T. Tachikawa, K. Nose, T. Ohmori, M. Adachi (Eds.)

New Trends in the Molecular and Biological Basis for Clinical Oncology

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Springer

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Foreword

On behalf of Showa University, I am pleased to publish the proceedings of The 4th Annual Meeting of the Showa International Symposium for Life Sciences, *New Trends in the Molecular and Biological Basis for Clinical Oncology.*

This symposium aims for the improvement in the prevention and therapeutics for intractable diseases and has been held annually for the past four years. It always provides us with a great opportunity to share the latest knowledge in fundamental, translational, and clinical fields about intractable diseases. In last year's symposium we focused on medical oncology. The proceedings is composed of 18 articles presenting the latest data about new strategies for cancer therapeutics. Six specialists of the contributors are invited from all over the world.

I hope that this book will furnish valuable information for the development of clinical as well as basic cancer research to all who are working in this field.

Katsuji Oguchi, M.D., Ph.D.
Chairman, Board of Directors of Showa University
Tokyo, Japan
June 2008

Foreword

Recently, many cancer patients have experienced the hope of being treated with the latest cancer therapy by specialists in oncology. It is obvious, however, that the number of oncologists is absolutely inadequate to meet the demand nationwide, because medical oncology has not been authorized in the ministry's curriculum guideline and cancer therapeutics has not been included among the special subjects of medical schools in Japan. Accordingly, the establishment of an education system for oncology to produce many experts in cancer therapeutics is the prime task of medical schools. Consequently, many medical schools in Japan have begun to set up departments of clinical oncology in their hospitals, and we also have decided to establish such a department in our hospital. I believe that the work of clinical oncology should be further accelerated for the benefit of cancer patients in this country.

Especially under these circumstance, it is my great pleasure to publish *New Trends in the Molecular and Biological Basis for Clinical Oncology*, the proceedings of The 4th Annual Meeting of the Showa International Symposium for Life Sciences, which was held at Showa University on October 6th, 2007. On behalf of the university, I am grateful to all the contributors to this book, who are active leaders in clinical oncology and in cancer research.

Akiyoshi Hosoyamada, M.D., Ph.D.
President, Showa University
Tokyo, Japan
June 2008

Foreword

A long time has passed since cancer became the primary cause of death in Japan. In fact, the number of cancer patients is still growing, and one-third of clinical deaths are caused by this disease. It is estimated that in tandem with the rapid transition to an aging society, the increment in the number of cancer patients will accelerate. It is obvious that the conquest of cancer is still one of the largest medical problems to be solved.

Recently, remarkable progress in cancer therapy has been made possible by better understanding of the molecular and cell biology of cancer and by the technology that has resulted in the discovery of new drugs. The molecular target cancer drugs are being developed constantly and with astonishing speed, and at the same time many large-scale clinical studies are being conducted all over the world. In order to utilize these cancer drugs properly, the efficacy of each of them must be proved by their own clinical studies. However, evaluation in clinical studies is not sufficient to select the optimal drug for each individual patient, because the impact of the molecular target drugs is dependent on the "individuality" of cancer. For this purpose, we have to solve the following additional problems:

1) Proof that a molecular target drug can actually inhibit the expected target in vivo (proof of principle)
2) Detection of a clinical marker from patient materials correlated with drug efficacy (surrogate marker)

As these challenges can be met only through close cooperation between basic and clinical cancer research, I think that we should establish an efficient new research system, breaking down the barrier between those two areas of research. There is only cancer research for the benefit of patients. We must be united as one body of researchers, wishing to cure cancer.

