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HEAD AND NECK SQUAMOUS CELL CARCINOMA CELL LINES: ESTABLISHED MODELS AND RATIONALE FOR SELECTION

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Abstract: *Background.* Head and neck squamous cell carcinoma (HNSCC) cell lines are important preclinical models in the search for novel and targeted therapies to treat head and neck cancer. Unlike many other cancer types, a wide variety of primary and metastatic HNSCC cell lines are available. An easily accessible guide that organizes important characteristics of HNSCC cell lines would be valuable for the selection of appropriate HNSCC cell lines for in vitro or in vivo studies.

Methods. A literature search was performed.

Results. Cell growth and culture parameters from HNSCC cell lines were catalogued into tables or lists of selected characteristics. Methods for establishing cancer cell lines and basic cell culture maintenance techniques were reviewed.

Conclusions. A compendium of HNSCC cell line characteristics is useful for organizing the accumulating information regarding cell line characteristics to assist investigators with the development of appropriate preclinical models. © 2006 Wiley Periodicals, Inc. *Head Neck* **29:** 163–188, 2007

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Head and neck cancers are the eighth most common tumor in the world, accounting for 390,000 new cases of cancer in 2000.[1] In the United States, there are approximately 30,000 new cases of head and neck cancer each year and 8,000 related deaths.[2] Head and neck squamous cell carcinoma (HNSCC) accounts for over 90% of all head and neck cancers.[3] Unfortunately, the mortality rates for this disease have not improved in the past 40 years despite advances in the delivery of treatment and in surgical reconstruction. Patients diagnosed with HNSCC in the United States have

a 60% mortality rate even with standard therapy including radiation, surgery, and/or chemotherapy.[4] Five-year survival is only 40%, primarily because of invasive spread and regional metastasis.[5] Head and neck cancers consistently metastasize to the cervical lymph nodes before spreading to distant sites, such as the lung and liver. Current research is focused on understanding the molecular mechanisms of HNSCC development and progression to facilitate the design of novel therapies that may improve survival.

Immortalized cell lines derived from HNSCC tumors have been an invaluable tool for researchers investigating detailed molecular, biochemical, genetic, and immunological properties of head and neck cancer. Advantages of using cell culture include sample homogeneity, cost, and the avoidance of legal and ethical issues associated with animal experimentation.[6] HNSCC cell lines such as Hep2, Hep3, and KB were some of the first HNSCC tumor cell lines to be developed as early as the 1950s.[7] Establishing HNSCC cell lines has proven challenging. Obstacles include fibroblast overgrowth, long quiescent periods before the cells can be subcultured, and the dependence on feeder layers in primary and secondary cultures.[7–9] With technical improvements, such as the use of complement-mediated lysis to selectively deplete fibroblasts, mitomycin C-treated mouse 3T3 fibroblast feeder layers, and explant outgrowth followed by differential trypsinization, successful permanent culture of HNSCC cell lines has become more feasible.[9–11] In fact, more than 300 reported HNSCC cell lines have been established compared with approximately 70, 60, and 10 cell lines derived from breast, colon, and prostate cancers, respectively.[12–14]

ESTABLISHMENT OF HNSCC TUMOR CELL LINE

The most popular method for establishing a new HNSCC cell line is called the explant culture method.[15] Establishing a new cancer cell line depends on several factors, with the most important being the method of obtaining the specimen. Surgically removing fresh tumor tissue under aseptic conditions specifically for laboratory use from non-necrotic and uninfected areas greatly increases the success rate of a long-term culture.[16] The fresh specimen may be treated with a triple antibiotic solution consisting of penicillin, streptomycin, and amphotericin B. Minced tumor fragments are grown in minimal culture medium supplemented with amino acids and serum. As the epithelial cells are growing, fibroblasts are routinely removed either with a cell scraper or by differential trypsinization. Differential trypsinization involves adding trypsin to dislodge the fibroblasts under visualization with an inverted microscope and blocking the trypsin activity with serum-containing medium before the epithelial cells detach. An alternative method using a feeder layer was described by Rheinwald and Beckett.[9] Instead of placing minced tumor fragments into culture flasks with medium, the feeder layer method uses culture flasks that contain mitomycin C-treated 3T3 mouse-fibroblast feeder cell monolayers. The feeder cells and fibroblasts are then removed with EDTA inoculations and vigorous pipetting.

CANCER CELL LINE MAINTENANCE

For cancer cells to survive and grow in culture, the in vitro environment must be carefully maintained. Three cell culture conditions that influence tumor cell growth will be discussed: culture medium, culture substrate, and physiochemical variables. Nutrition for the cells is supplied by the medium, either with or without serum. The medium contains amino acids, glucose, vitamins, and salts that are necessary to support cellular functions and cell synthesis. More often than not, serum, a chemically undefined mixture of hormones, growth factors, lipids, transport proteins, enzyme cofactors, and attachment factors, is added to culture medium to promote cell growth. The serum is isolated by removing the supernatant from clotted blood, usually from a calf or a fetal bovine source because of its high content of embryonic growth factors.[17] One needs to weigh the benefits and disadvantages of adding or withholding serum from medium. The major benefit from adding serum is that the proteins and factors in the serum promote faster tumor cell growth; however, these factors and proteins are relatively expensive and not well-defined. They could potentially interfere with experiments that study the effects of specific exogenous growth factors. Additionally, the cell-to-surface interaction is important for cell proliferation. Cancer cell cultures are usually grown as monolayers on polystyrene plastic; however, there are some exceptions, such as the multicellular tumor spheroid and the soft agar models. Tumor cells lose the requirement for anchorage-dependent growth, enabling some cell lines to grow as 3-dimensional spheroids in suspension culture or as suspensions on top of an

agar medium. These 2 models, which will be discussed later in this review, may reflect in vivo behavior more accurately and are used to investigate specific tumor cell characteristics such as drug response or metastatic potential. Finally, physiochemical variables, such as the CO_2 concentration and temperature, need to be maintained within certain limits for optimal cell growth. For human cancer cell lines, the optimal temperature is 37°C and the preferred CO_2 atmosphere is 5%.[18]

Once the conditions for cancer cell culture growth are established, it is important to routinely examine the cell cultures both macroscopically and microscopically for cell morphology, cell density, and the presence of contaminants. Macroscopically, the color and turbidity of the culture medium can describe the cell density or presence of microbiological contaminants. For example, the culture medium often turns from pink to yellow when the cells in culture have depleted the nutrients in the medium. Cloudy culture medium often indicates the presence of bacteria or fungi in the culture. Microscopically, it is important to check for signs of cell deterioration such as granularity around the nucleus and cytoplasmic vacuolation. The interval between changing medium and subculturing cells depends on the rate of growth or metabolism of the cancer cells; cultures that grow more rapidly require more frequent changes. When cells occupy the entire surface of a flask, the monolayer culture is considered confluent, and the cells need to be subcultured to reduce the cell density to a level where the cells can achieve optimal growth. Subculturing cells requires the use of proteolytic enzymes such as trypsin (0.01–0.5%) and/or 1 m*M* EDTA to break the cell-to-cell and cell-to-substrate interactions, thereby releasing the cells from the monolayer culture into single cell suspensions. These single cell suspensions can be used for future passages, for cryopreservation, or for setting up experiments.

