Mistletoe: From Mythology to Evidence-Based Medicine
Translational Research in Biomedicine

Vol. 4

Series Editor

Samuel H.H. Chan  Kaohsiung

Associate Editor

Julie Y.H. Chan  Kaohsiung

The Chang Gung Medical Foundation is the patron of this book series.
Mistletoe: From Mythology to Evidence-Based Medicine

Volume Editors

Kurt S. Zänker  Witten
Srini V. Kaveri  Paris/Mumbai

5 figures, 5 in color, 5 tables, 2015
Contents

VI Foreword
Chan, S.H.H. (Kaohsiung)

VII Preface
Zänker, K.S. (Witten); Kaveri, S.V. (Paris/Mumbai)

1 Mistletoe through Cultural and Medical History: The All-Healing Plant Proves to Be a Cancer-Specific Remedy
Ramm, H. (Arlesheim)

11 Chemical Constituents of Viscum album L.: Implications for the Pharmaceutical Preparation of Mistletoe
Urech, K.; Baumgartner, S. (Arlesheim)

24 The Anti-Cancer Activity of Mistletoe Preparations, as Related to Their Polyphenolic Profiles
Schramm, H.M. (Arlesheim)

39 From Berlin and Witten to Southampton and Hamburg: 25 Years of Mistletoe Research Cooperation
Schumacher, U.; Pfüller, U. (Hamburg)

48 Mistletoe Compounds as Anti-Cancer Drugs: Effects and Mechanisms in the Treatment of Glioblastoma
Schötterl, S.; Naumann, U. (Tübingen)

57 Cancer Surgery and Supportive Mistletoe Therapy: From Scepticism to Randomised Clinical Trials
Galun, D. (Belgrade); Tröger, W. (Freiburg); Milicevic, M. (Belgrade)

67 Dissecting the Anti-Inflammatory Effects of Viscum album: Inhibition of Cytokine-Induced Expression of Cyclo-Oxygenase-2 and Secretion of Prostaglandin E2
Elluru, S.R. (Linköping); Saha, C.; Hedge, P. (Paris/Compiègne); Friboulet, A. (Compiègne); Bayry, J.; Kaveri, S.V. (Paris)

74 Dancing with the Devil: Cancer-Related Fatigue, from Inflammation to Treatment Options
Zänker, K.S. (Witten)

82 Author Index
83 Subject Index
Foreword

Welcome to Volume Four of *Translational Research in Biomedicine*, a monograph series dedicated to the dissemination of seminal information in contemporary biomedicine with a translational orientation. This volume marks the second installment of this series under the generous patronage of Chang Gung Medical Foundation of Taiwan. This patronage substantially reduces the increasing financial constraints on scientific publication and allows us to concentrate on publishing text on timely and crucial themes in translational medicine.

This volume is designed to be a key reference on mistletoe. It is intended to reveal all of the conflicts of interest, bias, omissions, and scientific censorship related to the use of mistletoe in oncology. In the spirit of translational medicine, this volume will provide readers with an understanding of the mythology, the culture, the contextuality and the personalized treatment associated with mistletoe, along with fundamental knowledge based on molecular biology, chemistry and biochemistry. Whereas the majority of the literature on plant and natural products has a preferential Eastern flavor, this volume is unique in its own right because it represents our contemporary understanding of mistletoe from a European perspective.

I wish to express my deepest appreciation to Professors Kurt S. Zänker and Srinivasa V. Kaveri, whose patience and sustaining efforts have made this timely volume, or ‘Mistletoe: From Mythology to Evidence-Based Medicine’, a reality. I also wish to acknowledge the capable hands of Thomas Nold and Ricarda Cueni at S. Karger AG during the development and production of this volume. Last but not least, the publication of *Translational Research in Biomedicine* would not have been possible without the foresight, enthusiasm and whole-hearted support of my dear friend Dr. Thomas Karger.

*Samuel H.H. Chan*

Series Editor
Preface

It is a great honor for us (Kurt S. Zänker (Witten) and Srini V. Kaveri (Paris/Mumbai)) to edit this book on mistletoe, *From Mythology to Evidence-Based Medicine*, within the book series *Translational Research in Biomedicine*, published by Karger, as guest editors. With his outstanding reputation in biomedicine and the peer-reviewed approval of the chapters’ content, the Series Editor – Samuel H.H. Chan (Kaohsiung) – is a guarantor of a high international scientific standard for revealing and disseminating experimental and clinical results, embedded into a cultural context, regarding the use of mistletoe preparations in biomedicine.

