doi:10.1017/S0022215116004904

Free Papers (F866)

ID: 866.2

Inflammatory, invasive and neoplastic features of primary and secondary cholesteatomas: immunohistochemical and histological findings

Presenting Author: **Nadir Yildirim**
Nadir Yildirim[1], Ayşenur Deger[2], Onur Erdogan[3], Sinan Aksoy[3]
[1]*Dumlupinar Universitesi Medical Faculty,* [2]*DPU Medical Faculty Department of Pathology,* [3]*DPU Medical Faculty Department of ORL-HNS*

Learning Objectives: Objective: Etio-pathogenesis of middle ear cholesteatoma has not been wholly understood. Acquired cholesteatomas are classified into epitympanic/primary (PAK) and mesotympanic/secondary (SAK) subtypes. Herewith, we aimed to investigate the expression of multiple inflammatory, invasive and neoplastic markers in cholesteatomas using immunohistochemistry (IHC) and hematoxylene-eosin (H&E) staining with special reference to the PAK and SAK.

Objective: Etio-pathogenesis of middle ear cholesteatoma has not been wholly understood. Acquired cholesteatomas are classified into epitympanic/primary (PAK) and mesotympanic/secondary (SAK) subtypes. Herewith, we aimed to investigate the expression of multiple inflammatory, invasive and neoplastic markers in cholesteatomas using immunohistochemistry (IHC) and hematoxylene-eosin (H&E) staining with special reference to the PAK and SAK.

Material-Method: We statistically compared 74 (33 primary, 41 secondary) cholesteatoma matrices and normal (control) skin samples harvested from operated cholesteatoma patients for 10 different markers within, and between the subgroups using IHC and H&E staining. Evaluating pathologist was blinded.

Results: Statistically, staining scores for IHC markers of Ki67, collagen type-4, Proliferating cell nuclear antigen (PCNA), keratinocyte growth factor (KGF), fibronectin (FN), interleukin1α (IL-1α), tumor necrosis factor-α (TNF-α); and staining with H&E for vascularization and lymphocyte numbers were significantly higher in cholesteatomas than control materials of both subgroups except for collagen type-7. However, no difference in significances was found between the subgroups.

Conclusion: These results indicate that acquired cholesteatoma is pathologically the same invasive, inflammatory and hyperproliferative disease at different locations, irrespective of their different etio-pathology. Non-expression of collagen type-7 in cholesteatoma might be related to its interfacing location in uninvolved part of the basal membrane.

doi:10.1017/S0022215116004928

Free Papers (F866)

ID: 866.4

Regional differences of mouse utricle hair cells proliferation and differentiation and establishment of the planar cell polarity

Presenting Author: **Dongdong Ren**

Dongdong Ren, Xiaoyu Yang, Rui Ma, Xinwei Wang, Xiaoqing Qian, Juanmei Yang, Fanglu Chi
Eye & Ent Hospital of Fudan University

Learning Objectives: Cochlear sensory epithelial cells stop proliferation from the apical turn, while the earliest differentiated cochlear hair cell originates from the basal turn. Up to now, very few studies have been done to characterize the vestibular hair cells proliferation and differentiation. Planar cell polarity (PCP) is a special cell arrangement regularity. Vestibular organ has special cell polarity, with hair cell arrangement closely correlated with the function of vestibule. Whether the PCP establishment has the relationship with vestibular HC differentiation is still unknown .In this study, By collecting the embryonic utricles at the different stages, first we observed the 3D-schematic view of PCP in E18.5 mouse vestibular system, which showed the different PCP in five sensory organs. We choose utricle as an example, we found that the number of Edu/Myosin7a double positive cells peaks at E11.5 in medial extrastriola(MES) and striola zone of utricle. In the lateral extrastriola(LES), the number peaks at E13.5. Besides, at E12.5, P27 and Math1 positive cells were mainly observed in striola. At E13.5, P27 and Math1 positive cells occur in striola and MES. Edu positive cells decrease first in striola and then in MES. Interestingly, the PCP of hair cells stereocilia bundles also established first in the striola and MES region at E13.5. After overexpression of Emx2 in the E13.5 utricle epithelia, PCP of cultured utricle epithelia was disturbed, the orientation of HCs along the supposed LPR(line of polarity reversal) was not opposite, especially the orientation of the hair bundle arranged as a circular. Here we discovered the regional difference in the timing of terminal mitosis of hair cell precursors could account for the difference in their planar cell polarity . PCP of utricle epithelia regional establishment is consistant with HC proliferation and differentiation. Emx2 plays the role of the regional polarity formation in the developing utricle epithelia.

doi:10.1017/S002221511600493X

Free Papers (F866)

ID: 866.5

Comparative Genomic Hybridization Analysis of Patients with Severe Cisplatin Ototoxicity

Presenting Author: **Yüksel Olgun**

Yüksel Olgun[1], Ayşe Banu Demir[2], Zekiye Altun[2], Günay Kırkım[3], Enis Alpin Güneri[3], Safiye Aktaş[2]

[1]Dokuz Eylül University School of Medicine, [2]Dokuz Eylül University Institute of Oncology Department of Basic Oncology, [3]Dokuz Eylül University School of Medicine Department of Otorhinolaryngology

Learning Objectives:

Introduction: Cisplatin (CDDP) is a widely used chemotherapeutic drug with important side-effects, such as ototoxicity. CDDP ototoxicity affects individuals variably, which is mostly due to individual genetic factors. Aim of this study is to analyse the genetic background of the patients in which severe ototoxicity occured.

