The 2015 World Health Organization Classification of Lung Tumors

Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification

William D. Travis, MD, Elisabeth Brambilla, MD,† Andrew G. Nicholson, MD,‡ Yasushi Yatabe, MD,§ John H. M. Austin, MD,‖ Mary Beth Beasley, MD,¶ Lucian. R. Chirieac, MD,# Sanja Dacic, MD,** Edwina Duhig, MD,†† Douglas B. Flieder, MD,‡‡ Kim Geisinger, MD,§§ Fred R. Hirsch, MD,‖‖ Yuichi Ishikawa, MD,¶¶ Keith M. Kerr, MD,## Masayuki Noguchi, MD,*** Giuseppe Pelosi, MD,††† Charles A. Powell, MD,‡‡‡ Ming Sound Tsao, MD,§§§ and Ignacio Wistuba, MD,‖‖‖*

On Behalf of the WHO Panel

Abstract: The 2015 World Health Organization (WHO) Classification of Tumors of the Lung, Pleura, Thymus and Heart has just been published with numerous important changes from the 2004 WHO classification. The most significant changes in this edition involve (1) use of immunohistochemistry throughout the classification, (2) a new emphasis on genetic studies, in particular, integration of molecular testing to help personalize treatment strategies for advanced lung cancer patients, (3) a new classification for small biopsies and cytology similar to that proposed in the 2011 Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society classification, (4) a completely different approach to lung adenocarcinoma as proposed by the 2011 Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society classification, (5) restricting the diagnosis of large cell carcinoma only to resected tumors that lack any clear morphologic or immunohistochemical differentiation with reclassification of the remaining former large cell carcinoma subtypes into different categories, (6) reclassifying squamous cell carcinomas into keratinizing, nonkeratinizing, and basaloid subtypes with the nonkeratinizing tumors requiring immunohistochemistry proof of squamous differentiation, (7) grouping of neuroendocrine tumors together in one category, (8) adding *NUT* carcinoma, (9) changing the term sclerosing hemangioma to sclerosing pneumocytoma, (10) changing the name hamartoma to "pulmonary hamartoma," (11) creating a group of PEComatous tumors that include (a) lymphangioleiomyomatosis, (b) PEComa, benign (with clear cell tumor as a variant) and (c) PEComa, malignant, (12) introducing the entity pulmonary myxoid sarcoma with an *EWSR1–CREB1* translocation, (13) adding the entities myoepithelioma and myoepithelial carcinomas, which can show *EWSR1* gene rearrangements, (14) recognition of usefulness of *WWTR1–CAMTA1* fusions in diagnosis of epithelioid hemangioendotheliomas, (15) adding Erdheim–Chester disease to the lymphoproliferative tumor, and (16) a group of tumors of ectopic origin to include germ cell tumors, intrapulmonary thymoma, melanoma and meningioma.

Key Words: WHO classification, Lung tumors, Lung cancer, Lung adenocarcinoma, Squamous cell carcinoma, Small cell carcinoma, Large cell carcinoma, Carcinoid.

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*Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York; †Dept d'Anatomie et Cytologie Pathologiques, CHU Albert Michallon, University Joseph Fourier; INSERM U823 Institut Albert Bonniot, Grenoble, France; ‡Department of Pathology, Royal Brompton Hospital, London, United Kingdom; §Department of Pathology, Aichi Cancer Center, Nagoya, Japan; ‖Department of Radiology, Columbia University Medical Center, New York, New York; ¶Department of Pathology, Ichan School of Medicine at Mt Sinai, New York, New York; #Department of Pathology, Brigham and Women's Hospital, Boston, Massachusetts; **Department of Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania; ††Sullivan Nicolaides Pathology, The John Flynn Hospital, Tugun, Queensland, Australia; ‡‡Department of Pathology, Fox Chase Cancer Center, Philadelphia, Pennsylvania; §§Department of Pathology, University of Mississippi Medical Center, Jackson, Mississippi; ‖‖University of Colorado Cancer Center UCHSC, Aurora, Colorado; ¶¶Department of Pathology, The JFCR Cancer Institute, Tokyo, Japan; ##Department of Pathology, Aberdeen Royal Infirmary, Aberdeen, Scotland, United Kingdom; ***Department of Pathology; Institute of Basic Medical Sciences, University of Tsukuba, Tsukuba, Japan; †††Department of Pathology and Laboratory Medicine, Istituto Nazionale Tumori, Milan, Italy; ‡‡‡Division of Pulmonary Critical Care and Sleep Medicine, Ichan School of Medicine at Mt Siai, New York, New York; §§§Department of Pathology, Princess Margaret Hospital, Toronto, Canada; and ‖‖‖Department of Pathology, MD Anderson Cancer Center, Houston, Texas.