There is a constant risk of contaminating cell cultures with either microbes or different cancer cell lines. Most of this discussion will address microbial contamination (bacteria, fungus, and mycoplasma) and the methods for monitoring and treating them. Bacterial or fungal contamination is often noticed macroscopically as cloudiness in the medium, fuzzy fungal balls, or microscopically as fine granules. Toxic contamination can cause cultured cells to die and slough off the plate surface, often seen as significant movement under low power. Antibiotics, such as penicillin and streptomycin, may be used to treat unique or irreplaceable cultures that have been contaminated; otherwise, it is recommended that the contaminated cultures be discarded. The concern with using antibiotics prophylactically is developing a source of drug-resistant strains of bacteria that can chronically contaminate the cultures. Mycoplasma are small prokaryotes whose presence in cell cultures cannot be noticed macroscopically or microscopically. Often, these microbes grow insidiously and do not kill the host cells. Despite no apparent influence on cultured cell growth or behavior, the presence of mycoplasma may indeed alter any parameter measured in cell culture or in experimental investigations.[19,20] By depriving the cultured cells of medium components and degrading specific amino acids, mycoplasma can initiate a range of effects such as altering signal transduction, cytokine and growth factor expression, cancer cell growth, and cell membrane composition.[20] A popular choice for detecting mycoplasma contamination is with the use of polymerase chain reaction technology to detect mycoplasma-specific sequences. It is a sensitive and specific option for routinely screening growing cell lines or for testing cell lines newly introduced in the laboratory. To salvage irreplaceable cell lines, three groups of antibiotics (tetracycline, macrolides, quinolones) are effective in treating mycoplasma infections.[20]

CHARACTERISTICS OF HNSCC CELL LINES

The large number of available HNSCC cell lines underscores the importance of categorizing tumor cell line characteristics to help researchers select a cell line that best suits their needs. This review has organized HNSCC cell lines into practical and useful Appendix tables based upon important characteristics. More detailed information regarding specific cell lines and models can be found in the primary references.

Tumor Cell Line Name and Patient Demographics. Appendix Table A1 includes general characteristics and procurement information, such as tumor cell line name, patient data, and TNM stage. The cell lines that are available from the American Type Culture Collection (ATCC) are noted. The table also provides primary references for the cell lines and additional references focused upon chromosomal and molecular genetic characteristics. The genetics references are not intended

to be exhaustive, but provide researchers a starting point for further investigation.

HNSCC usually arises in patients with a history of tobacco and/or alcohol use, suggesting that alcohol and the carcinogens found in tobacco synergistically enhance the development of mutations responsible for HNSCC. Furthermore, areas of the upper aerodigestive tract, which are exposed to the highest levels of carcinogens in smokers, also experience high frequencies of HNSCC, further suggesting that changes at the chromosomal level lead to tumorigenesis.[21,22] As further evidence of the genetic basis for HNSCC, other malignancies such as esophageal and lung cancers, which share a common carcinogenic association to tobacco, have demonstrated deletions in chromosome 3p.[23–30] In fact, Cowan et al observed that 6 of 10 HNSCC cell lines demonstrated deletions in regions of chromosome 3p that contain tumor suppressor genes.[29,31] Other studies investigating chromosomal aberrations have reported 11q13 amplification in 20% to 50% of HNSCC cases and its association with poor clinical prognosis and increased metastasis.[32–34] The 11q13 locus contains genes that code for cyclin D1, 2 members of the fibroblast growth factor family, and cortactin. Overexpression of cyclin D1 and cortactin may play a role in HNSCC tumor progression.[29,35–38] Mutations of the *TP53* tumor suppressor gene are a well-recognized step in carcinogenesis. Specific *TP53* genetic alterations in HNSCC cell lines have been characterized (Appendix Table A2). Chromosomal alterations and instability enable the multistep process of genetic changes in HNSCC.[29,39–41] Whether the disruption is a loss of function of tumor suppressor genes or overexpression of oncogenes, or an alteration of chromosomal constitution, genetic changes are at the foundation of the series of changes that lead to rapid cell growth, tumor proliferation, and metastatic invasion. The chromosomal and genetic heterogeneity present in the primary tumor remain evident in cell lines despite continued passage in vitro. Further investigations to elucidate the relationship between genetic alterations at the cytogenetic and molecular level with tumor behavior and clinical outcome will continue to be critical.[29,31]

Site of Origin of Tumor Cell Lines. By organizing cell lines according to the site of origin, site-specific characteristics of HNSCC may be investigated with the possibility of developing more specific and targeted therapies. In the past, head and neck cancer has been studied as an aggregate of tumors from different sites in the upper aerodigestive tract. Appendix Table A3 organizes the tumor cell lines on the basis of the anatomic site of origin. The sites of origin are divided into 7 categories: facial skin, nasal/paranasal sinus, oral cavity, oral pharynx, hypopharynx, pharynx, and larynx. As shown in Appendix Table A3, most of the HNSCC cell lines are derived from tumors that either originated from the oral cavity or the larynx.

Doubling Times of Tumor Cell Lines. Doubling times are an important parameter used to measure the cellular response to experimental changes in culture conditions such as nutrient concentrations, hormones, or drugs[42] (Appendix Table A4). From a practical standpoint, knowledge of doubling times facilitates the daily maintenance of HNSCC cell cultures. Experiments can be planned so that cells will be in log phase when they are treated with reagents. The standard cycle of cell growth begins with negligible growth during the lag phase. After trypsinization, the cells adapt to the new environment by replacing elements of the glycocalyx lost during trypsinization, attaching to the substrate and spreading out. Following the lag phase, cells proceed into exponential growth during log phase. This is the optimal time for sampling because the population is most uniform and cell viability is high. The doubling time is measured during this phase. Cells are counted during the log phase, and the average doubling time is determined by plotting the cell counts as a function of time.[43] Another method for measuring doubling time is to calculate the time necessary for the cells to increase twofold in the middle of the log phase.[42] Toward the end of the log phase, adherent cells become confluent, cell division slows, and steady-state equilibrium between cell growth and cell death is achieved in stationary phase. In normal cells, a phenomenon termed contact inhibition has been observed when the cells become confluent during the stationary phase, suggesting that direct contact between neighboring cells reduces cell motility, membrane ruffling, and cell growth. However, HNSCC cell lines with regular culture medium replenishment will continue to proliferate beyond confluence to form multilayers of cells. The decline phase begins when nutrients are depleted and toxic by-products of metabolism accumulate leading to cell death.[42,44]

In Vivo Xenograft Growth of Tumor Cell Lines. Tumor cell lines or explants introduced as xenografts in mice can potentially model complex interactions

between the tumor and its host. Despite limitations, there is no current technology or in vitro assay that can predict the activity of antineoplastic drugs as accurately or demonstrate the tumorigenic and metastatic properties of tumors as fully as xenograft animal models. Appendix Table A5 catalogues the HNSCC cell lines that have grown as xenografts in mice. The athymic nude mouse was first described by Pantelouris in 1968.[45] In 1969, Polvsen and Rygaard were the first to xenograft a human colon adenocarcinoma into a nude mouse, and 3 years later, Polvsen and Rygaard were the first to transplant human tumor cells into the nude mouse model.[46,47] In 1984, Braakhuis et al[48] demonstrated that the nude mouse xenograft model could be used to study head and neck cancer by implanting 130 human head and neck biopsy explants into the subcutaneous tissue of nude mice.

The most commonly used immunodeficient mouse model to study head and neck cancer is the athymic nude mouse, which carries a homozygous *nu* mutation on mouse chromosome 11 leading to thymic dysgenesis.[46] While the primary immune defect of these mice is T-cell deficiency to prevent graft rejection, the athymic nude mouse is not completely immunodeficient. Although, functional T lymphocytes are effectively absent, B cells, natural killer (NK) cells, and macrophages are still present. Nevertheless, the nude mouse is more immunodeficient than animals that are rendered immunodeficient by artificial thymectomy or by other means of artificial immunosuppression. The benefits of using athymic nude mice include the following: thorough characterization and wide use; lack of hair that allows for visualization of subcutaneously xenografted tumors; immunodeficiency severe enough to support growth of wide range of tumor cells; and availability on different genetic backgrounds.[49] However, the nude mice retain normal levels of NK cells and macrophages. To eliminate NK cell activity and improve tumor establishment, nude mice can be pretreated with cyclophosphamide.[50] A less commonly used immunodeficient mouse model is the severe combined immunodeficiency (SCID) mouse. The benefit of using a SCID mouse is that the more severe immunodeficiency resulting in arrested T-cell and B-cell development allows for a higher percentage of engraftment, more enhanced tumor growth, and less tumor regression.[49] However, the disadvantages of SCID mice are that they experience a high incidence of thymic lymphomas, which may shorten their lifespan, and their severe immunodeficiency makes them harder to maintain.[49,51]

