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Review

Cell junction proteins within the cochlea: A review of recent research

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Abstract

Cell–cell junctions in the cochlea are highly complex and well organized. The role of these junctions is to maintain structural and functional integrity of the cochlea. In this review, we describe classification of cell junction-associated proteins identified within the cochlea and provide a brief overview of the function of these proteins in adherent junctions, gap junctions and tight junctions.

Keywords: Cochlea; Cell junction; Junction proteins

Contents

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As a sound sensor in a living organism, the cochlea is a highly sophisticated and complex organ. Its structural integrity at both cellular and tissue levels is critical to ensure normal auditory functions (Slepecky, 1996; Raphael and Altschuler, 2003; Yates, 1995). Cell junctions between sensory cells in the organ of Corti and supporting cells and between supporting cells exist in particular ways to maintain the well-organized structure of the auditory sensor in the three dimensional space, which plays irreplaceable roles in sustaining mechanical connections among cochlear cells, in ensuring the integrity of sensory epithelia and in controlling ion concentrations in the endo- and perilymph (Slepecky, 1996; Müller and Littlewood-Evans, 2001; Tsuprun and Santi, 2002; Edelman, 1986; Schwander et al., 2010; Leonova and Raphael, 1997). There are mainly three types of cell junctions in mammals: i.e. the adherens junction, gap junction and tight junction (Alberts et al., 2008). This review provides a brief summary of functions of these junctions in the cochlea.

1. Adherens junction

Adherens junction refers to the connection to one or multiple lipid-anchored proteins (as well as actins) on the inside of a cell, and with transmembrane adhesion proteins or extracellular matrix of neighboring cells (Alberts et al., 2008). In the cochlea, adherens junction is closely related to physiological processes such as cochlear development, growth of auditory neurons, immune mediation and planar cell alignment.

1.1. Adherens junction and cochlear development

Cadherin is a super family of transmembrane glycoproteins that mediate calcium-dependent intercellular adhesion. It is the main element in mediating adherens junction and is involved in cochlear development. T-cadherin is expressed in the sub-domain in all types of fibroblasts and pillar cells. Expression of E-cadherin opposes that of N-cadherin and both do not overlap T-cadherin expression. E-cadherin expression is positive in all cochlear epithelial cells (including outer hair cells, OHCs) except inner hair cells (IHCs) and the part of the Kolliker's organ in contact with IHCs. During development, E-cadherin is found between OHCs, pillar cells and Deiters cells, responsible for maintaining the distribution and alignment of the reticular lamina (Whitlon, 1993), which is the barrier separating the endo- and perilymph. Cochlear functions depend on its integrity. Expression of N-cadherin is seen in IHCs during development, but never in OHCs. Hensen cells show high levels of E-cadherin expression when differentiating. The β-catenin, which is connected to cadherin, is found in the cell membrane in all epithelial cells, especially in the modiolar extremity of Kolliker's organ, but not in fibroblasts. The polysialylated neuronal cell adhesion molecule (PSA-NCAM) is present around the IHC and may be involved in plasticity of neuron synapses (Simonneau et al., 2003).

The coxsackievirus and adenovirus receptor (CAR) is another type of adhesion proteins and is expressed at high levels in cell junctions of most cochlear cells in newborn mice, but only in supporting cells and stria vascularis cells in adult mice (Excoffon et al., 2006). It is therefore possible that this protein molecule is involved in early stage sensory epithelial differentiation and maturation. Its expression in only the supporting cells and stria vascularis cells in a matured cochlea indicates that these two types of cells may retain potentials of proliferation and differentiation under certain conditions.

1.2. Adherens junction and neuron growth

In the mouse cochlea, the neuronal cell adhesion molecule (NCAM), polysialic acid (PSA), NCAM-L1, E-cadherin, syndecan-1 and tenascin-C are expressed at different levels in different regions and different types of cells, resulting in different attractions among different cells, which lead to variations in micro-environments in different areas in the cochlea that modify the growth of afferent and efferent neurons (Whitlon et al., 1999). In mammal cochleae, a neuronal cell adhesion molecule in the immunoglobulin superfamily, the L1, is capable of regulating the growth of type I spiral ganglion neurons and guides the extension of neuron dendrites toward IHCs and not OHCs (Brand et al., 2013).

1.3. Adherens junction and immune mediation

Glycosylation-dependent cell adhesion molecule-1 (Gly-CAM-1) is found in the lateral wall, tectorial membrane, modiolus, organ of Corti and modiolar veins in the cochlea. It recognizes leukocyte L-selectin and participates in inflammatory responses in epithelial tissues (Kanoh et al., 1999). As a signal receptor, T-Cadherin may be involved in responses to hair cell injuries. Its mRNA expression is higher in the spiral ganglion (SG) and stria vascularis (SV) than in the organ of Corti (OG) (Listyo et al., 2011).

1.4. Adherens junction and planar cell alignment

Adhesion proteins can influence alignment of sensory epithelial cells. The p120-catenin can interact with cellular skeletons to form a molecular spring of structural mechanical significance (Garcia-Anoveros and Duggan, 2007). When the gene for p120-catenin is conditionally knocked out, the dynamic distribution of E-cadherin and N-cadherin will change and planar cell polarity (PCP) will be affected, seen as significant changes in cellular contact and geometry (Chacon-Heszele et al., 2012). Nectin-1 and Nectin-3 are also capable of influencing cochlear cells alignment. They are immunoglobulin-like adhesion molecules expressed in hair cells and supporting cells in mice. Their interaction mediates attachment between these two types of cells, leading to alignment of hair cells and supporting cells in a checkerboard pattern (Togashi et al., 2011).

Also, the Wnt/β-catenin signal pathway regulates the proliferation and differentiation of cochlear IHCs (Jacques et al., 2012). During early stages of cochlear development, inhibitory