Hajime Yasuhara, M.D., Ph.D.
Dean, Showa University School of Medicine
Tokyo, Japan
June 2008

Preface

Several years ago, molecular target anticancer drugs began to be used in the clinical field, showing outstanding clinical efficacy. These newly developed drugs have a great effect even on intractable cancers such as hepatoma and renal cell carcinoma. Fortunately, we are now facing a surge of new findings in the development of cancer therapy. Cancer research is becoming a multidisciplinary field that includes nearly all areas of science and technology. In fact, many anticancer drugs are developed by basic cancer research that is increasingly influenced by clinical observations. At the same time, the molecular and genetic observations of epidemiology have great influence on research protocols in both the laboratory and the clinic. We are convinced that such cooperation across basic, translational, and clinical research fields will rapidly advance cancer therapeutics beneficial to cancer patients.

Under these circumstances, we held The 4th Annual Meeting of Showa International Symposium for Life Sciences with the theme "New Trends in the Molecular and Biological Basis for Clinical Oncology" at Showa University, Tokyo, in October 2007. This book contains the materials from that symposium in which new strategies for the development of cancer therapeutics were discussed. In the first chapter, we focus on the cancer therapy targeting receptor tyrosine kinases aimed at clinical utilization of new signaling regulations. The second chapter explains the interaction between cancer progression and extracellular environments such as inflammatory cytokines and the extracellular matrix. The third describes investigation of the biomarkers for personalized cancer therapy, using microarray analysis and pharmacogenomics technology. This book also includes several reports of the latest investigations dealing with cancer cell biology and therapeutics.

We thank all the authors and others who have contributed to the publication of this book. We believe that its contents are valuable for investigators in cancer research and that their achievements will help to provide the best possible care for individual cancer patients in the near future.

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June 2008

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We would like to acknowledge the extraordinary contributions of Mrs. Noriko Shishido, who played a vital role in the preparation of this book and assumed responsibility for the organization and compilation of all the chapters. We are grateful for her dedication.

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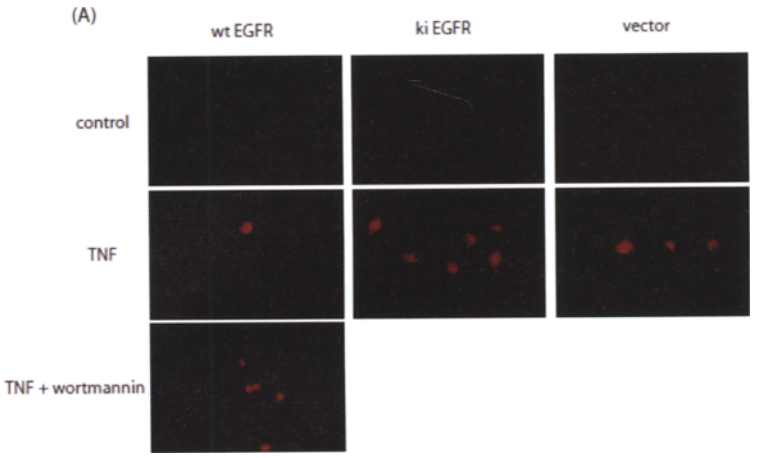
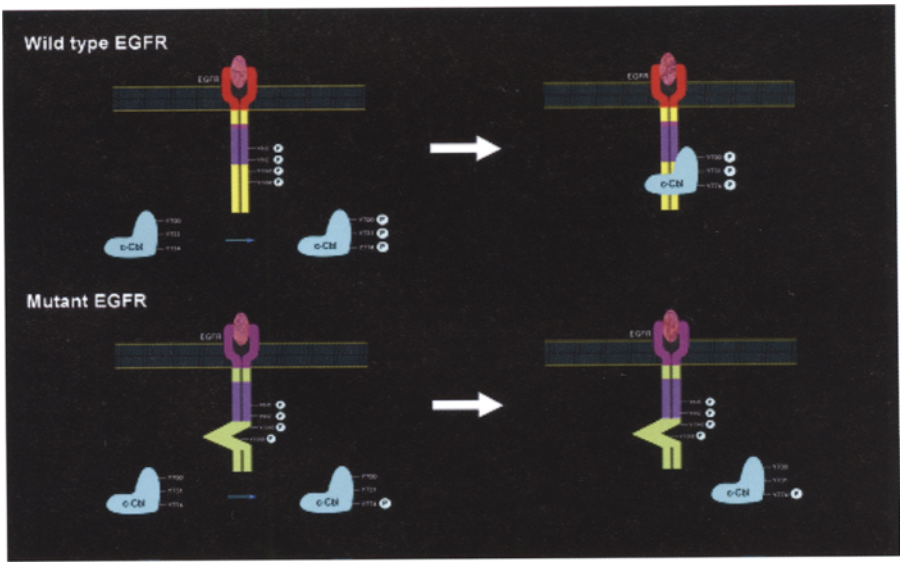
Color Plates