Several considerations need to be appreciated regarding the mouse xenograft model.[52] The xenograft in the mouse can be derived from either a tumor cell line or a patient biopsy explant. Tumor cell lines are histologically homogenous and undifferentiated, which ensures experimental uniformity and reproducibility. A drawback to using tumor cell lines is the concern that as they grow in vitro, they adapt to the culture environment and may develop genetic and phenotypic differences from the original tumor. The benefit of using biopsy explants is that they conserve morphological and molecular markers characteristics better than tumor cell lines; however, the disadvantage is the heterogeneous cell population found in the biopsy specimen and the difficulty associated with xenografting an explant. The site of xenograft implantation is also an important consideration. Most investigators implant HNSCC tumors into the subcutaneous tissue of the abdomen, nape of the neck, or the flank because of the relative ease in monitoring tumor growth and size; however, the subcutaneous implants show a benign growth pattern. Studies with tumor cells implanted into the subcutaneous tissue had difficulty demonstrating any significant invasion of surrounding tissues or metastatic activity.[47,48,53,54] Patients with head and neck cancer often have tumors that aggressively invade local surrounding tissues, so the subcutaneous model has its limitations. Orthotopic xenografts in the floor of mouth have been able to produce tumors that mimic histopathologic growth in the head and neck cancer patient, including invasion into surrounding tissues and spread to cervical lymph nodes.[55,56] Despite the recent developments of the murine model in head and neck cancer, it is important to recognize the limitations of the mouse xenograft model. Immunodeficient mouse strains have increased susceptibility to viral and bacterial infections, which limits the life span of the xenograft mouse to 4–6 months. In addition, immunodeficient mice have a different immunobiology when compared with the human host, which may result in different mechanisms and rates of tumor progression as well as treatment responses. Although beyond the scope of this review, the development of novel transgenic, knock-out and/or knock-in mice may provide more realistic models of human HNSCC in the setting of an intact immune system.

Tumor Cell Line Growth in Nonmonolayer Cultures. Soft agar growth demonstrates anchorage-independent proliferation potential, a hallmark of transformed cancer cells. Normally, non-

neoplastic cells require cell–matrix anchorage to survive; otherwise, a suspension-induced apoptosis known as anoikis occurs. Heterodimeric transmembrane cell surface receptors known as integrins bind to components of the extracellular matrix (ECM), and numerous studies have shown the disruption of these interactions lead to anoikis.[57–62] However, cancer cells have less stringent requirements for extracellular matrix adhesion, allowing them to resist anoikis and survive in an anchorage-independent manner. This property enables cancer cells to extravasate into lymphatic channels or blood vessels and invade a distant organ. Growth on soft agar becomes a reliable measure of the metastatic capability of tumor cells. Ten HNSCC cell lines have been reported to grow on soft-agar: HN-1,[8] HN-2,[8] UM-SCC-11A,[63] UM-SCC-14C,[64] UM-SCC-38,[64] TR126,[65] TR131,[65] TR146,[65] MDA-183,[23] and MDA-1483.[23] One challenge with this methodology is that most HNSCC cell lines do not grow in soft agar.

Spheroids offer a useful model of solid tumors because monolayer cultures lack the cell-to-cell interactions characteristic of tumors in vivo.[66] Spheroids are composed of an outer layer of proliferating cells, an inside layer of quiescent cells, and an inner core of necrotic cells. This arrangement reflects the growth pattern on solid tumors in vivo, with proliferating cells found closest to a nutrient and oxygen supply, quiescent cells found slightly farther, and necrotic cells found the farthest from capillaries.[67–75] There are 2 methods for culturing spheroids. The most popular approach involves the use of spinner flasks. Monolayer cell cultures are trypsinized and seeded in growth medium within spinner flasks. Rotation is achieved by spinning a stir bar in the spinner flask. Factors that affect spheroid formation include the type of cells, cell density at seeding, the rotation speed, the type of culture medium, and the incubation time. The advantage of using spinner flask cultures is the large number of spheroids formed from large-volume cultures and the considerable size of the spheroids.[67,76] Another method for forming spheroids is to use agar overlay cultures as first described by Yuhas.[77] Tumor cells obtained from confluent monolayer cultures are trypsinized into single-cell suspensions. These suspensions are seeded in a stationary, nonadherent mixture of complete growth medium and agarose.[67] When the spheroids are ready for experiments, it is critically important to select spheroids of the same size since a slight difference in diameter can result in a dramatic volume difference. Size uniformity can be achieved with the use of a Pasteur pipette and a low-power microscope, or for rapid harvesting of spheroids, the cultures may be filtered through a nylon sieve of decreasing mesh size to segregate spheroids, based on size and leaving the largest spheroids on top.[67] Eleven cell lines have been reported to cluster into 3-dimensional spheroidal cultures: Hep2,[78] FaDu,[79] HN-1,[80,81] UM-SCC-22B,[78] UM-SCC-30,[78] CAL27,[82] MDA-1483,[23,83] MDA-886LN,[83] MDA-686LN,[83] T1/CUHK,[84] and T2/CUHK.[84]

Spheroids may also be cultured from biopsy specimens and such cultures demonstrate ploidy stability suggesting that biopsies cultured in vivo maintain the cellular complexity of tumors in vivo.[85] Spheroid cultures derived from biopsy specimens do not experience the problematic clonal evolution of tumor cell subpopulations that has been attributed to the passage of monolayer cultures grown from biopsy specimens.[86] After a cell line has been passaged several times, there have been questions about its semblance to the original tumor.[85] However, genetic and molecular cytogenetic data show that HNSCC cells in culture closely resemble those in the primary tumors.[87,88]

A 3-dimensional spheroidal culture may be a better representation of the in vivo cellular complexity and heterogeneity found in the microenvironment of a tumor nodule than a monolayer culture. The 3-dimensional arrangement reflects several characteristics of tumor cells in vivo such as the irregular distribution of oxygen and nutrients found in tumor cells in vivo and cellular subpopulations of proliferating, quiescent, and necrotic cells. A model that better mimics tumor heterogeneity and intercellular contact should exhibit a more representative response to drug therapies. For example, studies using spheroid cell cultures have shown large variations in radiation and drug sensitivity, similar to those found with tumors in vivo.[74,89–94] Finally, spheroidal cultures are less affected by the culture conditions because of reduced cell-to-cell interactions.[67] A limiting factor to the use of tumor spheroids lies in the difficulty of establishing cell lines that can associate into spheroid clusters. Although both normal and transformed human cells may aggregate, only certain tumor cells will grow as spheroids. This review lists 11 reported HNSCC cell lines out of almost 300 total cell lines that can reassociate into spheroidal clusters. Across a wide range of different cancer types, only 5 of 22 human tumor xenografts and 16 of 27 tumor cell lines formed spheroids.[68,95]

SUMMARY

Head and neck cancer remains a significant public health concern. Despite current surgical treatments and adjunctive chemoradiation therapy, 5-year survival rates remain below 50%. This has prompted a greater need for investigating novel and targeted therapies. The use of HNSCC cell lines will be vital for these preclinical developments. Although the literature characterizing HNSCC cell lines is abundant, an easily accessible reference that organizes these data for researchers interested in selecting cell lines is necessary. This review provides a detailed catalogue of HNSCC cell line characteristics that will assist new and experienced investigators in their selection of appropriate preclinical models for further understanding head and neck tumor biology and therapeutic mechanisms.

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See Appendix in Next Page

APPENDIX

Table A1. Tumor cell line name and patient demographics.

