [22], paired SJs [23], smooth SJs [14], anastomosing SJs [24], scalariform junctions [25], and reticular SJs [26]. Indeed, these morphological differences among SJs have been used in an attempt to draw a phylogenetic tree of invertebrate species [27]. Interestingly, certain species of animals, including coelenterates, arthropods, echinoderms and hemichordates, possess multiple types of SJs in different types of epithelial cells [6,14,27].

3. Septate junctions as permeability barriers

Morphological features of SJs such as the septa between adjacent cells suggest that these junctions provide a paracellular diffusion barrier between the apical and the basolateral compartments of epithelia [28]. Several studies have reported that injected electron-dense solutes, such as lanthanum salts, are unable to penetrate through SJs [29–34]. In addition, genetic studies in *Drosophila* have shown that fluorescent-labeled dextrans (10 kDa) are unable to pass between epithelial cells in wild-type animals but penetrate the paracellular routes in mutants defective for SJ formation (see Section 4) [35]. These observations indicate that SJs regulate the paracellular flow of at least large molecules. In contrast, it has been reported that SJs in Malpighian tubules of *Rhodnius* are readily permeable to a variety of substances with smaller molecules, including sucrose, inulin and polyethylene glycol [36]. Thus, SJs apparently regulate paracellular flow in epithelial cells but the detailed properties of their barrier function remain obscure.

4. Septate junctions in *Drosophila*

Arthropods have two types of SJs: pleated SJs (pSJs) and smooth SJs (sSJs). pSJs are found in ectodermally-derived epithelia, such as the epidermis, foregut, hindgut, salivary glands, trachea and imaginal discs [6,7,14] (Fig. 1). In central and peripheral nerves, pSJs are observed between the glial cells that enwrap neurons, where they function as a blood–brain or blood–nerve barrier that insulates the neurons from the hemolymph [19,37]. sSJs are found in the endodermally-derived epithelia of the midgut and the gastric caeca [6,7,14]. Malpighian tubules and the outer epithelium of the proventriculus also possess sSJs although these organs are ectodermal derivatives. The criteria distinguishing these two types of SJs are the arrangement of the septa visualized in lanthanum-treated membrane preparations and the appearance of intramembrane particles observed in freeze-fracture images. In oblique sections of lanthanum-treated preparations, the septa of pSJs form regular undulating rows but those in sSJs are arranged in regularly spaced parallel lines [6] (Fig. 2A). In freeze-fracture images, the rows of intramembrane particles in pSJs are separated from one another, whereas in sSJs they are fused into ridges [6] (Fig. 2B). The intramembrane particles presumably correspond to transmembrane proteins within the SJs. This structural difference has been