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Scope of Viral Related Cancer – NPC (Nasopharyngeal Carcinoma)

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ABSTRACT
The cancer known as nasopharyngeal carcinoma (NPC) is rare throughout the world, but it is endemic in a few places, such as Southern China, Southeast Asia and North Africa. It is yet unknown what causes this exceptional geographic spread. Undifferentiated NPC has been related to Epstein-Barr virus (EBV) infection, yet EBV by itself is inadequate to bring about this cancer. The interaction of EBV with additional co-factors, such as environmental risk factors or genetic susceptibility, may contribute to the development of NPC carcinogenesis. Patients with early-stage NPC have a much lower chance of survival than those with late-stage NPC. EBV-related biomarkers have been employed for early identification and screening for NPC in a few high-incidence locations because of the close links between EBV infection and NPC risk. In this proposal latest updates are discussed about the functional, gene expression and proteomics studies.

I. INTRODUCTION

One of the cancer related to the Epstein-Barr virus (EBV) is nasopharyngeal carcinoma (NPC), which has a well-defined geographic distribution (1).Although several environmental exposures, such as consuming a lot of salt-preserved fish, smoking, and not eating enough fresh fruit and vegetables, are generally acknowledged as being risk factors for NPC (1,2).Since the 1970s, a few high-incidence areas in Southern China have used antibodies against EBV for early diagnosis and screening for NPC despite the disease's uncertain origin. In comparison to the conventional approach, recent studies have shown that a combination of IgA antibodies against the Epstein-Barr nuclear antigen 1 (EBNA1/IgA) and VCA/IgA assessed by enzyme-linked immunosorbent test (ELISA) has superior sensitivity, specificity, and positive predictive value.

FUNCTIONS

A rare sort cancer that affects the portion of the throat that connects the back of the nose to the back of the mouth is called nasopharyngeal carcinoma (the pharynx).It's important to distinguish between nasopharyngeal cancer and other throat-related cancers like laryngeal and oesophageal cancer.

Today's conventional treatment plan involves combining radiotherapy and chemotherapy. The best chemotherapy and radiation schedules, however, have not yet been identified (3). The low survival rate and significant incidence require the development of novel therapeutic strategies. Immunotherapy and treatment approaches that target particular molecules may enhance NPC outcomes (4). However, the lack of standard cell and animal models for monitoring genes impacting tumor growth and metastasis and the incomplete understanding of the genes connected to NPC formation restrict the development of novel therapies.

When compared to CNE-2 cells, NPC cell line S18, a subclone that was derived from human NPC undifferentiated cells (CNE-2 cells), demonstrates simple migration and invasion. Additionally, the S18 xenografted cancer model retains a growth rate that is comparable to the in situ cancer and has a large metastatic potential (5).

For the research of target genes in NPC, regulation of target gene expression in the S18 cell line is thought to be of major value. In eucaryon, the Tet-Off Advanced System is a highly developed instrument for gene regulation. The response element containing the target gene, such as pTRE-Tight-X, and the doxycycline-dependent regulator, such as pTet-Off Advanced, are the two essential parts of the Tet-Off Advanced system. A double-stable cell line with integrated copies of the regulator and responder plasmids is the goal of the Tet-Off Advanced system (6, 7).

Doxycycline's presence in the culture media keeps the transcription of the target gene in this cell line in the "off" state, while its removal may cause transcription activation. Even though this approach seems to be helpful, additional research is necessary to develop an inducible system. Furthermore, it is known that different cell

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types have an impact on how well doxycycline-controlled gene induction works. To the best of our knowledge, no work has examined the possibility of this method demonstrating high efficacy of target gene transcriptional stimulation in NPC cell lines. A NPC S18 Tet-Off cell line was created for the current work, and it successfully expressed a doxycycline-dependent regulator and had high transcriptional activity of target genes with a low background (8, 9).

GENE EXPRESSION

Most of the gene expression profile in NPC cells is unknown.There are a total of 42 genes that have been found to express themselves in both benign and malignant NPE cells. Malignant NPE cells overexpressed thirteen of these genes. These include the nuclear factor (NF90), the FOS-related antigen 1 (FRA-1), the cytoplasmic dynein light chain (HDLC1), the replication factor C (RFC1), the nucleoside diphosphate kinase B, the UV excision repair protein (RAD23A), the insulin-like growth factor receptor II, the transcription initiation factor TFIID subunit (TAFII31), the growth factor receptor-bound protein 2 (GRB2), the In contrast, malignant NPE cells showed reduced expression of nine genes.Calgranulins A and B, neutrophil activating protein (ENA-78), heat shock protein 27, integrin beta-1 and beta-4, cyclin-dependent kinase inhibitor 1A (p21), interleukin-8, and tyrosine protein kinase receptor are among them (RET). RT-PCR research supported the differential expression of calgranulin A, calgranulin B, ENA-78, FRA-1, and NF90 in benign and malignant nasopharyngeal epithelial cells (10).

