THYMIC MALIGNANCY

More Hands Produce Stronger Flames

Honorary Editors: Pier Luigi Filosso, Anja C. Roden

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Thymic Malignancy

方文涛 Joel Dunning (英) Robert J. Korst (美) 主编

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THYMIC MALIGNANCY (FIRST EDITION)

HONORARY EDITORS

Pier Luigi Filosso

Thoracic Surgery, University of Torino, Italy

Anja C. Roden

Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN 55905, USA

EDITORS

Wentao Fang

Department of Thoracic Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Joel Dunning

Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK

Robert J. Korst

Department of Thoracic Surgery, Icahn School of Medicine, Mount Sinai Health System, New York, NY, USA; Valley/ Mount Sinai Comprehensive Cancer Care, Paramus, NJ, USA

ASSOCIATE EDITORS

Jianhua Fu

Department of Thoracic Surgery, Guangdong Esophageal Cancer Institute, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center of Cancer Medicine, Guangzhou 510060, China

Zhentao Yu

Department of Esophageal Cancer, Tianjin Cancer Hospital, Tianjin 300060, China; Department of Thoracic Surgery, Zhejiang Cancer Hospital, Hangzhou 310022, China

Yin Li

Department of Thoracic Surgery, Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou 450008, China

Keneng Chen

Department of Thoracic Surgery, Beijing Cancer Hospital, Beijing 100142, China

Xiaolong Fu

Department of Radiation Oncology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200240, China

AUTHORS

Mark S. Allen

Division of General Thoracic Surgery, Mayo Clinic, Rochester, MN, USA

Florian Augustin

Department of Visceral, Transplant and Thoracic Surgery, Innsbruck Medical University, Austria

Hasan Fevzi Batirel

Department of Thoracic Surgery, Marmara University Faculty of Medicine, Istanbul, Turkey

Marcelo F. Benveniste

Department of Diagnostic Radiology, MD Anderson Cancer Center, Houston, TX, USA

Shanda H. Blackmon

Division of General Thoracic Surgery, Mayo Clinic, Rochester, MN, USA

Stephen D. Cassivi

Division of General Thoracic Surgery, Mayo Clinic, Rochester, MN, USA

Chun Chen

Department of Thoracic Surgery, Fujian Medical University Union Hospital, Fuzhou 350001, China

Keneng Chen

Department of Thoracic Surgery, Beijing Cancer Hospital, Beijing 100142, China

Hezhong Chen

Department of Cardiothoracic Surgery, Changhai Hospital, Shanghai 200433, China

Gang Chen

Department of Thoracic Surgery, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Wenhu Chen

Department of Thoracic Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Baishen Chen

Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Department of Thoracic Surgery, Sun Yat-sen Memorial Hospital, Sun Yatsen University, Guangzhou 510120, China

Ju Chen

Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Department of Thoracic Surgery, Sun Yat-sen Memorial Hospital, Sun Yatsen University, Guangzhou 510120, China

Zhenguang Chen

Department of Thoracic Surgery, The First Affiliated Hospital, Sun Yat-sen University, Guangdong, Guangzhou 510080, P.R. China

Se Hoon Choi

Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Neil A. Christie

Department of Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Giovanni Maria Comacchio

Division of Thoracic Surgery, Cardio-Thoracic and Vascular Sciences Department, University of Padova, Padova, Italy

Frank M. Corl

Department of Medical Illustration/Animation, Mayo Clinic, Rochester, MN, USA

Youbing Cui

Department of Thoracic Surgery, First Af liated Hospital of Jilin University, Changchun 130021, China

Anna De Rosa

Department of Clinical and Experimental Medicine, Neurology Unit, Robotic Multidisciplinary Centre for Surgery, Cardiothoracic and Vascular Surgery Department, University of Pisa, Italy

Frank Detterbeck

Section of Thoracic Surgery, Yale Thoracic Oncology Program, Yale University School of Medicine, New Haven, CT, USA

