ENT_BB CONNECTION

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "ENT BB Connection" which contains latest and interesting news.

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Multiple glucocorticoid receptor isoforms have been found in the nasal polyps of people with chronic rhinosinusitis.

A multifactorial inflammatory illness of the nasal and paranasal mucosa, chronic rhinosinusitis (CRS) manifests as a range of symptom clusters.[1] A increasing corpus of research points to significant variation in CRS patients' clinical characteristics and inflamatory endotypes.[2] With the identification of several GR isoforms, the conventional notion that glucocorticosteroid (GC) works via a glucocorticoid receptor (GR) protein has undergone a significant modification. We sought to determine whether numerous GR protein isoforms are expressed in chronic rhinosinusitis with nasal polyps (CRSwNP) and whether distinct endotypes of CRSwNP exhibit different patterns of GR protein isoform expression.[3]

48 people in total, comprising 10 control subjects who underwent septoplasty due to anatomic obstruction and 38 patients with CRSwNP, participated in the study. By using several GR antibodies and western blot analysis, the protein expression of numerous GR isoforms in nasal polyps (NPs) tissue and control mucosae was investigated.

Five bands were identified using both the total GR antibody (PA1-511A) and the GR-specific antibody, including three bands for known proteins (GR-A/B, GR-C, and GR-D) and two bands for unidentified proteins at 67 kDa and 60 kDa (PA1-516) (Fig.1). The CRSwNP group significantly raised GR-D intensity, which was abundant in nasal mucosa (PA1-511A: $P<0.001$ and $P=0.0018$; PA1-516: $P<0.003$ and $P=0.006$, respectively). The NE-CRSwNP group significantly increased GR-D intensity. Additionally, the NE-CRSwNP subgroup had significantly higher median intensities of the newly identified 67 kDa and 60 kDa bands than did the eosinophilic CRSwNP (E-CRSwNP) subgroup, which had median values even lower than the control group.

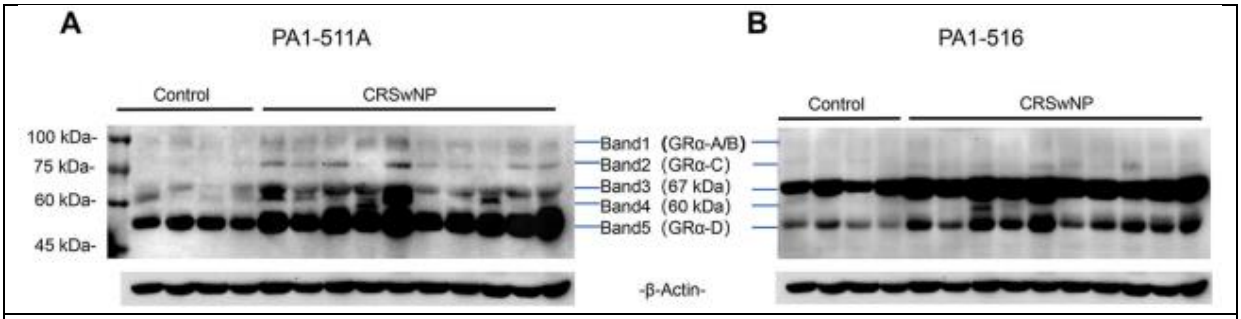

Fig.1 Western blots of representative GR bands in the CRSwNP group and control group. NP tissues and control mucosae were probed with a an anti-total GR antibody (PA1-511A) and b an anti-GRα antibody (PA1-516)

With a combination of various GR antibodies, this study is the first to show the existence of multiple GR isoforms in human nasal tissues. We also discovered that there were differences in the expression profiles of GR isoforms between the E-CRSwNP and NE-CRSwNP subgroups and between the CRSwNP and control groups depending on the illness and tissue.[3]

This study shows that several GR protein isoforms are expressed in nasal tissues. The disease- and tissue-specific expression patterns of GR protein isoforms differed between the CRSwNP and control groups as well as between the E-CRSwNP and NE-CRSwNP subgroups.

References:
1. Vlaminck S, Acke F, Scadding GK, Lambrecht BN, Gevaert P. Pathophysiological and Clinical Aspects of Chronic Rhinosinusitis: Current Concepts. Front Allergy. 2021 Oct 27;2:741788.
2. Saydy N, Moubayed SP, Desrosiers M. Patient perspectives on endoscopic sinus surgery for chronic rhinosinusitis. J Otolaryngol Head Neck Surg. 2021;50(1):34.
3. Shao S, Wang Y, Zhao Y, Xu Y, Wang T, Du K, Bao S, Wang X, Zhang L. Identification of multiple isoforms of glucocorticoid receptor in nasal polyps of patients with chronic rhinosinusitis. J Otolaryngol Head Neck Surg. 2022 Jun 11;51(1):25.

