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ORIGINAL PAPER

The Significance of Relative Claudin Expression in Odontogenic Tumors

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Abstract

Claudins are integral to the structure and function of tight junctions. Altered claudin expression has been shown to affect disease behavior and patient prognosis in various neoplasms. The objectives of this study were to analyze the claudin-1, -4 and -7 expression in odontogenic tumors and characterize their expression pattern in distinct tumor cell types in relation to the recurrence potential. Sixty-nine cases of odontogenic tumors, including 43 ameloblastomas (AM), 17 adenomatoid odontogenic tumors (AOT), 6 ameloblastic fibromas (AF) and 3 ameloblastic carcinomas (AC) were investigated for claudin-1, -4 and -7 expression immunohistochemically. The staining was analyzed semi-quantitatively and categorized into 4 levels, based on the percentage of positively stained neoplastic epithelial cells. Claudin-1 was expressed in all AOT and AF cases, whereas most AC (66.7%) showed no expression. The claudin-1 staining was moderate-to-intense in the odontogenic epithelium of AF. In contrast, its staining of ameloblast-like cells and stellate reticulum-like cells in AM was weak. Claudin-7 expression was noted in all tumor types studied, while the expression of claudin-4 was limited and mainly localized in the squamous differentiated cells of AM and AC. AM showed significantly higher claudin-4, but lower claudin-7 expression than AOT. In addition, AC showed diminished claudin-1 immunoreactivity, compared to AOT. Low claudin-1 expression in AM was significantly associated with the increased clinical recurrence. The loss of claudin-1 may underlie the locally invasive nature of AM.

Keywords Claudin · Ameloblastoma · Adenomatoid odontogenic tumor · Ameloblastic fibroma · Ameloblastic carcinoma

Introduction

Differentiated epithelial cells are characterized by their ability to form polarity architecture and cell–cell adhesion. These features help create a protective barrier between internal human tissues and surrounding environment. At the most apical portion, tight junctions (zonula occludens) serve this property by regulating the diffusion of ions and molecules along paracellular channels [1]. Emerging studies have shown that tight junction is also involved in the intracellular signaling and regulation of the epithelial cell proliferation, polarity and differentiation [2].

Tight junctions are composed of 3 transmembrane components, i.e., claudins, occludins and junctional adhesion molecules. Claudins are the major transmembrane proteins, inherent to the structure and function of tight junctions. They localize exclusively on tight junctions and form the indispensable backbone of tight junctions by creating intercellular sealing strands. In addition, zona occludens combine with other intracellular membrane proteins to help construct frameworks connecting these transmembrane proteins with the actin cytoskeleton. To date, 27 claudin members are identified in mammals [3]. They show diverse expression pattern among different cell types and tissues. Some claudin members are expressed solely in specific cell or tissue types. Epithelial cells typically express multiple claudins and different claudin combinations influence the tight junction formation. In addition, claudins may interact with other proteins and participate in the cell–cell and cell-extracellular

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