Cell line	Sex	TNM stage	Reference	Genetics references
Hep2*	M	–	1, 2	–
Hep3	M	–	1, 2	–
KB*	M	–	3	–
RPMI 2650	–	–	4	–
Detroit 562*	F	–	5	–
FaDu*	M	–	6	–
SW579*	M	–	7	–
A-253*	M	–	8	–
T3M-1	M	–	9	9
HLac78	–	T2N2M0	10, 11	11
HLac79	–	–	11	11
HSmC78	–	T2N2M0	10, 11	11
HPaC79	–	–	11	–
MC	F	–	12	–
HN-1	M	T2N1M0	13	13, 14
HN-2	M	T3N0M0	13	13, 14
HN-3	M	T3N0M0	13	13, 14
HN-4	M	T2N0M0	13	13
HN-5	M	T2N0M0	13	14
HN-6	M	T2N0M0	13,15	14
HN-6Rr	M	–	15	–
HN-6nl	M	–	15	–
HN-6n2	M	–	15	14
HN-7	M	T2N0M0	13	–
HN-8	M	T2N0M0	13	–
HN-9	F	T2N0M0	13	–
HN-10	M	T2N0M0	13	–
UM-SCC-1	M	T2N0M0	16	7
UM-SCC-2	F	T2N0M0	16	17
UM-SCC-3	F	T1N0M0	16	17, 18
UM-SCC-4	F	T3N2aM0	19	17
UM-SCC-5	M	T2N1M0	19	17, 18, 20
UM-SCC-6	M	T2N0M0	19	17, 18
UM-SCC-7	M	T2N1M0	19	17, 18
UM-SCC-8	F	T2N1M0	19	7, 17, 18, 20
UM-SCC-9	F	T2N0M0	19	17, 18, 20
UM-SCC-10A	M	T3N0M0	19	7, 17, 18, 20, 21
UM-SCC-10B	M	T3N1M0	22	7, 18, 20
UM-SCC-11A	M	T2N2aM0	19	7, 17, 18, 20
UM-SCC-11B	M	T2N2aM0	7	7, 17, 18, 20
UM-SCC-12	M	T2N1M0	19	17
UM-SCC-13	M	T3N0M0	7	17
UM-SCC-14A	F	T1N0M0	19	7, 17, 18, 20, 21
UM-SCC-14B	F	T1N0M0	19	7, 17, 18, 20, 21
UM-SCC-14C	F	T1N0M0	19	7, 17, 18, 20, 21
UM-SCC-15	M	T4N1M0	7	7
UM-SCC-16	F	T2N0M0	22	7, 17, 20
UM-SCC-17A	F	T1N0M0	23	7, 17, 20, 23, 24
UM-SCC-17as	F	T1N0M0	23	23
UM-SCC-17B	F	T1N0M0	23	7, 17, 20, 23, 24
UM-SCC-18	M	T3N1M0	7	–
UM-SCC-19	M	T2N1M0	7	7, 17
UM-SCC-20	M	T2N1M0	7	17, 18
UM-SCC-21A	M	T2N1M0	25, 26	7, 17, 20, 26
UM-SCC-21B	M	T2N1M0	18, 26	7, 17, 18, 20, 26
UM-SCC-22A	F	T2N1M0	7	7, 17, 18
UM-SCC-22B	F	T2N1M0	19	7, 17, 18
UM-SCC-23	F	T2N0M0	22	7, 18

Table A1. (Continued).

Cell line	Sex	TNM stage	Reference	Genetics references
UM-SCC-24	M	T1N0M0	7	–
UM-SCC-25	M	T3N0M0	7	17
UM-SCC-26	M	T3N1M0	7	17
UM-SCC-27	M	T1N0M0	7	–
UM-SCC-28	F	T1N0M0	7	17
UM-SCC-29	M	T3N2aM0	7	17
UM-SCC-30	F	T3N1M0	7	17
UM-SCC-31	M	T3N0M0	7	–
UM-SCC-32	M	T3N1M0	7	–
UM-SCC-33	F	T4N3aM0	7	–
UM-SCC-34	M	T3N1M0	7	–
UM-SCC-35	M	T4N1M0	19	17
UM-SCC-36	M	T2N0M0	7	–
UM-SCC-37	M	T2N0M0	7	–
UM-SCC-38	M	T2N2aM0	19, 26	7, 17, 18, 26
UM-SCC-39	M	T3N3aM0	7	–
UM-SCC-40	M	T3N0M0	7	–
UM-SCC-41	M	T2N1M0	7	–
UM-SCC-42	M	T4N3bM0	7	–
UM-SCC-43	M	–	7	–
UM-SCC-44	M	T4N2bM0	7	–
UM-SCC-45	F	T4N2bM0	7	–
UM-SCC-46	F	–	7	27
UM-SCC-47	M	T3N1M0	7	27
UM-SCC-48	M	T4N0M0	7	–
UM-SCC-49	M	T2N1M0	7	17, 18
UM-SCC-50	F	T4N3bM0	7	–
UM-SCC-51	M	T3N3bM0	7	17, 18
UM-SCC-52	F	T3N3cM0	7	–
UM-SCC-53	M	T3N1M0	7	–
UM-SCC-54	M	T3N0M0	7	–
UM-SCC-55	M	–	7	–
UM-SCC-57	M	–	7	–
UM-SCC-58	F	–	7	–
UM-SCC-59	F	T3N2bM0	7	–
UM-SCC-60	–	–	7	–
UM-SCC-62	M	T3N1M0	7	–
UM-SCC-63	M	–	22	7
UM-SCC-65	M	–	7	17
UM-SCC-66	M	–	7	–
UM-SCC-67	M	–	7	–
UM-SCC-68A	M	–	7	–
UM-SCC-68B	M	–	7	–
UM-SCC-69	M	T4N0M0	19	7, 18, 21
UM-SCC-70	M	–	7	–
UM-SCC-71	M	–	7	–
UM-SCC-72	M	–	7	–
UM-SCC-73A	M	–	7	17
UM-SCC-73B	M	–	7	17
UM-SCC-74A	M	T3N0M0	7	–
UM-SCC-74B	M	T3N0M0	7	–
UM-SCC-75	F	–	7	–
UM-SCC-76	M	–	7	–
UM-SCC-77	F	–	7	–
UM-SCC-78A	M	–	7	–
UM-SCC-78B	M	–	7	–
UM-SCC-79	M	–	7	–
UM-SCC-80	M	T4N1M0	7	7, 18, 21
UM-SCC-81A	M	T2N0M0	7	24
UM-SCC-81B	M	T2N0M0	7	7, 24
UM-SCC-82A	F	T2N0M0	7	7, 17, 18, 21

Table A1. (Continued).

Cell line	Sex	TNM stage	Reference	Genetics references
UM-SCC-82B	F	–	7	17, 18, 21
UM-SCC-83A	M	–	7	7, 24
UM-SCC-83B	M	–	7	7, 24
UM-SCC-84	M	T2N0M0	7	–
UM-SCC-85	M	–	7	–
UM-SCC-86	F	–	7	24
UM-SCC-87	M	T3N0M0	7	7, 24
UM-SCC-88	F	T3N1M1	7	–
UM-SCC-89	M	T3N0M0	7	24
UM-SCC-90	M	T4N3M0	7	7, 24
UM-SCC-91	M	T4N0M0	7	24
UM-SCC-92	F	T2N0M0	7	–
UM-SCC-93	F	T4N0M0	7	7, 24
UM-SCC-94	M	T4N2aM0	7	24
UM-SCC-95	M	T4N1M0	7	–
UM-SCC-96	F	T3N3M0	7	–
UM-SCC-97	F	T1N0M0	7	–
UM-SCC-98	M	T4N0M0	7	–
UM-SCC-99	M	T3N0M0	7	–
UM-SCC-100	F	T4N3M0	7	–
UM-SCC-101A	F	T2N3M0	7	7
UM-SCC-101B	F	T2N3M0	7	–
SCC-4*	M	T3N0M0	28	–
SCC-9*	M	T2N1	28	–
SCC-12	M	–	28	–
SCC-13	F	–	28	–
SCC-15*	M	T4N1M0	28	–
SCC-25*	M	T2N1	28, 29	7
SCC-35	–	T4N0	29, 30	7
SCC-49	–	T2N0	30	–
SCC-61	–	T4N2b	29, 30	7
SCC-66	–	T4N0	30	–
SCC-68	M	T4N10M0	7	–
SCC-71	–	T4N1	30	–
SCC-73	–	T4N0	30	–
SCC-74	F	T4N0M0	7	–
SCC-76	–	T4N0	30	–
SCC-182	M	T3N0M0	7	–
SCC-200	M	T2N2M0	7	–
SCC-203	M	T2N2M0	7	–
SCC-210	M	T3N0M0	7	–
SCC-213	M	T4N0M0	7	–
SCC-220	M	T4N1M0	7	–
JSQ-3	–	T3N0	29, 31	7
JSQ-13	–	–	32	–
SQ-9G	–	T3N1	30	7
SQ-20B	–	T2N0	29, 30	7
SQ-29	–	T3N1	30	–
SQ-31	–	T2N0	29, 30	7
SQ-38	–	T3N0	30	7
SQ-39	–	T3N2a	30	–
SQ-43	–	T1N0	30	–
SQ-50	–	T4N2	7	–
HN-SCC-3	–	T3N3bM0	31	–
HN-SCC-28	–	–	31	–
HN-SCC-29	–	–	32	–
HN-SCC-42	–	–	32	–
HN-SCC-58	–	T4N1M0	31	–
HN-SCC-68	–	–	32	–
HN-SCC-80	–	–	32	–
HN-SCC-104	–	T3N3aM0	31	–

Table A1. (Continued).