Evoked otoacoustic emissions and a contralateral suppression test are used to evaluate the auditory system in autistic children

The brain can modify the cochlear response thanks to the efferent auditory system, especially through the medial olivocochlear system (MOC). Studies on humans have shown that otoacoustic emissions (OAE) are suppressed in the presence of ipsilateral (IAS) and/or contralateral (CAS) acoustic stimulation, likely because the medial olivocochlear reflex is activated (MOCR).[1] A group of complex, rapidly expanding neurodevelopmental and behavioural problems are known as autism spectrum disorders (ASDs).[2] Children with autism spectrum disorders may also experience impaired hearing, ear discomfort, and auditory hypersensitivity. This study measured evoked OAEs and contralateral OAE suppression (CLS) to assess the cochlea, MOS, and brainstem function in autistic children.[3]

In all, 65 children participated in the study. 55 children between the ages of 6 and 13 who had normal hearing and neurodevelopment but had been labelled as autism made up the study group. Ten healthy children (aged 6 to 12) from the control group were in good health and had normal hearing. Cochlear activity was measured using transient-evoked OAE measurements, while MOS efferent activity was measured using CLS values. All patients' left and right ears were examined for transient-evoked OAEs (TEOAEs) and CLS of TEOAE. Spontaneous, transient, and dP ILO292 were assessed in a silent environment.

In the research and control groups, the average age was 9.1 years (range: 6-13 and 6-12 years, respectively). Regarding age, there was no discernible difference between the groups (P >.05). The OAE and CLS values for the right ear are shown in (Table 1 and Figure 1). The

study found no statistically significant differences between these values for the right ear for the study group (P >.05). The OAE values were, however, substantially greater than the CLS values for the left ear (P< .05). The OAE values for the control group's left and right ears were greater than the CLS values for both ears (P< .05.)

Table 1: Left and Right Ear OAE and CLS Values for All Patients.			
Side of ear	OAE	CLS	P
Right ear	15.79	14.59	.211
Left ear	14.56	14.10	.002
Right ear (control group)	14.91	14.43	<.001
Left ear (control group)	14.56	14.08	.008

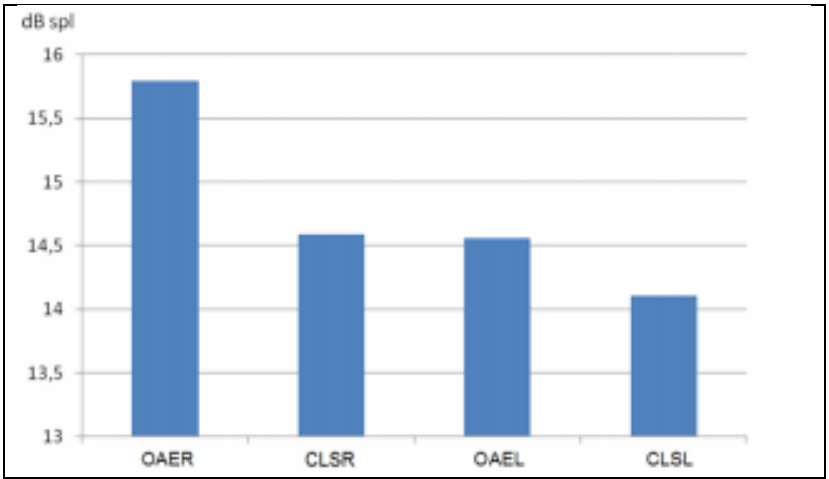

Fig. 1: Left and right ear OAE and CLS values for the study group. CLS indicates contralateral suppression; OAE, otoacoustic emission.

In this study, evoked OAE and noninvasive CLS tests were used to assess the cochlea, MOS, and brainstem function in autistic children. We found no difference between the study and control groups' average ages. The OAE values were substantially greater than the CLS values in the left ear (P< .05).

In conclusion, MOS performs better in the right ear than the left in autistic youngsters with normal hearing. The disparities between the left and right ears and peripheral auditory lateralization, in our opinion, may be caused by asymmetries.