Jianyong Ding

Department of Thoracic Surgery, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Wentao Fang

Department of Thoracic Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Olivia Fanucchi

Department of Cardiac, Thoracic and Vascular Surgery, Thoracic Surgery Division, University of Pisa, Italy

Pier Luigi Filosso

Department of Thoracic Surgery, University of Torino, Turin, Italy

Jianhua Fu

Department of Thoracic Surgery, Guangdong Esophageal Cancer Institute, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center of Cancer Medicine, Guangzhou 510060, China

Xiangfeng Gan

Department of Thoracic Surgery, General Hospital of Ningxia Medical University, Yinchuan 750004, China

Lanting Gao

Department of Radiation Oncology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Nicolas Girard

Department of Respiratory Medicine and Thoracic Oncology, Hospices Civils de Lyon, Lyon, France

Zhitao Gu

Department of Thoracic Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Francesco Guerrera

Department of Thoracic Surgery, University of Torino, Turin, Italy

Ayumi Hachimaru

Division of Thoracic and Cardiovascular Surgery, Fujita Health University School of Medicine, 1-98 Dengakugakubo Kutsukake, Toyoake, Aichi 470-1192, Japan

Yongtao Han

Department of Thoracic Surgery, Sichuan Cancer Hospital, Chengdu 610041, China

Yong Han

Department of Thoracic Surgery, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Nicholas R. Hess

University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Monique Hochstenbag

Department of Cardiothoracic Surgery, University Medical Centre of Maastricht, Netherlands

Lijun Huang

Department of Thoracic Surgery, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Lei Jiang

Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University, Shanghai 200433, China

Gening Jiang

Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University, Shanghai 200433, China

Shinji Kaneda

Division of Thoracic and Cardiovascular Surgery, Fujita Health University School of Medicine, 1-98 Dengakugakubo Kutsukake, Toyoake, Aichi 470-1192, Japan

Marlies Keijzers

Department of Cardiothoracic Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

Hyeong Ryul Kim

Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Yong-Hee Kim

Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Dong Kwan Kim

Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Kazuya Kondo

Department of Oncological Medical Services, Graduate School of Biomedical Sciences, Tokushima University, Tokushima 770-8509, Japan

Robert J. Korst

Department of Thoracic Surgery, Icahn School of Medicine, Mount Sinai Health System, New York, NY, USA; Valley/Mount Sinai Comprehensive Cancer Care, Paramus, NJ, USA

Geun Dong Lee

Department of Thoracic Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

Ryan M. Levy

Department of Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Hecheng Li

Department of Thoracic Surgery, Ruijin Hospital, Shanghai Jiao Tong University school of Medicine, Shanghai 200025, China

Hui Liu

Department of Radiation Oncology, Sun Yat-sen University Cancer Center, Guangzhou 510060, China

Yin Li

Department of Thoracic Surgery, Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou 450008, China

Xiao Li

Department of Thoracic Surgery, Peking University People's Hospital, Beijing, China

Xiaofei Li

Department of Thoracic Surgery, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Guanghui Liang

Department of Thoracic Surgery, Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou 450008, China

Lei Lin

Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University, Shanghai 200433, China

Yongyu Liu

Department of Thoracic Surgery, Liaoning Cancer Hospital, Shenyang 110042, China

Yangchun Liu

Department of Thoracic Surgery, Jiangxi People's Hospital, Nanchang 330006, China

Yuan Liu

Department of Thoracic Surgery, Shanghai Chest Hospital, Jiao Tong University, Shanghai 200030, China

Qianwen Liu

Department of Thoracic Surgery, Guangdong Esophageal Cancer Institute, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center of Cancer Medicine, Guangzhou 510060, China

Ming Liu

Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University, Shanghai 200433, China

Qiang Lu

Department of Thoracic Surgery, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Marco Lucchi

Division of Thoracic Surgery, Robotic Multidisciplinary Centre for Surgery, Cardiothoracic and Vascular Surgery Department, University of Pisa, Italy