Cell line	Sex	TNM stage	Reference	Genetics references
HN-SCC-109A	–	–	32	–
HN-SCC-131	–	–	31	–
HN-SCC-135	–	T1N1MO	29	7
HN-SCC-151	–	T3N0M0	29	7
HN-SCC-167	–	T3N0M0	29	7
HN-SCC-294	–	T2N0M0	29	7
PCI-1	M	–	33, 34	7, 33
PCI-2	M	T3N0M0	33	7, 33
PCI-3	–	T3N0M0	33	7, 33
PCI-4A	M	T3N0M0	33, 34	7, 33
PCI-4B	M	T3N0M0	33, 34	7, 33
PCI-5	M	T3N1M0	33	7, 33
PCI-6A	M	T3N3M0	33, 34	7, 33
PCI-6B	M	T3N3M0	33, 34	7, 33
PCI-7	M	T4N2M0	33	7, 33
PCI-8	M	T3N0M0	33	33
PCI-9A		T4N3M0	33	7, 33
PCI-9B	M	T4N3M0	33	7, 33
PCI-10	M	T3N1M0	33	7, 33
PCI-11	M	T4N1M0	33, 34	7, 33
PCI-12	M	–	33	7, 33
PCI-13	M	T4N1M0	33, 34	7, 33
PCI-14	M	–	33	–
PCI-15A	M	T2N1M0	33, 34	–
PCI-15B	M	T2N1M0	33, 34	–
PCI-16	M	T2N1M0	33	–
PCI-17	F	T2N0M0	33	–
PCI-18	M	–	33	–
PCI-19	M	T3N0M0	7	–
PCI-20	M	–	7	–
PCI-21	M	T3N2M0	7	–
PCI-22A	M	T4N1M0	34, 35	–
PCI-22B	M	T4N1M0	34, 35	–
PCI-23	F	T2N0M0	36	–
PCI-24	M	T2N0M0	33	–
PCI-25	M	T4N1M0	34, 35	–
PCI-26	M	T3N0M0	34	–
PCI-27	M	T4N0M0	7	–
PCI-28	M	T3N2M0	34, 35	–
PCI-29	F	T4N0M0	7	–
PCI-30	M	T3N1M0	34, 36	–
PCI-31	M	T3N0M0	34	–
PCI-32	M	T4N0M0	37	–
PCI-33	M	–	34	–
PCI-34	M	T4N2M0	34	–
PCI-35	M	T3N1M0	7	–
PCI-36	F	T2N0M0	34	–
PCI-37A	M	T3N2M0	34	–
PCI-37B	M	T3N2M0	34	–
PCI-38	M	T3N1M0	34, 36	–
PCI-39	M	T2N0M0	34	–
PCI-40	M	T4N2M0	7	–
PCI-41	F	T2N0M0	7	–
PCI-42	M	T4N2M0	7	–
PCI-43	M	T1N0M0	7	–
PCI-44	M	T4N0M0	7	–
PCI-45	M	T4N3M0	7	–
PCI-46	M	T2N2M0	7	–
PCI-47	F	T3N0M0	7	–
PCI-50	M	T2N0M0	38	–
PCI-51	M	T1N2M0	39	–

Table A1. (Continued).

Cell line	Sex	TNM stage	Reference	Genetics references
PCI-52	M	T1N2M0	40	–
PCI-100	M	T3N1M0	7	–
PCI-101	M	T4N2M0	7	–
PCI-102	M	T2N0M0	7	–
PCI-103	M	T3N0M0	7	–
PCI-104	M	T4N3M0	7	–
PCI-105	M	T3N0M0	7	–
PCI-106	F	T4N2M0	7	–
UT-SCC-1A	F	T2N1M0	19, 41	7
UT-SCC-1B	F	T4N1M0	42	7
UT-SCC-2	M	T4N1M0	19, 41	7
UT-SCC-4	F	T4N0M0	41	7
UT-SCC-5	M	T1N1M0	42	7
UT-SCC-6A	F	T2N1M0	42	7, 43
UT-SCC-6B	F	T2N1M0	42	7
UT-SCC-7	M	T1N0M0	41	7
UT-SCC-8	M	T2N0M0	42	7, 43
UT-SCC-9	M	T2N0M0	42	7, 43
UT-SCC-10	M	T1N0M0	42	7, 43
UT-SCC-11	M	T1N0M0	41	7
UT-SCC-12A	F	T2N0M0	41	7
UT-SCC-12B	F	T2N0M0	42	7
UT-SCC-13	M	T3N0M0	42	7
UT-SCC-14	M	T3N1M0	42	7
UT-SCC-15	M	T1N0M0	7	7
UT-SCC-16A	F	T3N0M0	41	7, 43
UT-SCC-16B	F	T3N0M0	42	7
UT-SCC-17	M	T2N0M0	7	7
UT-SCC-18	M	T3N1M0	42	7, 43
UT-SCC-19A	M	T4N0M0	44	7, 43
UT-SCC-19B	M	T4N0M0	44	7
UT-SCC-20A	F	T1N0M0	42	7
UT-SCC-20B	F	–	42	7
UT-SCC-21	M	T3N0M0	7	7
UT-SCC-22	M	T1N0M0	44	7
UT-SCC-23	M	T3N0M0	7	7
UT-SCC-24A	M	T2N0M0	42	7
UT-SCC-24B	M	T2N0M0	42	7, 43
UT-SCC-25	M	T2N0M0	42	7
UT-SCC-26A	M	T1N2M0	42	7
UT-SCC-26B	M	T1N2M0	42	7
UT-SCC-27	M	T2N0M0	7	7
UT-SCC-28	F	T2N0M0	7	7
UT-SCC-29	M	T2N0M0	42, 44	7, 43
UT-SCC-30	F	T3N1M0	7	7
UT-SCC-31	M	T3N2bM0	7	7
UT-SCC-32	M	T3N0M0	7	7
UT-SCC-33	F	T2N0M0	7	7
UT-SCC-34	M	T4N0M0	7	7
UT-SCC-35	M	T2N0M0	7	7
UT-SCC-36	M	T4N1M0	7	7
UT-SCC-37	F	T2N0M0	7	–
UT-SCC-38	M	T2N0M0	7	–
UT-SCC-39	M	T2N0M0	7	–
UT-SCC-40	M	T3N0M0	7	–
UT-SCC-41	M	T3N0M0	7	–
UT-SCC-42A	M	T4N3M0	7	–
UT-SCC-42B	M	T4N3M0	7	–
UT-SCC-43A	F	T4N1M0	7	–
UT-SCC-43B	F	T4N1M0	7	–
UT-SCC-44	F	T4N2bM0	7	–

Table A1. (Continued).