Part I: Yamaoka et al (Fig.1A)



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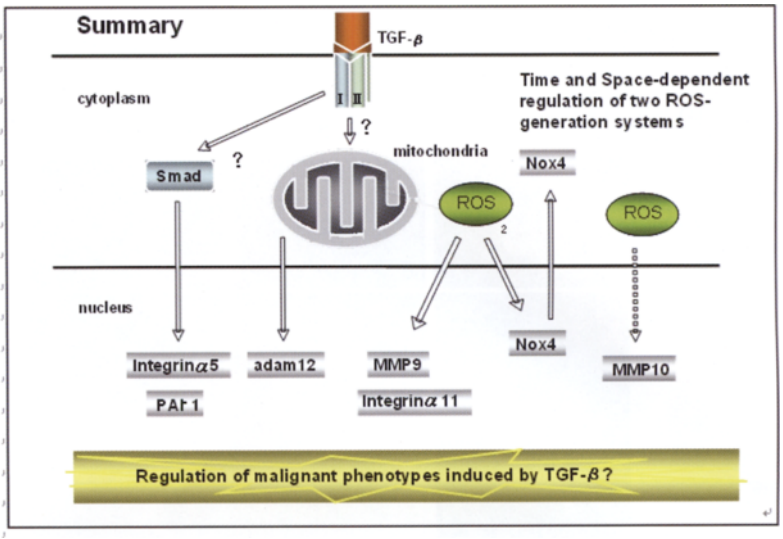

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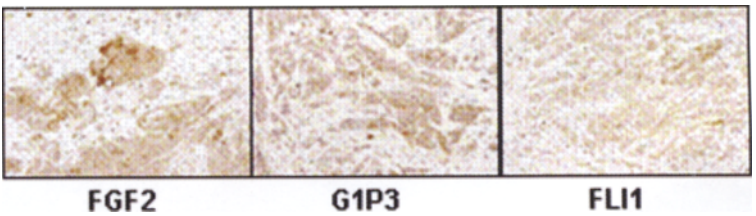