James D. Luketich

Department of Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Changxing Lv

Department of Radiation Oncology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Jianqun Ma

Department of Thoracic Surgery, Harbin Medical University Cancer Hospital, Harbin 150040, Heilongjiang, China

Ke Ma

Department of Thoracic Surgery, Sichuan Cancer Hospital, Chengdu 610041, China

Zhao Ma

Department of Esophageal Cancer, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center of Cancer, Key Laboratory of Cancer Prevention and Therapy of Tianjin City, Tianjin 300060, China

Ryo Maeda

Division of Thoracic and Cardiovascular Surgery, Fujita Health University School of Medicine, 1-98 Dengakugakubo Kutsukake, Toyoake, Aichi 470-1192, Japan

Jos G. Maessen

Department of Cardiothoracic Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

Michelangelo Maestri

Department of Clinical and Experimental Medicine, Neurology Unit, Robotic Multidisciplinary Centre for Surgery, Cardiothoracic and Vascular Surgery Department, University of Pisa, Italy

Teng Mao

Department of Thoracic Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Mirella Marino

Department of Pathology, Regina Elena National Cancer Institute, Rome, Italy

Edith M. Marom

Department of Diagnostic Radiology, Chaim Sheba Medical Center, Ramat-Gan, Israel

Giuseppe Marulli

Division of Thoracic Surgery, Cardio-Thoracic and Vascular Sciences Department, University of Padova, Padova, Italy

Alexander Marx

Institute of Pathology, University Medical Centre Mannheim, University of Heidelberg, Mannheim, Germany

Franca Melfi

Division of Thoracic Surgery, Robotic Multidisciplinary Centre for Surgery, Cardiothoracic and Vascular Surgery Department, University of Pisa, Italy

Claire Merveilleux du Vignaux

Department of Respiratory Medicine and Thoracic Oncology, Hospices Civils de Lyon, Lyon, France

Alfredo Mussi

Division of Thoracic Surgery, Robotic Multidisciplinary Centre for Surgery, Cardiothoracic and Vascular Surgery Department, University of Pisa, Italy

Francis C. Nichols

Division of General Thoracic Surgery, Mayo Clinic, Rochester, MN, USA

Berker Ozkan

Department of Thoracic Surgery, Istanbul Medical School, Istanbul University, Istanbul, Turkey

Sukhmani K. Padda

Department of Medicine (Oncology), Stanford University/ Stanford Cancer Institute, Stanford, CA, USA

Giovannella Palmieri

Rare Tumors Reference Center, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy

Liewen Pang

Department of Thoracic Surgery, Huashan Hospital, Fudan University, Shanghai 200032, China

Qingsong Pang

Department of Radiotherapy, Tianjin Medical University Cancer Hospital, Tianjin, China

Seung-Il Park

Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Arjun Pennathur

Department of Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Edoardo Pescarmona

Department of Pathology, Regina Elena National Cancer Institute, Rome, Italy

Afroditi Petsa

Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK

Kevin Phan

The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia

Federico Rea

Department of Cardiac, Thoracic and Vascular Sciences, Thoracic Surgery Division, University of Padova, Italy

Roberta Ricciardi

Department of Clinical and Experimental Medicine, Neurology Unit, Division of Thoracic Surgery, Robotic Multidisciplinary Centre for Surgery, Cardiothoracic and Vascular Surgery Department, University of Pisa, Italy

Anja C. Roden

Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN 55905, USA

Phillip G. Rowse

Division of General Thoracic Surgery, Mayo Clinic, Rochester, MN, USA

Enrico Ruffini

Department of Thoracic Surgery, University of Torino, Turin, Italy

Tommaso Salvitti

Department of Pathology, Regina Elena National Cancer Institute, Rome, Italy

Alberto Sandri

Department of Thoracic Surgery, University of Torino, Turin, Italy

Inderpal S. Sarkaria

Department of Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Thomas A. Schmid

Department of Visceral, Transplant and Thoracic Surgery, Innsbruck Medical University, Austria