Cell line	Sex	TNM stage	Reference	Genetics references
UT-SCC-45	M	T3N1M0	7	–
UT-SCC-46A	M	T1N0M0	7	–
UT-SCC-46B	M	T1N0M0	7	–
UT-SCC-47	M	T2N0M0	7	–
UT-SCC-48	M	T3N0M0	7	–
UT-SCC-49	M	T2N0M0	7	–
UT-SCC-50	M	T2N0	7	–
UT-SCC-51	M	T2N0M0	7	–
UT-SCC-52	M	T2N1M0	7	–
UT-SCC-53	M	T4N2cM0	7	–
UT-SCC-54A	F	T2N0M0	7	–
UT-SCC-54B	F	T2N0M0	7	–
UT-SCC-55	M	T4N1M0	7	–
EV-SCC-1	M	T2N0M0	22	–
EV-SCC-2	M	T2N2aM0	7	–
EV-SCC-3	M	T2N2bM0	22	–
EV-SCC-4	M	T3N1M0	22	–
EV-SCC-7	M	T4N0M0	7	–
EV-SCC-10M	M	T4N1M0	7	–
EV-SCC-14M	M	T2N2bM0	7	–
EV-SCC-17P	M	T4N0M0	7	–
EV-SCC-17M	M	T4N0M0	7	–
EV-SCC-18	M	T3N1M0	7	–
EV-SCC-19P	M	T3N1M0	7	–
EV-SCC-19M	M	T3N1M0	7	–
HFH-SCC-3	M	T1N0M0	21	21
HFH-SCC-4	M	T4N0M0	21	21
HFH-SCC-6	M	T2N1M0	21	21, 45
HFH-SCC-8	M	T1N1M0	21	46
HFH-SCC-11	M	T3N0M0	21	21
HFH-SCC-12	M	T2N2bM0	21	21
HFH-SCC-15	F	–	21	21
HFH-SCC-16	M	T2N2M0	21	21
HFH-SCC-17	–	NS	18	18
HFH-SCC-19	M	T1N2M0	21	21
HFH-SCC-20	M	T4N3M0	21	21
HFH-SCC-28	M	T2N0M0	21	21
HFH-SCC-29	F	–	21	21
HFH-SCC-33	M	T4N2M0	21	21
HFH-SCC-42	M	T2N0M0	21	21
AMC-HN-1	M	T1N0M0	47	47
AMC-HN-2	M	T4N2M0	47	47
AMC-HN-3	M	T3N1M0	47	47
AMC-HN-4	F	T4N0M0	47	47
AMC-HN-5	M	T3N0M0	47	47
AMC-HN-6	M	T4N2M0	47	47
AMC-HN-7	M	T4N2M0	47	47
AMC-HN-8	M	T3N2M0	47	47
AMC-HN-9	F	T4N2M0	47	47
UD-SCC-1	M	T3N2bM0	48	48
UD-SCC-2	M	T1N2M0	48	48
UD-SCC-3	M	T2N2cM0	48	48
UD-SCC-4	M	T3N1M0	48	48
UD-SCC-5	M	T1N1M0	7	48
UD-SCC-6	M	T2N0M0	7	48
HNSCCUM-01T	M	T2N2cM0	7	–
HNSCCUM-02T	M	T3N3bM0	7	–
HNSCCUM-03T	M	T3N2bM0	7	–
HNSCCUM-04N	M	T1N1M0	7	–
HNSCCUM-05N	M	T1N2bM0	7	–
HNSCCUM-06N	M	T2N2cM0	7	–

Table A1. (Continued).

Cell line	Sex	TNM stage	Reference	Genetics references
HNSCCUM-07N	M	T2N2bM0	7	–
TU-138	M	T3N0M0	49	–
TU-158 LN	M	T2N2aM0	49	–
TU-159	M	T3N0M0	49	–
TU-167	F	T4N2bM0	49	–
TU-177	M	T3N0M0	49	–
TU-182	F	T3N2bM0	49	–
TU-202	–	–	7	–
TU-212	M	T2N2cM0	49	–
TU-212 LN	M	T2N2cM0	49	–
TU-358B	–	–	7	–
TU-686	–	–	7	–
CAL 33	–	–	50	50
CAL 27*	M	–	50	50
TR126	F	–	51	–
TR131	M	–	51	–
TR138	M	–	51	–
TR146	F	–	51	–
MDA-183	M	T3N0M0	52	7, 52
MDA-1483	M	T2N1M0	52	7, 52
584A2	–	–	53	53
MDA-886LN	M	T3N3a	54	–
T1/CUHK	–	–	55	55
T2/CUHK	–	–	55	55
MDA-686Ln	–	–	56	–
HTB43	–	–	57	–
UPCI:SCC003	F	T1N0	58, 59	58–60
UPCI:SCC016	F	T1N0	58, 59	58, 59
UPCI:SCC029	M	T4N2	58, 59	58, 59
UPCI:SCC030	M	T4N2B	58, 59	58, 59
UPCI:SCC032	M	T2N2B	58, 59, 61	58, 59, 61
UPCI:SCC036	M	T3N1	58, 59, 61	58, 59, 61
UPCI:SCC040	M	T2N2	58, 59	58, 59, 62–67
UPCI:SCC056	M	T3N2B	58, 59, 61	58, 59, 61, 63, 65
UPCI:SCC070	F	T3N1	58, 59, 61	58, 59, 61
UPCI:SCC072	F	T3N2B	58, 59, 61	58, 59, 61
UPCI:SCC074	F	T4N1	59, 61	59, 61
UPCI:SCC075	M	T3N2B	58, 59, 61	58, 59, 61
UPCI:SCC077	M	T2N2	58, 59, 61	58, 59, 61
UPCI:SCC078	M	T2N0	58, 59, 61	58, 59, 61, 68
UPCI:SCC080	M	T1N0	58, 59	58, 59
UPCI:SCC081	F	T4N0	59, 61	59, 61
UPCI:SCC084	M	T2N2B	58, 59, 61	58, 59, 61
UPCI:SCC089	M	T4N2B	59, 61	59, 61
UPCI:SCC090	M	T2N0	59, 62, 69	59, 62, 69
UPCI:SCC099	M	T1N0	58, 59	58, 59
UPCI:SCC103	F	T1N0	58, 59, 61	58, 59, 61, 64, 66, 68
UPCI:SCC104	M	T4NX	58, 59, 61	58, 59, 61
UPCI:SCC105	M	T2N0	58, 59, 61	58, 59, 61
UPCI:SCC111	F	T1N1	58, 59, 61	58, 59, 61
UPCI:SCC114	M	T2N0	58, 59, 61	58, 59, 61, 63, 65, 70
UPCI:SCC116	M	T2N0	58, 59, 61	58, 59, 61
UPCI:SCC122	M	T1N1	58, 59, 61	58, 59, 61
UPCI:SCC125	F	T4N2B	58, 59, 61	58, 59, 61
UPCI:SCC131	M	T2N2	58, 59, 61	58–61, 67
UPCI:SCC136	F	T3N2	58, 59, 61	58, 59, 61
UPCI:SCC142	M	T4NX	58, 59, 61	58, 59, 61
UPCI:SCC154	M	T4N2	58, 59	58, 59
UPCI:SCC172	M	–	58, 59	58–60
UPCI:SCC182	M	T2N1	58, 59	58, 59
JHU-11-SCC	M	T3N0	71–73	–

Table A1. (Continued).

Cell line	Sex	TNM stage	Reference	Genetics references
JHU-12-SCC	F	T1N2b	71	–
JHU-20-SCC	M	T2N2b	72–74	–
JHU-22-SCC	M	T3N2b	72–74	–
JHU-29-SCC	M	T4N0	71	–

**HNSCC cell lines available from the American Type Culture Collection (ATCC).*

Table A2. *TP53* gene mutations.