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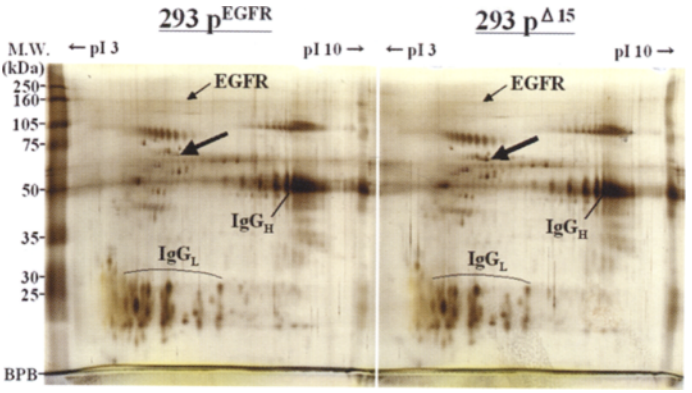
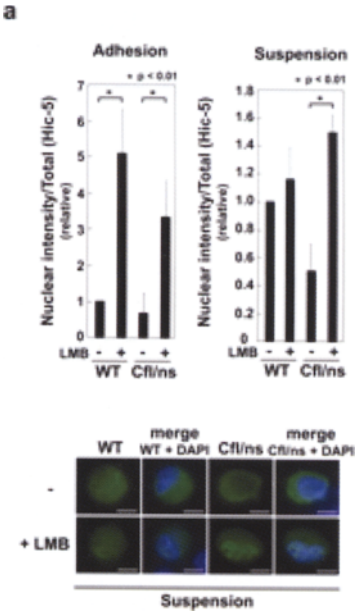
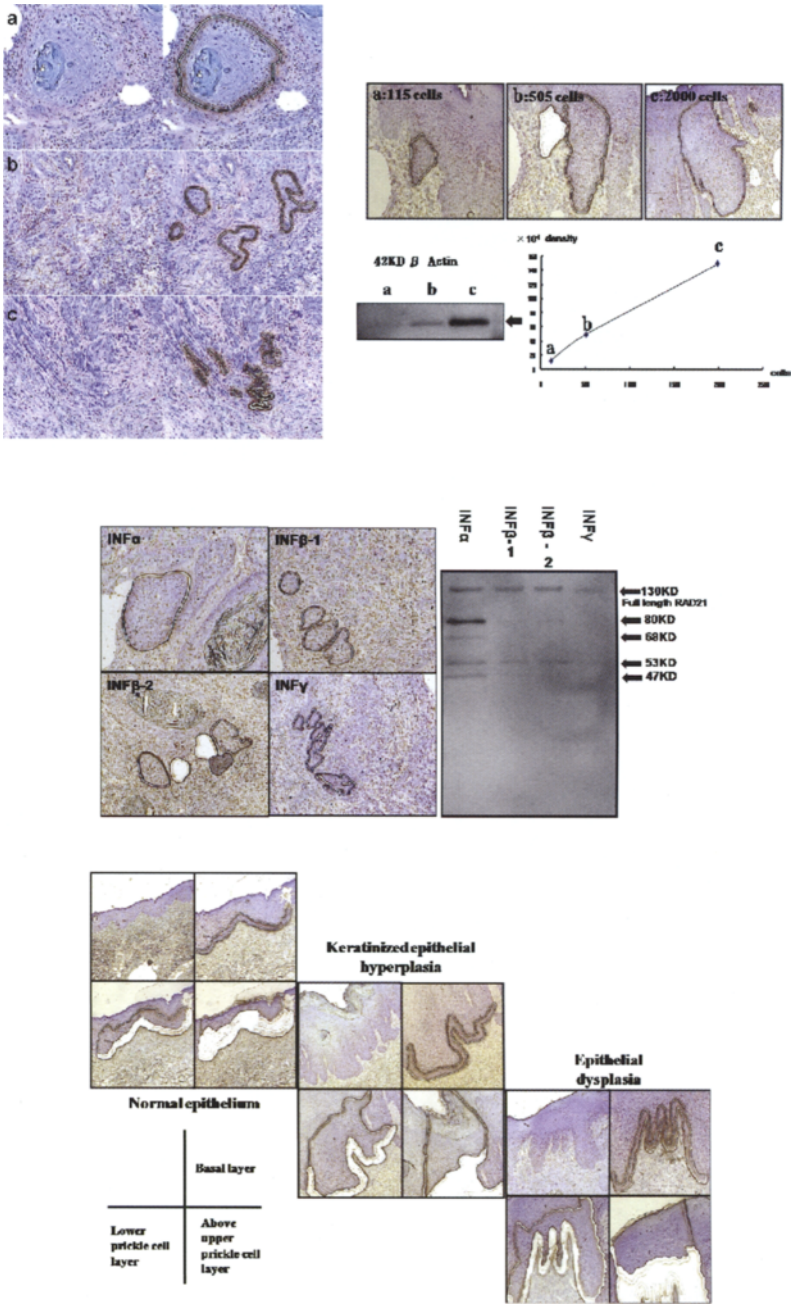


Part IV: Kadofuku et al (Fig.1)



Part IV: Mori et al (Fig.3a)



Part IV: Yamamoto et al (Figs.1, 3-5)