References:

1. Miranda FA, Aguilar-Vidal E. Magnitude of the contralateral efferent olivocochlear effect as a function of the frequency. J Otol. 2022 Apr;17(2):67-71

2. Bharath R, Moodithaya SS, Halahalli H, Undaru SB, Nallilu SK, Mirajkar AM. Evaluation of sympathetic sudomotor responses to auditory stimuli in children with autism spectrum disorders. Indian J Psychiatry. 2020 Sep-Oct;62(5):494-500.
3. Aslan E, Guzel I, Caypinar B, Samanci B, Oysu C. Evaluation of the Auditory System in Autistic Children Using Evoked Otoacoustic Emissions and a Contralateral Suppression Test. Ear Nose Throat J. 2022 Feb 18:145561319838934.

Prediction of survival rate in Head and Neck Squamous cell carcinoma patients with Nine Gene Signature and Nomogram

Worldwide, Head and neck squamous cell carcinoma (HNSCC) stands as the sixth commonest cancer[1]. Even though the advances in treatment the overall 5-year survival is still under 50%[2]. Various studies show that gene signatures can predict the prognosis of patients with HNSCC and Gene expression datasets are characterized by high dimensionality, small sample sizes, and sample imbalance. The tumour microenvironment (TME) of HNSCC harbours transformed cells, immune cells, and stromal cellular elements and may have adverse or beneficial consequences[3]. The TME can promote tumour growth and progression through the immune cells which are affected easily. In this study, gene expression profiles of HNSCC TME-related genes were obtained and utilized to create a robust prognostic model and establish a prognostic nomogram expression data and clinical data.

A total of 213 samples (199 HNSCC tissue samples and 14 normal tissue samples) of HNSCC gene expression data were downloaded. To retrieve HNSCC gene expression data and clinical data The Cancer Genome Atlas (TCGA) was used. A total of 511 patients TCGA HNSCC clinical data was also downloaded. Almost all the clinical characteristics, including survival status, survival outcomes, age, gender, grade, Tumour Node Metastases (TNM) classification, and stage, were all collected. To externally validate the reliability of the nine-gene signature GSE16076 dataset with 270 samples (including gene expression data and clinical data) from the Gene Expression Omnibus (GEO) database was downloaded. To extract TME-related genes Intersecting analysis was adopted between the gene expression matrix of HNSCC patients from TCGA database and Non negative matrix factorization (NMF) clustering algorithm was applied to the TME-related genes to categorize HNSCC patients by using the "NMF" R package.

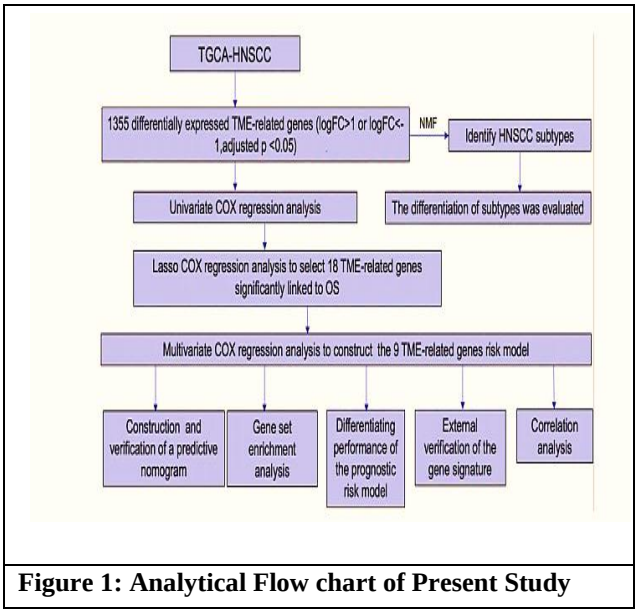

Figure 1: Analytical Flow chart of Present Study

Univariate Cox regression analysis, LASSO Cox regression analysis, and multivariate Cox regression analysis were used to analyse TME-related prognosis genes. To construct a prognostic risk model and a prognostic gene signature they selected the nine genes and also nomogram was entrenched by using clinical parameters and risk score, as following the data Figure 1 describes the analytical flow of the study.

A total of 193 patients who were involved in the survival analysis and were randomly assigned into the training set and testing set. Training set data has been retrieved using the "survival" R package and subjected to univariate Cox regression analysis, which detected 18 TME- related genes. To establish the prognostic risk model nine genes (GTSE1, LRRN4CL, CRYAB, SHOX2, ASNS, KRT23, ANGPT2, HOXA9, and CARD11) were determined by using multivariate Cox regression analysis. Nine genes and their corresponding regression coefficients were used to calculate risk scores for each sample using the formula.