Cell line	Mutation	Protein detection IB/IHC*	References
Ca9-22	R248W	+	–
FS-1	R273H	+	–
HSC-3	aa305-306 INSERTION	+	–
HSC-4	R248Q	+	–
HSQ-89	G266E	+	–
K562	wt	–	–
Kuma-3	C176F	+	–
MO24	wt	–	33
PCI-13	E286K		33, 37, 75
PCI-30	wt		33, 37, 75
PCI-4B			33, 37, 75
SCC-4	T150L	+	33
SCC-9	del275–285	–	33
TE-11	R110L	+	–
UD-SCC-1	Skip exon 3	–/–	48, 76
UD-SCC-2		–/–	48, 76
UD-SCC-3		–/–	48, 76
UD-SCC-5	H179Y	+/+	48, 76
UD-SCC-6	Y220C	+/+	48, 76
UD-SCC-7A/B/C	R248L	+/+	48, 76
UD-SCC-8	T155N	+/+	48, 76
UM-SCC-1			16, 77
UM-SCC-5	V157F		16, 77
UM-SCC-6			16, 77
UM-SCC-10A/B	G245C	+/+	16, 76, 77
UM-SCC-11B	C242S	+/+	16, 76, 77
UM-SCC-12	Q110 stop		16, 77
UM-SCC-13	Y163C		16, 77
UM-SCC-14A/B/C	R280S	+/+	16, 76, 77
UM-SCC-17A/B	wt	–/–	16, 76, 77
UM-SCC-22A/B	Y220C	+/+	16, 76, 77
UM-SCC-23	C176F		16, 77
UM-SCC-25	wt		16, 77
UM-SCC-36	R158P		16, 77
UM-SCC-46	P278A		16, 77
UM-SCC-47	wt		16, 77
UM-SCC-54			16, 77
UM-SCC-57	R273L		16, 77
UM-SCC-68	R248W		16, 77
UM-SCC-72	wt		16, 77
UM-SCC-74A	wt		16, 77
UM-SCC-74B	wt		16, 77
UM-SCC-81A	wt		16, 77
UM-SCC-81B	H193R		16, 77
UPCI:SCC-16	R282W		78
UPCI:SCC-29B	R280T		78
UPCI:SCC-32	Del2bp		78
UPCI:SCC-36	I195F		78
UPCI:SCC-70	R248Q		78
UPCI:SCC-72	H179N		78

Table A2. (Continued).

Cell line	Mutation	Protein detection IB/IHC*	References
UPCI:SCC-77	Del1bp		78
UPCI:SCC-84	Del1bp		78
UPCI:SCC-99	P177R		78
UPCI:SCC-103	R306X		78
UPCI:SCC-105	T155P		78
UPCI:SCC-111	H189Y		78
UPCI:SCC-114	R248Q		78
UPCI:SCC-116	R175H		78
UPCI:SCC-122	R273H		78
UPCI:SCC-125	P151H		78
UPCI:SCC-136	E224X		78
UPCI:SCC-172	T155P		78
UPCI:SCC-182	E294X		78
UT-MUC-1			19, 79, 80
UT-SCC-1A			19, 79, 80
UT-SCC-2			19, 79, 80
UT-SCC-4			19, 79, 80
UT-SCC-5			19, 79, 80
UT-SCC-6A/B			19, 79, 80
UT-SCC-7	G266E	+/+	19, 79, 80
UT-SCC-8			19, 79, 80
UT-SCC-9		–/–	19, 79, 80
UT-SCC-14	Skip exon 8 insertion intron 8	+/+	19, 79, 80
UT-SCC-15	N77 del116	–/–	19, 79, 80
UT-SCC-15			19, 79, 80
UT-SCC-16A			19, 79, 80
UT-SCC-20B			19, 79, 80
UT-SCC-22	C238F	+/+	19, 79, 80
UT-SCC-23		–/–	19, 79, 80
UT-SCC-24A/B	NT 775ins49	–/–	19, 79, 80
UT-SCC-33	R282W	+/+	19, 79, 80
UT-SCC-34		–/–	19, 79, 80
UT-SCC-50	Skip exon 9	–/–	19, 79, 80

Abbreviations: IB, immunoblot; IHC, immunohistochemistry.

Table A3. Tumor cell line and anatomic site of origin.

Oral cavity	Oropharynx	Hypopharynx	Larynx	Paranasal/nasal sinus	Facial skin
Hep3 (HeLa?)	UM-SCC-4	FaDu	Hep2 (HeLa?)	RPMI 2650	UM-SCC-21A
KB (HeLa?)	UM-SCC-6	UM-SCC-15	HLac78	MC	UM-SCC-21B
SW579	UM-SCC-18	UM-SCC-22A	HLac79	UM-SCC-3	UM-SCC-63
A-253	UM-SCC-19	UM-SCC-22B	HN-2	UM-SCC-33	SCC-12
T3M-1	UM-SCC-26	UM-SCC-30	HN-4	UM-SCC-85	SCC-13
HN-1	UM-SCC-31	UM-SCC-37	HN-8	UT-SCC-53	PCI-20
HN-3	UM-SCC-34	UM-SCC-39	HN-9	AMC-HN-5	UT-SCC-7
HN-5	UM-SCC-35	UM-SCC-42	HN- 10		UT-SCC-12A
HN-6	UM-SCC-38	UM-SCC-53	UM-SCC-5		UT-SCC-12B
HN-6Rr	UM-SCC-50	UM-SCC-60	UM-SCC-10A		
HN-6Rr	UM-SCC-62	UM-SCC-80	UM-SCC-10B		
HN-6Rr	UM-SCC-65	UM-SCC-88	UM-SCC-11A		
HN-7	UM-SCC-81B	SCC-35	UM-SCC-11B		
UM-SCC-1	UM-SCC-87	SQ-31	UM-SCC-12		
UM-SCC-9	UM-SCC-89	HN-SCC-104	UM-SCC-13		
UM-SCC-14A	UM-SCC-91	PCI-5	UM-SCC-16		
UM-SCC-14B	UM-SCC-95	PCI-8	UM-SCC-17A		
UM-SCC-14C	UM-SCC-99	PCI-11	UM-SCC-17as		
UM-SCC-27	UM-SCC-100	PCI-12	UM-SCC-17B		
UM-SCC-32	UM-SCC-101A	PCI-21	UM-SCC-20		
UM-SCC-44	UM-SCC-101B	PCI-32	UM-SCC-23		
UM-SCC-45	SCC-49	PCI-40	UM-SCC-24		
UM-SCC-47	SCC-71	PCI-104	UM-SCC-25		

Table A3. (Continued).

Oral cavity	Oropharynx	Hypopharynx	Larynx	Paranasal/nasal sinus	Facial skin
UM-SCC-48	SCC-200	PCI-105	UM-SCC-28		
UM-SCC-49	SQ-9G	PCI-106	UM-SCC-36		
UM-SCC-51	HN-SCC-3	UT-SCC-26A	UM-SCC-46		
UM-SCC-55	HN-SCC-167	UT-SCC-26B	UM-SCC-52		
UM-SCC-59	PCI-6A	EV-SCC-10M	UM-SCC-54		
UM-SCC-69	PCI-6B	HFH-SCC-6	UM-SCC-57		
UM-SCC-73A	PCI-7	AMC-HN-2	UM-SCC-66		
UM-SCC-82A	PCI-9A	UD-SCC-2	UM-SCC-67		
UM-SCC-82B	PCI-9B	HNSCCUM-01T	UM-SCC-68A		
UM-SCC-83A	PCI-10	HNSCCUM-03T	UM-SCC-72		
UM-SCC-83B	PCI-41	HNSCCUM-06N	UM-SCC-76		
UM-SCC-84	PCI-46	HNSCCUM-07N	UM-SCC-81A		
UM-SCC-86	PCI-51	TU-212	UM-SCC-90		
UM-SCC-92	EV-SCC-3	TU-212 LN	UM-SCC-93		
UM-SCC-96	HFH-SCC-19		UM-SCC-94		
UM-SCC-97	HFH-SCC-20		UM-SCC-98		
SCC-4	UD-SCC-1		SQ-20B		
SCC-9	UD-SCC-4		SQ-43		
SCC-15	HNSCCUM-02T		SQ-50		
SCC-25	HNSCCUM-05N		HN-SCC-28		
SCC-61	TU-158 LN		PCI-1		
SCC-66	TU-159		PCI-4A		
SCC-68	TU-182		PCI-4B		
SCC-73	MDA-183		PCI-14		
SCC-182	JHU-20-SCC		PCI-16		
SCC-210	JHU-29-SCC		PCI-17		
SCC-213	UPCI:SCC003		PCI-18		
SCC-220	UPCI:SCC036		PCI-19		
JSQ-3	UPCI:SCC072		PCI-25		
SQ-29	UPCI:SCC080		PCI-26		
SQ-38	UPCI:SCC089		PCI-28		
SQ-39	UPCI:SCC090		PCI-29		
HN-SCC-131			PCI-35		
HN-SCC-135			PCI-37A		
HN-SCC-151			PCI-37B		
HN-SCC-294			PCI-39		
PCI-2			PCI-43		
PCI-3			PCI-44		
PCI-13			PCI-47		
PCI-15A			PCI-52		
PCI-15B			PCI-102		
PCI-22A			PCI-103		
PCI-22B			UT-SCC-6A		
PCI-23			UT-SCC-6B		
PCI-24			UT-SCC-8		
PCI-27			UT-SCC-9		
PCI-30			UT-SCC-11		
PCI-31			UT-SCC-13		
PCI-33			UT-SCC-17		
PCI-34			UT-SCC-19A		
PCI-36			UT-SCC-19B		
PCI-38			UT-SCC-22		
PCI-42			UT-SCC-23		
PCI-45			UT-SCC-29		
PCI-50			UT-SCC-34		
PCI-100			UT-SCC-35		
PCI-101			UT-SCC-38		
UT-SCC-1A			UT-SCC-39		
UT-SCC-1B			UT-SCC-42A		
UT-SCC-2			UT-SCC-42B		
UT-SCC-5			UT-SCC-49		
UT-SCC-10			UT-SCC-50		
UT-SCC-14			UT-SCC-51		
UT-SCC-16A			EV-SCC-18		
UT-SCC-16B			HFH-SCC-3		
UT-SCC-18			HFH-SCC-11		
UT-SCC-20A			HFH-SCC-12		
UT-SCC-20B			HFH-SCC-16		

Table A3. (Continued).