Yi Shen

Department of Thoracic Surgery, Affiliated Hospital of Qingdao University, Qingdao 266001, China

K. Robert Shen

Division of General Thoracic Surgery, Mayo Clinic, Rochester, MN, USA

Zhuojian Shen

Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Department of Thoracic Surgery, Sun Yat-sen Memorial Hospital, Sun Yatsen University, Guangzhou 510120, China

Yan Shen

Department of Radiology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Lei Su

Department of Thoracic Surgery, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

Takashi Suda

Division of Thoracic and Cardiovascular Surgery, Fujita Health University School of Medicine, 1-98 Dengakugakubo Kutsukake, Toyoake, Aichi 470-1192, Japan

Yasushi Takagi

Division of Thoracic and Cardiovascular Surgery, Fujita Health University School of Medicine, 1-98 Dengakugakubo Kutsukake, Toyoake, Aichi 470-1192, Japan

Lijie Tan

Department of Thoracic Surgery, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Liejie Tan

Department of Thoracic Surgery, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Qunyou Tan

Department of Thoracic Surgery, Daping Hospital, Research Institute of Surgery Third Military Medical University, Chongqing 400042, China

Richard Tjahjono

The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia

Sachiko Tochii

Division of Thoracic and Cardiovascular Surgery, Fujita Health University School of Medicine, 1-98 Dengakugakubo Kutsukake, Toyoake, Aichi 470-1192, Japan

Daisuke Tochii

Division of Thoracic and Cardiovascular Surgery, Fujita Health University School of Medicine, 1-98 Dengakugakubo Kutsukake, Toyoake, Aichi 470-1192, Japan

Alper Toker

Department of Thoracic Surgery, Istanbul Medical School, Istanbul University, Istanbul, Turkey

Federico Venuta

Department of Thoracic Surgery, University of Rome Sapienza, Policlinico Umberto I, Fondazione Eleonora Lorilard Spencer Cenci, Rome, Italy

Heather A. Wakelee

Department of Medicine (Oncology), Stanford University/ Stanford Cancer Institute, Stanford, CA, USA

Yun Wang

Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu 610041, China

Changlu Wang

Department of Radiation Oncology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Fangrui Wang

Department of Thoracic Surgery, Huashan Hospital, Fudan University, Shanghai 200040, China

Hao Wang

Department of Thoracic Surgery, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Juzheng Wang

Department of Thoracic Surgery, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Minghui Wang

Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Department of Thoracic Surgery, Sun Yat-sen Memorial Hospital, Sun Yatsen University, Guangzhou 510120, China

Yucheng Wei

Department of Thoracic Surgery, Affiliated Hospital of Qingdao University, Qingdao 266001, China

Christel Weiss

Department of Medical Statistics and Biomathematics, University Medical Centre Mannheim, University of Heidelberg, Mannheim, Germany

Dennis A. Wigle

Division of General Thoracic Surgery, Mayo Clinic, Rochester, MN, USA

Jie Wu

Department of Pathology, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Liang Wu

Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University, Shanghai 200433, China

Jin Xiang

Department of Pathology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center of Cancer Medicine, Guangzhou 510060, China

Ashleigh Xie

The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia

Xuan Xie

Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Department of Thoracic Surgery, Sun Yat-sen Memorial Hospital, Sun Yatsen University, Guangzhou 510120, China

Xia Xu

Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Department of Thoracic Surgery, Sun Yat-sen Memorial Hospital, Sun Yatsen University, Guangzhou 510120, China

Tristan D. Yan

The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia; Department of Cardiothoracic Surgery, Royal Prince Alfred Hospital, Sydney, Australia; University of Sydney, Sydney, Australia

Fu Yang

Department of Thoracic Surgery, Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai 200080, China

Jianding Ye

Department of Radiology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China

Zhentao Yu

Department of Esophageal Cancer, Tianjin Cancer Hospital, Tianjin 300060, China

Jie Yue

Department of Esophageal Cancer, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center of Cancer, Key Laboratory of Cancer Prevention and Therapy of Tianjin City, Tianjin 300060, China