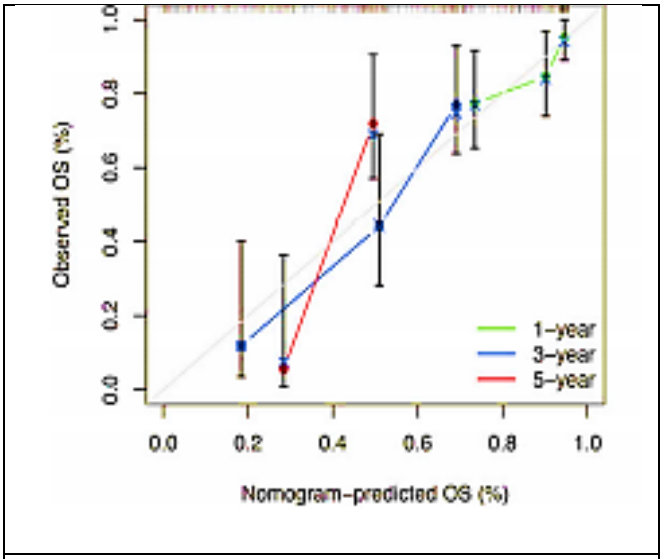

Figure 2: Internal validation of Nomogram

Patients with risk scores above the median scores were assigned to the high-risk group, whereas those with scores below the median risk score were assigned to the low-risk group Moreover, HNSCC patients in the high-risk group showed significantly poorer OS than those in the low-risk group.

For predicting the 1-, 3-, and 5-year OS for patients with HNSCC Seven independent prognostic factors were used to construct a nomogram. As shown in the Fig: 2 calibration curves showed that the nomogram accurately predicted the 1-, 3-, and 5-year OS. The estimated probability ROC curves were used to evaluate the sensitivity and specificity of the nine-gene signature in determining the survival. Nine-gene signature considered as reliable and stable based on the results of time-independent ROC analysis and survival analysis. Moreover, the nomogram showed better performance than conventional clinical parameters, especially in predicting short term (1-year or 3-year) survival.

Clinically, because of its high heterogeneity HNSCC is difficult to treat, so recent studies describes that signatures based on aberrantly expressed genes can predict cancer prognosis[4] As ASNS gene plays a major role in detecting the prognosis of HNSCC, as its high expression promotes growth, metastasis, and chemo resistance in neoplastic cells and low

expression of ASNS impaired metabolic function in specified cancer models as it plays major role in prognosis of HNSCC[5]. ANGPT2 is associated with shorter OS in HNSCC[6].
As CARM1 silencing suppresses tumour invasion in oral squamous cell carcinoma cells effectively. For predicting the prognosis of HNSCC, use of nine-gene signature not reported previously. Based on the gene expression profile, risk score of nine prognostic genes was determined. As this gene signature is affordable and eliminates the requirement for whole-genome sequencing, can be used in various clinical centers. Especially in predicting the short term survival, nomogram has showed good performance when compared to the clinical parameters.

This study established and verified a TME-related nine-gene signature and nomogram, which might have the potential to act as new therapeutic targets for HNSCC patients. The nine gene signature and nomogram can be used to guide clinical decisions regarding HNSCC treatment

References:

1. Yang F, Zhou LQ, Yang HW, Wang YJ. Nine-gene signature and nomogram for predicting survival in patients with head and neck squamous cell carcinoma. Front Genet. 2022 Aug 24;13:927614
2. Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE, Grandis JR. Head and neck squamous cell carcinoma. Nat Rev Dis Primers. 2020 Nov 26; 6(1):92.
3. Nieto MA, Huang RY, Jackson RA, Thiery JP. EMT: 2016. Cell. 2016 Jun 30;166(1):21-45.
4. Ferris RL. Immunology and Immunotherapy of Head and Neck Cancer. J Clin Oncol. 2015 Oct 10;33(29):3293-304.
5. Chiu, M., Taurino, G., Bianchi, M. G., Kilberg, M. S., and Bussolati, O. Asparagine synthetase in cancer: Beyond acute lymphoblastic leukemia. Front. Oncol. 2019; 9, 1480.
6. Arends R, Guo X, Baverel PG, González-García I, Xie J, Morsli N, Yovine A, Roskos LK. Association of circulating protein biomarkers with clinical outcomes of durvalumab in head and neck squamous cell carcinoma. Oncoimmunology. 2021 Mar 17;10(1):1898104.
7. Lyu, X. Y., Shui, Y. S., Wang, L., Jiang, Q. S., Meng, L. X., Zhan, H. Y., et al.. WDR5 promotes the tumorigenesis of oral squamous cell carcinoma via CARM1/β-catenin axis. Odontology. 2022;110 (1), 138–147.

