

BOOK SERIES - 50th Year of Hacettepe University
Series Editor: Adil Denizli

RESTORATIVE MEDICINE

İbrahim Vargel
Editor



**HACETTEPE
UNIVERSITY
2018**

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Adil Denizli *Series, Editor*

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Kitapta yer alan yazı, resim ve şekil 5846 sayılı yasanın hükümlerine göre kısmen ya da tamamen basılamaz, dolaylı dahi olsa kullanılamaz, teksir, fotokopi ya da başka bir teknikle çoğaltılamaz. Her hakkı saklıdır, HACETTEPE ÜNİVERSİTESİ'ne aittir.

PREFACE

We have proudly celebrated the 50th anniversary of the foundation of Hacettepe University. We take pride in being one of the most successful universities in Turkey and being ranked among the leading universities in the World. Since the year 1967, when Hacettepe earned the status of ‘University’, it has never given up on its principle of continuously going ahead and reaching for the very best. Hacettepe, always preserving its values and basic principles, has become a pioneer university that has been intertwined with the society and pursued innovations, achieving many “firsts” ahead of others.

From medicine to biology, philosophy, statistics, physics and chemistry; from history of arts to the English, German and French languages; from sociology to engineering, fine arts and conservatory, Hacettepe University started almost 50 years ago developing interdisciplinary collaborations across a wide range of scientific fields, a research trend which has achieved a status of global recognition in the 21st century.

Hacettepe University, which was recognized as “Research University” by the decision of Council of Higher Education, dated September 26, 2017, has built a strong “brand” image over these 50 years with its qualified and unique contributions to science in Turkey and has been the country’s gateway to global scientific advances. It has graduated tens of thousands of students, each of whom has been our source of pride with their contributions to science, society and humanity as well as with their worldwide achievements. So have its graduates always been proud of Hacettepe.

Hacettepe University owes its success to its people who have always aimed to move forward by promoting interdisciplinarity and without giving up on the understanding “To the leading edge... Toward being the best...”

The Turkish and English series of books you are presented have been prepared in memory of the 50th anniversary of Hacettepe University by Prof. Dr. Adil Denizli, a distinguished researcher and faculty member who has heartily devoted himself to his university and science. Among the editors and authors of the book series are respected scientists from Hacettepe University, Turkey and abroad. The series covers the studies from the multi-/interdisciplinary research areas of sciences, mainly from Medicine, Science and Engineering Sciences, which particularly stand out among the World’s and Hacettepe’s research interests.

Readers benefiting from these books will certainly appreciate the value of the profound contributions Hacettepe University made to science both in the country and in the World

each time they see the name of “Hacettepe University” in the context of the authors, editors, footnotes, citations and bibliographies. This work is an expression of respect for Hacettepe University and for those who have meticulously served in this university for 50 years with an interdisciplinary understanding.

Thank you Adil Denizli... I would like to express my sincere gratitude and thanks to all those who have contributed to this precious work.

I wish many 50 more years to go forward in line with our motto “To the leading edge... Toward being the best...”

Prof. Dr. A. Haluk ÖZEN
Rector

PREFACE

In 1954 “Hacettepe” was founded in two chambers of an old Ankara house as a Chair of Child Health, then in 1967 officially earned “university” status. Hacettepe University celebrated its 50th anniversary in 2017 by proud of rich heritage and the positive, life-changing impact globally through the strength of our research, teaching, innovation and enterprise. In just 50 years Hacettepe University has managed to forge a powerful global reputation as a strong research-led university. To celebrate 50th anniversary numerous standout events were planned and performed by proud of past and dreaming of the future.

The Hacettepe Book Series are published to honor the five decades of work not only for the field but also for society at large and to leave the scientific mark of Hacettepe University to the history.