Peng Zhang

Department of Endocrinology, Tianjin Medical University General Hospital, Tianjin 300052, China

Renquan Zhang

Department of Thoracic Surgery, First Af liated Hospital of Anhui Medical University, Hefei 230022, China

Jie Zhang

Department of Pathology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200032, China

Hongdian Zhang

Department of Esophageal Cancer, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center of Cancer, Key Laboratory of Cancer Prevention and Therapy of Tianjin City, Tianjin 300060, China

Huizhong Zhang

Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Department of Thoracic Surgery, Sun Yat-sen Memorial Hospital, Sun Yatsen University, Guangzhou 510120, China

Jinbo Zhao

Department of Thoracic Surgery, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Yizhuo Zhao

Department of Pulmonary Medicine, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China

Zhengwei Zhao

Department of Thoracic Surgery, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Xinming Zhou

Department of Thoracic Surgery, Zhejiang Cancer Hospital, Hangzhou 310022, China

Yongan Zhou

Department of Thoracic Surgery, Tangdu Hospital, the Fourth Military Medical University, Xi'an 710038, China

Chengchu Zhu

Department of Cardiothoracic Surgery, Taizhou Hospital, Wenzhou Medical University, Linhai, Zhejiang, People's Republic of China

Lei Zhu

Department of Pathology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200032, China

Cover Image Illustrator

Zhijing Xu, Shanghai, China

Executive Typesetting Editor

Beibei Chen, AME Publishing Company

We are pleased to announce that the "AME Research Time Medical Book Series" co-launched by AME Publishing Company, Central South University Press and DXY.cn will be published as scheduled.

Finishing my medical degree after 4 years and 3 months of study, I decided to quit going on to become a doctor only after 3 months of training. After that, I had been muddling through days and nights until I started engaging in medical academic publishing. Even 10 years after graduation, I had not totally lost the affection for being a doctor. Occasionally, that subconscious feeling would inadvertently arise from the bottom of my heart.

In April 2011, Mr. Tiantian Li, the founder of DXY.cn, and I had a business trip to Philadelphia, where we visited the Mütter Museum. As part of The College of Physicians of Philadelphia, the museum was founded in 1858 and has now become an exhibition hall of various diseases, injuries, deformities, as well as ancient medical instruments and the development of biology. It displays more than 20,000 pieces of items including pictures of wounded bodies at sites of battle, remains of conjoined twins, skeletons of dwarfs, and colons with pathological changes. They even exhibited several exclusive collections such as a soap-like female body and the skull of a two-headed child. This museum is widely known as "BIRTHPLACE OF AMERICAN MEDICINE". Entering an auditorium, we were introduced by the narrator that the inauguration ceremony of the Perelman School of Medicine at the University of Pennsylvania would take place there every year. I asked Mr. Li, "If it was at this auditorium that you had the inauguration ceremony, would you give up being a doctor?" "No," he answered.

In May 2013, we attended a meeting of British Medical Journal (BMJ) and afterwards a gala dinner was held to present awards to a number of outstanding medical teams. The event was hosted annually by the Editor-in-Chief of BMJ and a famous BBC host. Surprisingly, during the award presentation, the speeches made by BMJ never mentioned any high impact papers the teams had published in whichever prestigious journals over the past years. Instead, they laid emphasis on the contributions they had made on improving medical services in certain fields, alleviating the suffering of patients, and reducing the medical expenses.

Many friends of mine wondered what AME means.

AME is an acronym of "Academic Made Easy, Excellent and Enthusiastic". On September 3, 2014, I posted three pictures to social media feeds and asked my friends to select their favourite version of the AME promotional leaflet. Unexpectedly we obtained a perfect translation of "AME" from Dr. Yaxing Shen, Department of Thoracic Surgery, Zhongshan Hospital, Shanghai, who wrote: enjoy a grander sight by devoting to academia (in Chinese, it was adapted from the verse of a famous Chinese poem).