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Address for correspondence: William D. Travis, MD, Department of Pathology, Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065. E-mail: travisw@mskcc.org

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The 2015 World Health Organization (WHO) Classification of Tumors of the Lung, Pleura, Thymus and Heart has just been published (Table 1).[1] This follows previous WHO

TABLE 1. 2015 WHO Classification of Lung Tumors[a,b,c]

Histologic Type and Subtypes	ICDO Code
Epithelial tumors	
Adenocarcinoma	8140/3
Lepidic adenocarcinoma[e]	8250/3[d]
Acinar adenocarcinoma	8551/3[d]
Papillary adenocarcinoma	8260/3
Micropapillary adenocarcinoma[e]	8265/3
Solid adenocarcinoma	8230/3
Invasive mucinous adenocarcinoma[e]	8253/3[d]
Mixed invasive mucinous and nonmucinous adenocarcinoma	8254/3[d]
Colloid adenocarcinoma	8480/3
Fetal adenocarcinoma	8333/3
Enteric adenocarcinoma[e]	8144/3
Minimally invasive adenocarcinoma[e]	
Nonmucinous	8256/3[d]
Mucinous	8257/3[d]
Preinvasive lesions	
Atypical adenomatous hyperplasia	8250/0[d]
Adenocarcinoma in situ[e]	
Nonmucinous	8250/2[d]
Mucinous	8253/2[d]
Squamous cell carcinoma	8070/3
Keratinizing squamous cell carcinoma[e]	8071/3
Nonkeratinizing squamous cell carcinoma[e]	8072/3
Basaloid squamous cell carcinoma[e]	8083/3
Preinvasive lesion	
Squamous cell carcinoma in situ	8070/2
Neuroendocrine tumors	
Small cell carcinoma	8041/3
Combined small cell carcinoma	8045/3
Large cell neuroendocrine carcinoma	8013/3
Combined large cell neuroendocrine carcinoma	8013/3
Carcinoid tumors	
Typical carcinoid tumor	8240/3
Atypical carcinoid tumor	8249/3
Preinvasive lesion	
Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia	8040/0[d]
Large cell carcinoma	8012/3
Adenosquamous carcinoma	8560/3
Sarcomatoid carcinomas	
Pleomorphic carcinoma	8022/3
Spindle cell carcinoma	8032/3
Giant cell carcinoma	8031/3
Carcinosarcoma	8980/3
Pulmonary blastoma	8972/3
Other and Unclassified carcinomas	
Lymphoepithelioma-like carcinoma	8082/3
NUT carcinoma[e]	8023/3[d]
Salivary gland-type tumors	
Mucoepidermoid carcinoma	8430/3
Adenoid cystic carcinoma	8200/3
Epithelial-myoepithelial carcinoma	8562/3
Pleomorphic adenoma	8940/0
Papillomas	
Squamous cell papilloma	8052/0
Exophytic	8052/0
Inverted	8053/0
Glandular papilloma	8260/0
Mixed squamous and glandular papilloma	8560/0
Adenomas	
Sclerosing pneumocytoma[e]	8832/0
Alveolar adenoma	8251/0
Papillary adenoma	8260/0
Mucinous cystadenoma	8470/0
Mucous gland adenoma	8480/0
Mesenchymal tumors	
Pulmonary hamartoma	8992/0[d]
Chondroma	9220/0
PEComatous tumors[e]	
Lymphangioleiomyomatosis	9174/1
PEComa, benign[e]	8714/0
Clear cell tumor	8005/0
PEComa, malignant[e]	8714/3
Congenital peribronchial myofibroblastic tumor	8827/1
Diffuse pulmonary lymphangiomatosis	
Inflammatory myofibroblastic tumor	8825/1
Epithelioid hemangioendothelioma	9133/3
Pleuropulmonary blastoma	8973/3
Synovial sarcoma	9040/3
Pulmonary artery intimal sarcoma	9137/3
Pulmonary myxoid sarcoma with *EWSR1–CREB1* translocation[e]	8842/3[d]
Myoepithelial tumors[e]	
Myoepithelioma	8982/0
Myoepithelial carcinoma	8982/3
Lymphohistiocytic tumors	
Extranodal marginal zone lymphomas of mucosa-associated Lymphoid tissue (MALT lymphoma)	9699/3
Diffuse large cell lymphoma	9680/3
Lymphomatoid granulomatosis	9766/1
Intravascular large B cell lymphoma[e]	9712/3
Pulmonary Langerhans cell histiocytosis	9751/1
Erdheim–Chester disease	9750/1
Tumors of ectopic origin	
Germ cell tumors	
Teratoma, mature	9080/0
Teratoma, immature	9080/1
Intrapulmonary thymoma	8580/3
Melanoma	8270/3
Meningioma, NOS	9530/0
Metastatic tumors	

[a]The morphology codes are from the ICDO.[2] Behavior is coded /0 for benign tumors, /1 for unspecified, borderline or uncertain behavior, /2 for carcinoma in situ and grade III intraepithelial neoplasia, and /3 for malignant tumors.

[b]The classification is modified from the previous WHO classification[3] taking into account changes in our understanding of these lesions.

[c]This table is reproduced from the 2015 WHO Classification by Travis et al.[1]

[d]These new codes were approved by the International Agency on Cancer Research/WHO Committee for ICDO.

[e]New terms changed or entities added since 2004 WHO Classification.[3]

LCNEC, large cell neuroendocrine carcinoma, WHO, World Health Organization; ICDO International Classification of Diseases for Oncology.