Adil Denizli, Ph.D

Editor

PREFACE

Restorative Medicine (RM) is a set of procedures aiming at re-establishment, regeneration of human cell, tissues, organs and their physiological functions. Through the process of research and development, clinical trials and actual treatment of patients; it requires employment of current approach and advanced technologies. There needs to be cooperation of multiple disciplines such as life sciences, basic science, medicine, surgery, dentistry, pharmacology, engineering, biotechnology and pharmaceutical industry, investing and legislation. RM involving researchers from a variety of disciplines, is progressing faster than the expected pace in both Turkey and the world. Therefore, there is a growing need of such a book covering knowledge and experience of the RM field for the benefit of various researchers.

Regeneration/restoration is necessary for organisms to repair and prevent tissue or organ damages that are resulted from physiological and pathological conditions. Aging comes with trauma or disease-related tissue/organ insufficiency. Traffic, work, or firearm related accidents are common in Turkey. Additionally, with the aging population, there is an increase in organ failure and chronic disease incidences (kidney, heart, liver failure and nervous system damage).

Another important health problem in Turkey is rare inherited genetic disorders, which occurs more frequently due to the high consanguineous marriage rate. These disorders are cumulatively plenty and account for a large portion of health care cost. The current therapies for those rare inherited disorders are causing pain, loss of function and decrease in life quality. There needs to be more effective and cost-efficient new therapies against those genetic disorders.

In 2016, United States Department of Health and Human Services announced the “2020 A New Vision: A Future for Regenerative Medicine” document. In that report, tissue/organ design as a result of collaboration of basic science, engineering and clinical sciences is emphasized and targeted therapies with the focus of patient is announced to be the priority. With this approach, development of RM field will be accelerated; tissue/organ products will be improved; sophisticated three-dimensional tissue/organs will be succeeded and full organ regeneration is foreseen to be possible within the next 20 years. Among this escalated field, the most critical point is having the product development, clinical applications and long-term monitoring in joint with ethical and legislative regulations regarding the high quality of life and safety of patients. The corresponding strategic objections are these:

1) basic science or preclinical research in stem cell biology and microenvironment, 2) research, development and production in the RM field, 3) clinical research and applications in the RM field, 4) raising the qualitative personnel, establishment of interdisciplinary RM-focused research groups and infrastructure, 5) monitoring and evaluation within an institutional administration model. This objective and collaboration is the backbone of successful RM applications.

Hacettepe University is an important academic institution with strong base on the multi-disciplinary structure, well-established graduate education and robust research on tissue engineering. Within research and development of the RM field, the main aim is to do research on candidate diseases, to establish corresponding clinical units, and to develop three-dimensional tissue/organs. The anticipated readers of this book are researchers among the above-mentioned fields. In collaboration with basic science, engineering and clinical sciences, the prioritized research areas are inherited or acquired abnormalities, sports injury, periodontal diseases, and cancers. Another potential application area is age-related degenerative disorders, such as neurological and cerebrovascular diseases. As a whole, the research experience acquired in molecular medicine is being translated into clinical applications. As researchers gain more experience with the help of technological advancement, regenerative medicine will become applicable to other diseases.

The process of translation of basic research into clinics requires both legal and ethical regulations, and the presence of experienced academic and administrative personnel. This process will be accelerated once we can establish the conditions to attract successful, qualified researchers abroad to return to Turkey. In this regard, Hacettepe University can offer an attractive research environment with its constituents such as the Faculty of Medicine, Faculty of Dentistry, Pharmacology, basic sciences and engineering in conjunction with multidisciplinary research programs (bio-engineering, stem cells, nanotechnology, nanomedicine, pharmaceutical biotechnology, biochemistry, etc.). It offers modern, strong academic establishment and graduate programs to the researchers at every level.

In summary, we invite young researchers to investigate, contemplate and build bridges in between clinic and laboratory. As it is emphasized in this book, restorative medicine requires the collaboration of multiple research areas. Young researchers should understand the clinical problems correctly and follow an accurate strategy. The key of the successful RM application is through the restored function with complete anatomic structure and aesthetic appearance. We planned and prepared this book as a guide to overcome the problems and insufficiencies of current therapies. There will be always a room for improvement and update.