AME is a young company with a pure dream. Whilst having a clear focus on research, we have been adhering to the core value "Patients come first". On April 24, 2014, we developed a public account on WeChat (a popular Chinese social media) and named it "Research Time". With a passion for clinical work, scientific research and the stories of science, "Research Time" disseminates cutting-edge breakthroughs in scientific research, provides moment-to-moment coverage of academic activities and shares rarely known behind-the-scene stories. With global vision, together we keep abreast of the advances in clinical research; together we meet and join our hands at the Research Time. We are committed to continue developing the AME platform to aid in the continual forward development and dissemination of medical science.

It is said that how one tastes wine indicates one's personality. We would say how one reads gives a better insight to it. The "AME Research Time Medical Books Series" brings together clinical work, scientific research and humanism. Like making a fine dinner, we hope to cook the most delicate cuisine with all the great tastes and aromas that everyone will enjoy.

Stephen Wang Founder & CEO, AME Publishing Company Thymic Epithelial Tumors (TETs) are rare neoplastic diseases, but the most common anterior mediastinal tumors in the adulthood. TETs are classified according to the World Health Organization (WHO) histopathological classification, which distinguishes thymomas from thymic carcinomas (tumors cathegory which also includes thymic neuroendocrine ones). Their rarity, along with the lack of randomized clinical trials (RCTs) make TETs' global management still questioned, and only few clinical recommendations currently exist.

The interest to the thymic disorders management has never been so strong as in the last few years. A huge number of articles about biology, associated parathymic syndromes, radiological tumor's appearance, surgery, induction/adjuvant medical therapy and radiotherapy have been published especially after 2014. These reflect of single Institution, multicenter experiences, or are the reults of retrospective societal databases. These datasets are commonly used to investigate the biological aggressiveness of the rare thymic tumours as well as their prognostic correlates.

Some recent examples of their usage and their effectiveness are the outcome of aggressive neoplasms (Thymic Carcinomas or Neuroendocrine Thymic tumors as well as their comparison), tumor's size as valuable predictor for complete resection and possible recurrence's development, the role of Myasthenia Gravis (MG) in thymomas outcome and, finally, the multimodality approach importance definitive demonstration while treating advanced lesions.

Last but not least, historically more than 15 different TETs' staging systems have been proposed and used, the most common of which were the Masaoka one and its update by Koga and Colleagues. Few years ago, under the International Association for the Study of Lung Cancer (IASLC) aegis, the need for a new TNM based staging system was evident, in accordance with other solid tumors. Therefore, merging the International Thymic Malignancy Interest Group (ITMIG), the European Society for Thoracic Surgeons (ESTS) and the Japanese Association for Research on the Thymus (JART) datasets, a retrospective analysis of the outcome of several thousand treated patients worldwide made the new TNM system final processing possible. Nowadays this represents the official staging system for thymic tumors.

The new prospective societal datasets development (ITMIG & ESTS, particularly) will furthermore improve our knowledge on some specific issues concerning TETs' treatment, and result are expected in few years. In particular, they will be focused on the optimal MG surgical management, the role of minimally-invasive procedures (VATS, robotic, transcervical or subxiphoid approaches), the role of lymphadenectomy, the correct indication for induction/adjuvant treatments in locally-aggressive lesions as well as the importance of personalised medicine, following the recent identification of molecular alterations occurring in the KIT, vascular endothelial growth factor receptors (VEGFRs) and mammalian target of rapamycin (mTOR) signalling pathways. This is the future.

This book is the result of the Authors' tremendous effort in collecting and making available all that was recently published on TET's diagnosis and management: they deserve a very major credit for putting this on.

Also AME Publishing Company, once again, demonstrated its extreme entrepreneurship, believing in the project and carefully curing it with a meticulous print apparel. The reading of this book should be suggested to all the researchers of thymic disorders and I'm sure this book will become a landmark text on this field.