Methods: 72 children who received CDDP chemotherapy between January 2013 and March 2015 were included in the study. Audiological evaluations were performed before and minimum three months after the therapy. Ototoxicity was evaluated using Muenster, Brock classifications. During routine controls, 5cc of peripheric blood samples were taken into EDTA-coated tubes. Peripheric blood mononuclear cell and subsequent DNA isolations were performed. In order to analyze the genetic background of patients, we performed comparative genomic hybridization(CGH) arrays for 5 patients with the most severe ototoxicity (Grade 3 and 4), among the studied 72 patients. Results were evaluated statistically by using "Agilent CytoGenomics Software".

Results: CGH analysis showed some common genetic differences among evaluated patients. Chr8.p23.1 (Defensin-family genes) deletion was seen in 3 patients. Chr11.q13.2 (NDUFV1) gain was observed among 4 patients. Chr14.q32.33 (ADAM6) amplification, Chr2.p21 (SIX3) amplification and Chr11.p15.5 (H19) gain were common in all patients. Chr20.q13.32 (GNAS) gain was also seen in 3 patients and this chromosomal region was deleted in one patient. Further assessments may be important to understand the roles of these genes in CDDP induced ototoxicity.

Conclusion: In order to minimize the risk for CDDP ototoxicity, identification of genetic differences is of great importance. Further studies on new candidate genes such as Defensin-family genes, ADAM6, SIX3, GNAS, NDUFV1, and H19 should be performed to better understand their effect on CDDP ototoxicity.

doi:10.1017/S0022215116004941

Free Papers (F866)

ID: 866.6

Network analysis of Innate Immune Interaction in Cholesteatoma

Presenting Author: **Anke Leichtle**

Anke Leichtle[1], Karl-Ludwig Bruchhage[2], Holger Sudhoff[3], Barbara Wollenberg[2]

[1]University of Lübeck, Lübeck, Germany, [2]Department of Otorhinoloaryngology, Head and Neck Surgery, University of Lübeck, Lübeck, Germany, [3]Department of Otorhinoloaryngology, Head and Neck Surgery Klinikum Bielefeld Bielefeld, Germany

Learning Objectives: Innate Immunity, Cholesteatoma, Network Analysis, Regulatory Network.

Introduction: The etiopathogenesis of Cholesteatoma is controversial, but it is associated with recurrent, persistent ear infections and bacteria. Thereby the interaction between pathogen susceptibility and innate immunity is relevant. Toll-like (TLRs) and Nod-like receptors (Nods) are known to be important participants in the innate immune response to pathogens at other sites, via elaboration of inflammatory cytokines. We explored the network of Innate Immune Receptor-signalling and cytokine production in cholesteatoma.

Methods: Cholesteatoma and control tissue of the external auditory canal skin (EAS) from patients undergoing surgery were evaluated for innate immune pattern and molecules. Cholesteatoma thickness and cellular infiltration were evaluated histologically. mRNA expression of receptors and downstream molecules were evaluated by microarray, real-time PCR, while protein levels were determined by Immunhistochemistry and bioinformatical network analysis.

Results: A subset of receptors involved and downstream molecules in Innate Immunity such as TLRs, Nods and TNF are expressed in cholesteatoma. NOD2 mRNA and protein, but not TLRs or Nod-receptors were significantly induced compared to control samples of the external auditory canal skin (EAS). Moreover, regulation of genes in an interaction network of the RIPK2 was detected. In addition to NOD2, NLRC4, PYCARD, the downstream molecules IRAK1 and anti-apoptotic regulator CFLAR, showed significant upregulation, whereas SMAD3, a pro-apoptotic inducer, was significantly downregulated.

Conclusions: The network interaction of innate immune regulation is important in the etiopathogenesis and growth of cholesteatoma.

doi:10.1017/S0022215116004953

Endoscopic Ear Surgery: Concept and Technique 2 (V867)

ID: 867.1

Teaching Videos of Endoscopic Middle Ear Anatomy: A Free Educational Resource

Presenting Author: **Alexander Saxby**

Alexander Saxby, Jonathan Kong, Nirmal Patel, Nicholas Jufas

Sydney Endoscopic Ear Surgery Research Group