PROTEOMICS STUDIES IN NASOPHARYNGEAL CARCINOMA:

The term "proteome" refers to the complete set of proteins that make up a genome, where a genome is a collection of genetic material that can be expressed as proteins (11).Proteomics fundamental and developmental phases depend on methods for separating and identifying proteins. In terms of technologies for protein separation and visualization, isotope-coded affinity tags (ICATs), stable isotope labelling of amino acids (SILAC), differential gel electrophoresis (DIGE), one-dimensional polyacrylamide gel electrophoresis (1-DE), two-dimensional polyacrylamide gel electrophoresis (2-DE), and isobaric tags for relative absolute quantitation (iTRAQ) are all gradually evolving and expanding. Technologies for protein identification include surface-enhanced laser desorption ionization time of flight mass spectrometry (SELDI-TOF MS), matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS), and liquid chromatography-electrospray ionization-mass spectrometry (12).

Even though large nasopharyngeal cancer (NPC) is typically successfully treated with radiotherapy, about 20% of patients still develop radioresistance. To better the situation, it would be extremely helpful to identify blood or biopsy biomarkers that can forecast the therapeutic response to radioresistance and that can diagnose NPC in its early phases. In NPC, proteomics is frequently used to compare differentially expressed proteins and look for biomarkers. The highest protein ranked is keratin, which is followed by annexin, heat shock protein, 14-3-3, nm-23 protein, cathepsin, heterogeneous nuclear ribonucleoproteins, enolase, triosephosphate isomerase, stathmin, prohibitin, and vimentin. This rating suggests that these proteins may be associated with NPCs and may be useful for further research.

NASOPHARYNGEAL CARCINOMA (NPC) CELL LINE

Poor differentiation and high metastasis are characteristics of the HNE1 (poorly differentiated nasopharyngeal carcinomas cell line), HNE2, HNE3, CNE-1 (human highly differentiated NPC cell line), CNE-2 (human poorly differentiated NPC cell line), 5-8F (high metastatic potential), 6-10B (without metastatic potential), S-18 (high-metastatic), NPC-TW02 (derived from a keratinizing carcinoma), The nasopharyngeal carcinoma cell lines include NPC-TW04 (derived from an undifferentiated carcinoma), NPC-BM1 (derived from a bone marrow biopsy of a female Taiwanese patient with NPC), HONE-1 (poorly differentiated nasopharyngeal carcinomas), HK1 (well-differentiated squamous nasopharyngeal carcinomas),NP69 is an usual nasopharyngeal cell line, but ATCC: HTB-43 and C666-1 are NPC cell lines.

A cell line (C666-1) derived from nasopharyngeal cancer that is not differentiated has been created (NPC). In extended cultures, this cell line continuously maintains Epstein-Barr virus (EBV). C666-1 is a subclone of its parent cell line, C666, which was created from a southern Chinese NPC xenograft. It lacks contact inhibition and develops as an adherent culture. Furthermore, it causes tumors in athymic nude mice. EBV-encoded

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RNAs are regularly expressed by the cells, and cytokeratin, an epithelial marker, is positively stained. Additionally, they exhibit the EBV latency II pattern because they express the EBNA1 protein, LMP1 transcript, and LMP2 transcript. The latent membrane protein 1 gene exhibits a 30-bp deletion at the carboxyl terminus and the virus genotype is EBV-1, which is consistent with observations in southern Chinese NPC tumors. A sub-diploid condition with a chromosomal modal number of 45 was discovered by cytogenetic investigation. Among NPC cell lines, C666-1 is distinctive because it contains EBV. Given that the majority of primary NPC biopsies from Chinese patients show the viral latency pattern and genotype, these cells may be an effective research tool (13).

II. CONCLUSION:

Due to significant advancements in diagnosis, staging, and treatment, the prognosis for NPC has significantly improved over the past few decades. Radiotherapy and chemotherapy control is no longer a major obstacle in the majority of cases due to modern care, and distant metastasis has taken over as the main cause of failure. There are still unanswered questions about improving risk classification, selecting the best radiotherapy volume management algorithms, and ordering chemoradiation combinations. Currently, research is being done on the applications of immunotherapy and particle treatment (such as protons) in the management of NPC. The clinical elements of NPC management in terms of diagnosis, staging, treatment, and disease surveillance are presented in detail, along with potential future tactics to boost the therapeutic ratio.

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