İbrahim Vargel, M.D
Editor

Restorative Medicine
İbrahim Vargel, Editor

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Prof. Dr. Ibrahim Vargel was born in 1955, Nazilli. He completed his primary, secondary and high school education in Nazilli and graduated from Gazi University, in 1977. He has taught physics, chemistry and biology at secondary schools for four years. He studied Chemical Engineering at Gazi University for two years. Dr. Vargel became a doctor in 1986 after starting his medical career by winning the Trabzon Medical Faculty of Hacettepe University in 1979. While he was a student at the Faculty of Medicine. He served as mandatory service in Haymana State Hospital and Hacettepe University Etimesgut Regional Hospital between 1986-1990. He graduated from Hacettepe University Faculty of Medicine Plastic Reconstructive and Aesthetic Surgery Department in 1997. During his specialization training, he completed his specialty thesis titled "Comparison of Conventional Nerve Grafts with Vascularized Nerve Grafts". In 2003, he was the first and only Ph.D. student in the Advanced Plastic Reconstructive and Aesthetic Surgery Sciences program, which was founded in 1998 at Hacettepe University Institute of Health Sciences with the contribution of Dr. Vargel. He completed his Ph.D. in doctoral dissertation titled "Effect of Calcitonin Gene-Related Peptide in Cranial Suture Fusion". In 2004, he started as Assistant Professor at Kırıkkale University Faculty of Medicine Plastic Reconstructive and Aesthetic Surgery Department. Dr. Vargel, who became Associate Professor in 2008, was appointed Chief of Staff at KKKU Medical Faculty Hospital in 2009. In between 2006 and 2013, he served as President of the KKKU Department of Plastic Rec. and Aesthetic Surgery. He left Kırıkkale University on December 2012 and started to work Faculty of Medicine at Hacettepe University. Between the years 2014-2018 Dr. Vargel made the head of the Department of Bioengineering at Hacettepe University. He received his Professor title at Hacettepe University in 2014. During his academic career, he worked as a researcher on International Expertissues, E-rare and Irses projects. He has been a facilitator and researcher in several national and international research for clinical problems. In 2007, he was an observer at the University of Michigan Craniofacial Surgery Center. He completed DAFP clinical fellowship program at Erasmus University in 2012 with YÖK Scholarship. He worked at the University of Pittsburgh Research Center in 2014 to conduct research in the fields of 'Tissue Engineering and Regenerative Medicine'. Dr. Vargel did some important collaborative research on the definition, treatment and etiology of unknown illnesses. His "ALX gene mutation frontonasal with developing dysplasia and clinical studies on the treatment algorithm" was chosen best clinical study in Turkey. In Vancouver, 2011, he represented Turkey at the ISAPS Congress. He was awarded with a special award by the Rectorate of Kırıkkale University twice in 2006 and 2011 due to scientific studies and international contributions to science. Another important area of clinical research is the initial identification and treatment of VMOS Syndrome. There are significant contributions and advances in the diagnosis and treatment of 9 diseases that have entered the OMIM catalog. He has "Hacettepe Journal of Biology and Chemistry" editorial board member' Gazi Medical Journal' cites 'Consulting and' Turkey Medical Sciences Journal of Plastic, Rek. and Esthetic Surgery. Member of the Advisory Board "(Kırıkkale University, Faculty of Medicine, 2006). Because of his clinical and experimental studies, he received five first, three second, one third and one incentive award in the field of Plastic Rec. and Aesthetic Surgery. Since 2006, he has been a faculty member and since 2015 he has been the President of the Department of Bioengineering. He has chapter translations in eight books and chapter authoring in eleven books, published 74 research articles in SCI scanned journals, 46 scientific books and book chapters. His studies has been cited in more than 11200. He is married (Dr. Serpil Vargel) and has a child (Dr. Özge Vargel Bölükbaşı).