A Case Report and Literature Review on Patient with Otitis externa

Otitis externa (OE) is an inflammation of the external auditory canal that can be either infectious or non-infectious. In some circumstances, inflammation may spread to the tragus or pinna of the outer ear. As it frequently happens in the summer and in tropical areas, and as having retained water in the ears increases the risk for it, it is also known as swimmer's ear.[1] In this study, a 20-year-old patient's case of swimmer's ear is presented.[2]

Case Presentation:

A patient, age 20, complained of left ear ache for one day when he arrived at the hospital. When the left ear is scratched with a finger because it itches, pain is felt in the left ear as well as behind the ear. The patient had previously gone through a swimming test as part of the

TNI admission test. He felt that there was still cotton in his ear after cleaning it. The patient also said that her hearing had diminished and that she had yellow ear discharge that stank when she cleaned it. a physical examination that falls within the norm. When the patient's left ear was examined locally, discharge, hyperemia, and a furuncle were discovered. Tympanic membrane testing is not possible for the patient. The patient was first treated by cleaning his ears with PZ 25cc. He was then given prescriptions for antibiotic cefadroxil 500mg 2x1, anti-inflammatory diclofenac sodium 25mg 1x1, and analgesic otopain ear drop 3 ddgtt1 left ear.

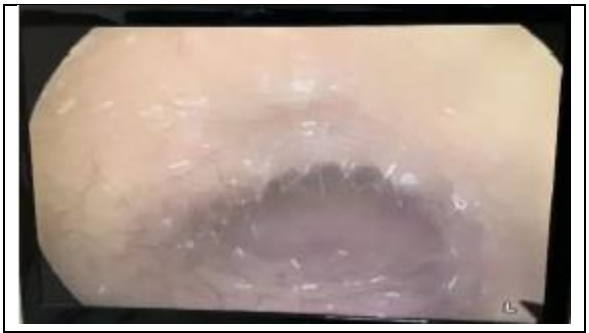

Fig.1: Left ear of a patient with circumscribed otitis externa

Following loss of the ear canal's protective squamous epithelial layer, a collection of acute or chronic inflammatory illnesses of the external auditory canal and auricle are referred to as otitis externa (OE). The cause of the inflammation may have been infectious (caused by bacteria, fungus, and viruses) or allergic (reactive). Otitis externa (OE) is a frequent infectious illness for which patients visit the ear, with an annual incidence rate of 1.2%.[3]

Patients with OE frequently experience earache, itching, auditory fullness, or hearing loss, and painful lymphadenopathy is a less frequent symptom. Patients frequently mention ear discharge as well. Atypical organisms, illness that is resistant to treatment, and antibiotic choices all make OE a clinical challenge. When treating OE patients, it's important to take into account a number of warning signs.[4]

Swimmer's ear, also known as otitis externa (OE), is an ear inflammation brought on by bacteria, fungus, or clusters of these organisms that thrive in moist environments. Using anamnesis, a local status evaluation, and assistance, to make a diagnosis. Pharmacology and spooling techniques can be used to manage OE and clean the ear.

References:

1. Medina-Blasini Y, Sharman T. Otitis Externa. [Updated 2022 Apr 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
2. Amanda Muhamad Bauzir, Arsiyoga Bimo Fadhyki, Muhammad Hanun Mahyuddin, & Ulaa Haniifah.. Swimmer’s Ear: A Case Report and Literature Review . *Asian Australasian Neuro and Health Science Journal (AANHS-J)*, 2022; *4*(2).

3. Aboutalebian S, Ahmadikia K, Fakhim H, Chabavizadeh J, Okhovat A, Nikaeen M, Mirhendi H. Direct Detection and Identification of the Most Common Bacteria and Fungi Causing Otitis Externa by a Stepwise Multiplex PCR. Front Cell Infect Microbiol. 2021 Mar 25;11:644060.
4. Khatri H, Huang J, Guazzo E, Bond C. Review article: Topical antibiotic treatments for acute otitis externa: Emergency care guidelines from an ear, nose and throat perspective. Emerg Med Australas. 2021 Dec;33(6):961-965.