Oral cavity	Oropharynx	Hypopharynx	Larynx	Paranasal/nasal sinus	Facial skin
UT-SCC-24A			HFH-SCC-28		
UT-SCC-24B			HFH-SCC-42		
UT-SCC-25			AMC-HN-3		
UT-SCC-27			AMC-HN-7		
UT-SCC-28			AMC-HN-8		
UT-SCC-30			HNSCCUM-04N		
UT-SCC-31			TU-177		
UT-SCC-32			TR 131		
UT-SCC-33			TR 138		
UT-SCC-36			584A2		
UT-SCC-37			MDA-886LN		
UT-SCC-40			JHU-11-SCC		
UT-SCC-41			JHU-22-SCC		
UT-SCC-43A					
UT-SCC-43B					
UT-SCC-44					
UT-SCC-45					
UT-SCC-46A					
UT-SCC-46B					
UT-SCC-47					
UT-SCC-52					
UT-SCC-54A					
UT-SCC-54B					
UT-SCC-55					
EV-SCC-4					
EV-SCC-7					
EV-SCC-14M					
EV-SCC-17P					
EV-SCC-17M					
EV-SCC-19P					
EV-SCC-19M					
HFH-SCC-4					
HFH-SCC-8					
HFH-SCC-15					
HFH-SCC-33					
AMC-HN-1					
AMC-HN-4					
AMC-HN-6					
UD-SCC-5					
UD-SCC-6					
TU-138					
TU-167					
TU-202					
CAL 33					
CAL 27					
TR 126					
TR 146					
MDA-1483					
T1/CUHK					
T2/CUHK					
JHU-12-SCC					
UPCI:SCC016					
UPCI:SCC029					
UPCI:SCC030					
UPCI:SCC032					
UPCI:SCC040					
UPCI:SCC056					
UPCI:SCC070					
UPCI:SCC074					
UPCI:SCC075					
UPCI:SCC077					
UPCI:SCC078					
UPCI:SCC081					
UPCI:SCC084					
UPCI:SCC099					
UPCI:SCC103					
UPCI:SCC104					

Table A3. (Continued).

Oral cavity	Oropharynx	Hypopharynx	Larynx	Paranasal/nasal sinus	Facial skin
UPCI:SCC105					
UPCI:SCC111					
UPCI:SCC114					
UPCI:SCC116					
UPCI:SCC122					
UPCI:SCC125					
UPCI:SCC131					
UPCI:SCC136					
UPCI:SCC142					
UPCI:SCC154					
UPCI:SCC172					
UPCI:SCC182					

Note: For references, please refer to Table A1.

Table A4. Doubling times of HNSCC cell lines.

Cell line	Doubling time, h	References	Cell line	Doubling time, h	References
T3M-1	17	9	PCI-22A	80	34
HN-1	36	13	PCI-22B	68	34
HN-2	48	13	PCI-25	200	34
HN-3	38	13	PCI-26	93	34
HN-4	100	13	PCI-28	240	34
HN-5	34	13	PCI-30	52	34
HN-6	32	13	PCI-33	102	34
HN-6Rr	30	15	PCI-34	73	34
HN-6nl	30	15	PCI-37A	80	34
HN-6n2	72	15	PCI-37B	91	34
HN-7	72	13	PCI-38	82	34
HN-8	170	13	PCI-39	104	34
HN-9	70	13	PCI-50	27.3	38
HN- 10	60	13	UT-SCC-1A	53	81
UM-SCC-1	37	81	UT-SCC-1B	62	81
UM-SCC-2	34	81	UT-SCC-2	32	81
UM-SCC-4	90	81	UT-SCC-4	88	81
UM-SCC-5	34	81	UT-SCC-5	45	81
UM-SCC-6	77	81	UT-SCC-6A	100	81
UM-SCC-8	37	81	UT-SCC-6B	91	81
UM-SCC-9	55	81	UT-SCC-7	43	81
UM-SCC-10B	36	81	UT-SCC-8	23	81
UM-SCC-11B	29	81	UT-SCC-9	43	81
UM-SCC-12	34	81	UD-SCC-1	32.5	48
UM-SCC-14A	40	81	UD-SCC-2	42	48
UM-SCC-14B	38	81	UD-SCC-3	31	48
UM-SCC-14C	43	81	UD-SCC-4	36	48
PCI-1	66	34	CAL 33	43	50
PCI-4A	58	7	CAL 27	35	50
PCI-4B	58	7	TR126	21	51
PCI-6A	68	34	TR131	34	51
PCI-6B	106	34	TR138	22	51
PCI-11	124	34	TR146	22	51
PCI-13	86	34	MDA-183	36	52
PCI-15A	126	34	MDA-1483	36	52
PCI-15B	66	34			

Table A5. HNSCC xenograft models.

Nude mice	References	Nude + Cycl	References	SCID	References
Hep2	82, 83	PCI-1	33	UM-SCC-11A	84
Hep3	85–87	PCI-2	33		
KB	88, 89	PCI-3	33		
Detroit 562	90, 91	PCI-4A	33		
FaDu	92, 93	PCI-4B	33		
SW579	94	PCI-5	33		
A-253	92	PCI-6A	33		
T3M-1	9	PCI-6B	33		
HLac78	95, 96	PCI-7	33		
HLac79	10, 95	PCI-8	33		
HSmC78	10	PCI-9A	33		
HN-2	13	PCI-9B	33		
HN-5	13	PCI-10	33		
HN-6	13	PCI-11	33		
UM-SCC-2	97, 98	PCI-12	33		
UM-SCC-3	97	PCI-14	7		
UM-SCC-4	7	PCI-15A	7		
UM-SCC-6	7	PCI-15B	7		
UM-SCC-7	7	PCI-16	7		
UM-SCC-10A	7	PCI-17	7		
UM-SCC-10B	7	PCI-18	7		
UM-SCC-11B	98				
UM-SCC-12	7				
UM-SCC-14A	7				
UM-SCC-16	7				
UM-SCC-17B	7				
UM-SCC-18	7				
UM-SCC-19	7				
UM-SCC-22B	99				
SCC-4	28				
SCC-9	28				
SCC-12	28				
SCC-13	28				
SCC-15	28				
SCC-25	28				
SCC-61	100				
JSQ-3	101				
SQ-20B	102–105				
PCI-13	7				
PCI-52	106				
UT-SCC-12A	107				
UT-SCC-14	108				
AMC-HN-1	47				
AMC-HN-2	47				
AMC-HN-3	47				
AMC-HN-4	47				
AMC-HN-5	47				
AMC-HN-6	47				
AMC-HN-7	47				
AMC-HN-8	47				
AMC-HN-9	47				
UD-SCC-1	48				
UD-SCC-2	48				
UD-SCC-3	48				
UD-SCC-4	48				
TU-138	109				
CAL 27	50				
CAL 33	50				
TR131	51				
TR138	51				
TR146	51				
MDA-183	52				
MDA-1483	52				
T1/CUHK	55				
T2/CUHK	55				

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