Pier Luigi Filosso, MD, FECTS

Associate Professor of Thoracic Surgery, University of Torino, Italy (Email: pierluigi.filosso@unito.it).

Preface for *Thymic Malignancy*: More Hands Produce Stronger Flames!

Thymic epithelial tumors (TET) are neoplasms that arise from the thymic gland usually in the prevascular mediastinum. They are considered malignant neoplasms as they can recur, metastasize and potentially lead to the death of the patient (1,2). However, many patients have a favorable outcome and eventually die of another cause. TET are rare with an incidence of 1.5 cases/million population/year. Because of their paucity and their usually favourable outcome, TET are difficult to study. While many single-institution studies of clinico-pathologic features have been published, these reports usually include a relative small number of cases. In addition, small case series to compare different treatment options are available, however, again, these studies in general lack power and are retrospective in nature. Prospective randomized clinical trials are extremely challenging and have not been performed on a large scale. However, such trials would be important as some TET behave in an aggressive manner and standardized treatment of these tumors is currently lacking.

The paucity of TET and their in general excellent prognosis requires "more hands to produce stronger flames". Joint global efforts are crucial to acquire a sufficient number of such cases for meaningful studies to advance our knowledge of the disease and its optimal treatment regimens. Within recent years, regional [Chinese Alliance for Research in Thymomas (ChART) (3), Japanese Association for Research of the Thymus (JART) (4), Surveillance, Epidemiology, and End Results (SEER) database (5)] and global [European Society of Thoracic Surgeon (ESTS) (6), International Thymic Malignancy Interest Group (ITMIG) (7)] organizations have been formed to bring physicians of various specialties including medical oncology, neurology, pathology, radiation oncology, radiology, and thoracic surgery, other health care personnel, patients and patient advocates from around the world together to study TET. Large regional and international databases comprised of patients with the disease are an important foundation of these studies. These databases are of retrospective and prospective nature and are used for the study of clinical features, pathologic subtypes and findings, surgical procedures, treatment strategies and outcomes as presented in many of the articles in this book. These databases will also potentially be advantageous to discern ethnic differences in the pathogenesis of the disease. Moreover, only these kind of global efforts and international collaboration will allow for future prospective randomized trials that might explore different treatment options and possibly personalized treatment.

To standardize treatment, global standardization of diagnosis and staging of TET are important. Therefore, major efforts have been undertaken within the last decade to enhance reproducibility of the pathologic subtyping of TETs and to develop a staging system that can be used for all subtypes of TET including thymoma, thymic carcinoma and thymic neuroendocrine tumors. As a result, the most recent WHO classification of TET was published in 2015 and pathologists are encouraged to use that for their diagnosis of TET and their subtypes (1,8) While over the years institutions have used the Masaoka staging (9) or the Masaoka-Koga staging (10) to stage thymomas and/or the TNM staging that was proposed by the WHO in 2004 (11) to stage thymic carcinomas, the International Association of the Study of Lung Cancer (IASLC) together with ITMIG proposed a staging for TET that now can be used for thymomas, thymic carcinomas and thymic neuroendocrine tumors (12) This proposed staging system was incorporated in the 8th AJCC/UICC TNM staging classification and is currently introduced or will be introduced shortly globally for staging of TET.

This book illustrates the remarkable results in the study of TET that have been accomplished through collaborative projects at regional and global level. Many of these projects were only possible thanks to established retrospective and prospective regional and international databases. These concerted efforts built a solid foundation for future projects such as the molecular study of TET and studies towards standardized and personal treatment of patients with these tumors amongst other projects. "More Hands Produce Stronger Flames!"

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Anja C. Roden, MD

Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN 55905, USA (Email: Roden.anja@mayo.edu). Thymic tumors are a series of malignancies with different biological behaviors, clinical manifestation, and prognosis. Because of their unique nature and rarity, many issues remain to be explored so as to improve management outcomes. And there has never been any book specialized in the disease. Therefore, I congratulate AME on publishing this series of papers as a monograph, which is certainly unprecedented.

