

Preface: Oncogenes and Tumor Suppressor Genes in Cancer: Honoring of Professor Demetrios A. Spandidos

This Special Issue is to honor Professor Demetrios A. Spandidos, currently Professor Emeritus at the School of Medicine of the University of Crete, Greece, as a recognition of his service and impact in the field of cancer research. As his former doctoral student, I feel honored to write this Preface to the Special Issue. Professor Spandidos has played a key role in the identification of cellular oncogenes, probably the most important discovery in the last few decades, which has entirely shifted the shape of modern research in Biomedical Sciences.

Professor Spandidos was born in Agios Constantinos, Sparta, Greece. He holds a Bachelor of Science degree in Chemistry from the Aristotelion University of Thessaloniki, Greece (1971). He received his Doctorate in Biochemistry from McGill University, Montreal, Canada in 1976, studying the transcription of Reovirus. He also holds a Doctorate of Science in Genetics from the University of Glasgow (1989) for his studies on the role of the *Ras* genes in carcinogenesis. He is a Fellow and Member of the Royal College of Pathologists (1997, 1988), London, United Kingdom, and a Fellow of the Royal Society of Health, London (1994). He holds a specialty in Clinical Chemistry (1998) from the Ministry of Health, Greece. He is also a corresponding Member of the Academia Nacional de Medicina de Buenos Aires, Argentina (1999). He has received the degrees of Doctor Honoris Causa from the Universities of Bucharest (2002) and Cluj-Napoca (2004) Romania, and he is a Fellow of the American Society of Angiology (2005). He was also a visiting Professor at the University of Catania, Italy (2005), an honorary Professor at the Fujian University, China (2013), and a visiting Professor at Kyoto University, Japan (2014).

In 1988, he was elected Professor in the Medical School University of Crete, Heraklion, Greece, and Director of Research at the National Hellenic Research Foundation in Athens, Greece. He held the

parallel positions for a decade, and from 1999 to 2015 he was exclusively Professor at the University of Crete. Currently, he is Professor Emeritus at the same University.

While a postdoctoral fellow at the University of Toronto (1976–1978), he was the first scientist in the field of oncology to develop and apply the gene transfer technique, which has become a very potent tool in oncogene investigations.^{1,2} At that time, he called these now well-known oncogenes “cancer genes.” His work assisted in the development of the gene transfer technology that has been of paramount importance in revealing new oncogenes, as well as implementing the molecular understanding of oncogenes and how the normal proto-oncogenes become activated into their malignant transforming cognates. Since then, an explosion of research has demonstrated the direct relevance of cellular oncogenes to cancer development, diagnosis, and treatment. These investigations are dependent on the technical and conceptual advances in the identification of cellular oncogenes and analyses of their roles in multistage carcinogenesis.

Professor Spandidos continued to contribute actively, playing a major role in his scientific investigations on the *Ras* oncogene. While at the Beatson Institute for Cancer Research in Glasgow, he performed notable and important investigations on the molecular mechanism of transformation of normal cells by the introduction of a single *Ras* gene using retroviral long terminal repeats (LTRs) and other strong promoters.³ Some other ideas of his that were very provocative at the time, like the dual function of *Ras Genes* as oncogenes and onco-suppressors,^{4,5} have now been proven correct.⁶ His most significant discoveries include the avian retrovirus,⁷ the involvement of the *ras* genes in colon tumours,⁸ the role of *ras* and *myc* genes in apoptosis,⁹ and the involvement of *c-myc*,¹⁰ *p53*,^{11,12} and *ras* in head and neck carcinomas¹³ and breast cancer.^{14,15}

Further publications of major significance derived from his research group at the University of Crete and other collaborators. These include the study on the role of *myc* and *ras* in cancer,⁹ the implication of p53 codon 72 polymorphism in bladder,¹⁶ breast,¹⁷ lung,¹⁸ and head and neck¹⁹ cancers, the expression of *ras*, *p53*, and *c-erbB-2* in advanced breast²⁰ and colorectal cancer,²¹ the role of the proteasome inhibitor NPI-0052 in the regulation of epithelial to mesenchymal transition,^{22,23} the role of dietary flavonoids in cancer therapy and prevention,²⁴ the role of growth factors in prostate,²⁵ lung,²⁶ and cervical cancers,²⁷ the overexpression of H-ras²⁸ and the implication of microsatellite instability in head and neck cancer,²⁹ the overexpression of the *p53* gene in head-and-neck cancer,³⁰ the expression of *BRCA1* and *Tpl-2/Cot* in breast cancer,^{31,32} the involvement of microRNAs in triple-negative breast³³ and bladder cancers,³⁴ the coderegulated genes of bladder cancer,^{35,36} and the genetics of nonmelanoma skin cancer,^{37–40} among many others.

Professor Spandidos has organized more than 27 international meetings on a variety of areas of oncology and molecular medicine. He has served on the editorial boards of a number of journals, including *Critical Reviews in Oncogenesis*, *The International Journal of Biological Markers*, and *Cancer Molecular Biology*. Notably, he has authored > 700 publications, which have received >13,000 citations (h-index: 56; Scopus), making him the most highly cited scientist of the 20th century in all sciences for research that has been conducted in the Balkan countries.

Importantly, Professor Spandidos has managed to establish a scientific tradition in biomedical sciences in Greece, including the successful creation of a school of talented scientists with international recognition. More than 100 graduate students have obtained their doctoral degrees under his supervision, and most of them have pursued careers abroad in leading institutions in the field of cancer research. As a fruit of his efforts, Greece has been put on the map of biomedical and cancer research at an international level.

In 1992, Professor Spandidos established Spandidos Publications, a publisher of scientific journals. Spandidos Publications has now developed into a

leading publishing group in the biomedical sciences field, being the third largest publisher in the world in the field of oncology and the fifth largest in the field of molecular medicine (Web of Science ISI ranking). Currently, Spandidos Publications publishes 8 journals with the highest standards of quality and with world-renowned scientists being members of their editorial boards: *International Journal of Molecular Medicine*, *International Journal of Oncology*, *Molecular Medicine Reports*, *Oncology Reports*, *Experimental and Therapeutic Medicine*, *Oncology Letters*, *Biomedical Reports*, and *Molecular and Clinical Oncology*. Professor Spandidos is the Editor-in-Chief of all of them, and the Deputy Editors are his two children, Drs Nikiforos-Anastasios and Athanasia.

Today, aged 71 years old, he remains a tireless investigator and a valued mentor for many students and colleagues. Esteemed Professor Demetrios A. Spandidos is an authentic role model and a living legend in cancer research.

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