We have been fortunate to recruit competent scientists who have been working in the field of translational mistletoe research for decades, and we thank them for their distinguished contributions.

Thomas Kuhn [1] fathered, defined and popularized the concept of ‘paradigm shift’. Currently, a long-standing, historically based view of medicine centered on the intuition, passion and creativity of the individual scientist is being replaced. The replacement is taking place stepwise via a series of peaceful interludes punctuated by biotechnologically and digitally violent revolutions that place value on data collection itself in biomedicine. The 21st century is predestined for a paradigm shift in biomedicine because exciting molecular biology results in biomedical research, the dramatic explosion of (nano-)biotechnology and the digital revolution provide the basis for P4 Medicine in cancer research [2]. A mandatory prerequisite in personalized medicine – and one of the P4 items – is to collect the greatest quantity of disease-related data sets possible in the hope of better diagnosis and treatment. However, where are the sophisticated algorithms for mining; integrating; modeling; and, at the patient’s end, dissecting the large, heterogeneous biological data sets to generate an individualized, actionable and meaningful model to determine what is the best individual therapy at the right time?

At this time, biomedicine is addressing two ideas: i) the idea of applying an object (disease)-orientated collection of computing-powered data sets – from bench to bytes to bedside – and ii) the conservative idea of converting what is perceived into a personal scientific concept to develop hypothesis-driven biomedical starting points for perceiving and reconstructing a patient’s individual world for better diagnosis and therapy.

It might sound complex, but behind these two ideas lie some simple concepts. In the future, for successful biomedicine, we need both, and both should provide mu-
tual assistance in order to facilitate biomedical applications of their directives to the well-being of patients.

Biomedicine is not only basic science but also humanities and cultural sciences. The history of medicine clearly shows that many fundamental discoveries and inventions in medicine are the results of the interactions of these entities.

This book is a treasure chest for all physicians and caregivers in biomedicine who want to see how mistletoe research developed into its translational and clinical applications today. For the first time, this book depicts the trajectory of mistletoe research in oncology from the beginning, following the philosophy – from mythology to evidence-based medicine – behind plotting the scientific course of human endeavors in a digital world.

The book starts with a chapter by Hartmut Ramm on the ancient use of mistletoe and its cultural myths in religion, in health and in disease. The molecular diversity of mistletoe constituents, as analyzed by modern chemical methods, is described by Konrad Urech and Stephan Baumgartner. The biodiversity of these substances is set in a functional context of anti-cancer activities by Henning Schramm. The chapters reporting on translational and clinical mistletoe research start with a chapter by Udo Schumacher and Uwe Pfüller, who give a timeline of important stages and results in the development of mistletoe research. Sonja Schötterle and Ulrike Naumann provide evidence that mistletoe-based drugs are candidates for use as concomitant therapeutics in parallel to standard therapy, e.g. for glioblastoma. Danijel Galun, Wilfried Tröger and Miroslav Milicevic give a summary of the use of mistletoe preparations as supportive care in cancer surgery, with special reference to pancreatic cancer. Sri Ramula Elluru, Chaitrali Saha, Pushpa Hedge et al. present translational results obtained for mistletoe preparations targeting cellular and molecular mechanisms of the immune system and inflammation. These translational research data provide a rationale for addressing cancer-related fatigue (CRF) clinically using mistletoe. It is very likely that inflammatory processes are involved in the etiology of CRF. Therefore, plant-derived anti-inflammatory substances, e.g. those derived from mistletoe preparations, might be the first candidates for fighting against CRF when applied together with conventional anti-tumor protocols. Kurt S. Zänker gives clinical evidence that CRF can be alleviated by the use of mistletoe preparations in oncology.

We are grateful to the publisher Karger (Switzerland) and to Samuel H.H. Chan (Kaohsiung), the Series Editor, for this platform to communicate a better understanding of the medical history; the plant chemistry; and the experimental, translational and functional activities of mistletoe constituents in the field of oncology to the appropriate scientific communities. Taken together, this information contributes to holistic and personalized medicine.

Winter 2014

Kurt S. Zänker, Witten
Srini V. Kaveri, Paris/Mumbai
Volume Editors

References