In recent years, two advances have contributed greatly to improved understanding of thymic tumors. The first is international and regional collaborations in joint studies for this relatively rare disease. Included in this compilation of related publications are the results from the Chinese Alliance for Research in Thymomas (ChART) retrospective studies that cover the most concerned questions in diagnosis and management of thymic malignancy (Part I. General concepts and strategies in the management of thymic malignancies). These include preoperative diagnosis, induction and adjuvant therapies, surgical procedures, and concomitant myasthenia. Although many of these still remain unsolved, it is a great step forward and help pave the way for future studies. And there is reason to believe that readers would benefit greatly from the comments on these studies by an international panel, many of them have been actively involved in the International Thymic Malignancy Interest Group (ITMIG).

The second and also a striking progress owes greatly to the advance in modern technology. Similar to the recent trend in lung and esophageal cancer surgery, minimally invasive approaches in thymic surgery has also attracted increasing attention and has contributed to improved outcome while maintaining similar oncological results. It is thus not surprising at all to notice that *Part II*, *Surgical therapies for thymic malignancies* of this book consists almost exclusively of topics on minimally invasive thymic surgery. A diversity of approaches is introduced here, including both left and right, subxiphoid VATS as well as robotic thymectomy. On top of these are introduction and perspectives on oncological principles and outcomes of minimally invasive surgery in management of thymic tumors. Hopefully this book would help disseminate the ideas of standardized management in thymic malignancy to many medical practitioners involved.

More hands build a higher flame. This book is not yet a comprehensive text that would solve all problems in the related area. Yet, it represents the state of the art in the management of thymic tumors and collected wisdom from colleagues in different specialties related to this interesting and important disease. The contents included here would be helpful for all medical professionals and researchers in the field and better inspire those interested to probe further for continuing improvement. We very much look forward to updating the contents and make it more educational in a future edition.

Wentao Fang, MD

Department of Thoracic Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai 200030, China (Email: vwtfang@hotmail.com; vwtfang12@shchest.org). Preface

Although tumors of the thymus gland are rare, they are not infrequently encountered by thoracic oncologic specialists. Thymic tumors have been managed for many decades using clinicians' anecdotal experience because their rarity has prohibited the performance of high quality clinical studies. Over the past decade, however, the landscape has begun to change for two major reasons. First, the development of formal research organizations dedicated to producing clinically applicable data for the everyday management of patients with thymic tumors has accelerated interest in these tumors. These organizations include the Chinese Alliance for Research in Thymomas (ChART), the Japanese Association for Research on the Thymus (JART) as well as the International Thymic Malignancy Interest Group (ITMIG). All of these organizations bring together physicians and researchers, working collaboratively, to try to answer clinically relevant questions regarding the management of patients with thymic tumors. Second, these organizations have dedicated resources and energy to develop multi-institutional databases (in the case of ITMIG, a multinational database) to serve as repositories of high quality patient data to be used for research purposes. Through this pooling of data and collaboration, research involving data from thousands of patients is now being performed with regularity, resulting in tangible benefits for patients.

This book represents a compilation of manuscripts that reflect recent contributions to the literature regarding thymic tumors. Several of these studies have resulted from analyses performed using the aforementioned large datasets compiled by investigators from all over the world, while others represent literature reviews by recognized experts in the field of thymic tumors, or single institutional experiences. Topics range from treatment strategies for complex cases to the technical aspects of cutting edge surgical techniques. Caregivers will find this collection of manuscripts an invaluable resource when involved in the management of patients with any type of thymic tumor, regardless of their specialty.

Robert J. Korst, MD

Department of Thoracic Surgery, Icahn School of Medicine, Mount Sinai Health System,
New York, NY, USA;
Valley/Mount Sinai Comprehensive Cancer Care,
Paramus, NJ, USA.
(Email: korsro@valleyhealth.com).