Special Issue "p53 in Cancer and beyond—40 Years after Its Discovery"

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Deadline for manuscript submissions: **closed (31 December 2019)**.

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Special Issue Editors

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Special Issue Information

Dear Colleagues,

The “p53 team” dictates cell fate and sacrifices cell life as demanded, for the greater good of the organism. The p53 team consists of its close family (*p53*, *p63*, and *p73* genes), a varied number of isoforms, and a plethora of downstream target genes. Together they control cell stemness, division, chromosome integrity, epigenetics, differentiation,

senescence and death; response to stress, infection and disease; reproduction, immunity, metabolism, and regeneration. As a consequence, p53 team function is central to our lives, from birth and development to aging and life span in both health and disease.

Forty years after its discovery, we aim to cover important and new aspects of p53 and its team, not only in cancer, but in all the diversity of p53-dependent activities. Authors are invited to review recent work or submit original research in all areas of recent and current p53 research, with an emphasis on work providing molecular insight, including but not limited to novel physiological and pathological functions, or regulatory mechanisms.

We welcome your contributions for this Special Issue on “p53 in Cancer and beyond—40 Years after Its Discovery”.

Dr. Marco M. Candeias
Dr. Rieko Ohki
Guest Editors

Manuscript Submission Information

Manuscripts should be submitted online at www.mdpi.com by registering and logging in to this website. Once you are registered, click here to go to the submission form. Manuscripts can be submitted until the deadline. All papers will be peer-reviewed. Accepted papers will be published continuously in the journal (as soon as accepted) and will be listed together on the special issue website. Research articles, review articles as well as short communications are invited. For planned papers, a title and short abstract (about 100 words) can be sent to the Editorial Office for announcement on this website.

Submitted manuscripts should not have been published previously, nor be under consideration for publication elsewhere (except conference proceedings papers). All manuscripts are thoroughly refereed through a single-blind peer-review process. A guide for authors and other relevant information for submission of manuscripts is available on the Instructions for Authors page. International Journal of Molecular Sciences is an international peer-reviewed open access semimonthly journal published by MDPI.

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Research

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SLMP53-1 Inhibits Tumor Cell Growth through Regulation of Glucose Metabolism and Angiogenesis in a P53-Dependent Manner

by Helena Ramos,Juliana Calheiros,Joana Almeida,Valentina Barcherini,Sónia Santos,Alexandra T. P. Carvalho,Maria M.M. Santos andLucília Saraiva

Int. J. Mol. Sci. 2020, 21(2), 596; https://doi.org/10.3390/ijms21020596 - 17 Jan 2020

Cited by 1

Abstract The Warburg effect is an emerging hallmark of cancer, which has the tumor suppressor p53 as its major regulator. Herein, we unveiled that p53 activation by (S)-tryptophanol-derived oxazoloisoindolinone (SLMP53-1) mediated the reprograming of glucose metabolism in cancer cells and xenograft human [...] Read more.

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The Influence of Quadruplex Structure in Proximity to P53 Target Sequences on the Transactivation Potential of P53 Alpha Isoforms

by Otília Porubiaková,Natália Bohálová,Alberto Inga,Natália Vadovičová,Jan Coufal,Miroslav Fojta andVáclav Brázda

Int. J. Mol. Sci. 2020, 21(1), 127; https://doi.org/10.3390/ijms21010127 - 24 Dec 2019

Abstract p53 is one of the most studied tumor suppressor proteins that plays an important role in basic biological processes including cell cycle, DNA damage response, apoptosis, and senescence. The human TP53 gene contains alternative promoters that produce N-terminally truncated proteins and can produce [...] Read more.

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Characterization of p53 Family Homologs in Evolutionary Remote Branches of Holozoa

by Martin Bartas,Václav Brázda,Jiří Červeň andPetr Pečinka

Int. J. Mol. Sci. 2020, 21(1), 6; https://doi.org/10.3390/ijms21010006 - 18 Dec 2019

Cited by 2

Abstract The p53 family of transcription factors plays key roles in development, genome stability, senescence and tumor development, and p53 is the most important tumor

suppressor protein in humans. Although intensively investigated for many years, its initial evolutionary history is not yet fully elucidated. [...] Read more.

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The Dual Interactions of p53 with MDM2 and p300: Implications for the Design of MDM2 Inhibitors

by Srinivasaraghavan Kannan,Anthony W. Partridge,David P. Lane andChandra S. Verma

Int. J. Mol. Sci. 2019, 20(23), 5996; https://doi.org/10.3390/ijms20235996 - 28 Nov 2019

Cited by 1

Abstract Proteins that limit the activity of the tumour suppressor protein p53 are increasingly being targeted for inhibition in a variety of cancers. In addition to the development of small molecules, there has been interest in developing constrained (stapled) peptide inhibitors. A stapled peptide [...] Read more.

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Coordination of miR-192 and miR-22 in p53-Mediated Cell Fate Decision

by Cheng-Yuan Sun,Xiao-Peng Zhang andWei Wang

Int. J. Mol. Sci. 2019, 20(19), 4768; https://doi.org/10.3390/ijms20194768 - 26 Sep 2019

Cited by 4

Abstract p53-targeted microRNAs (miRNAs) markedly affect cellular response to DNA damage. These miRNAs may contribute to either cell cycle arrest or apoptosis induction. However, how these miRNAs coordinate to modulate the decision between cell survival and death remains less understood. Here, we developed an [...] Read more.

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Review

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p53-PHLDA3-Akt Network: The Key Regulators of Neuroendocrine Tumorigenesis

by Yu Chen andRieko Ohki

Int. J. Mol. Sci. 2020, 21(11), 4098; https://doi.org/10.3390/ijms21114098 - 08 Jun 2020

Cited by 1

Abstract p53 is a well-known tumor suppressor gene and one of the most extensively studied genes in cancer research. p53 functions largely as a transcription factor and can trigger a variety of antiproliferative programs via induction of its target genes. We identified PHLDA3 as [...] Read more.

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PHLD Class Proteins: A Family of New Players in the p53 Network

by Taylor T. Fuselier andHua Lu

Int. J. Mol. Sci. 2020, 21(10), 3543; https://doi.org/10.3390/ijms21103543 - 17 May 2020

Abstract The Pleckstrin Homology-like Domain (PHLD) class of proteins are multifunctional proteins. The class is comprised of two families of proteins, PHLDA and PHLDB, each with 3 members. All members of the families possess a pleckstrin homology (PH) domain. Though identified nearly 30 years [...] Read more.

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P53: A Guardian of Immunity Becomes Its Saboteur through Mutation

by Arjelle Decasa Agupitan,Paul Neeson,Scott Williams,Jason Howitt,Sue Haupt andYgal Haupt

Int. J. Mol. Sci. 2020, 21(10), 3452; https://doi.org/10.3390/ijms21103452 - 13 May 2020

Cited by 6

Abstract Awareness of the importance of immunity in controlling cancer development triggered research into the impact of its key oncogenic drivers on the immune response, as well as their value as targets for immunotherapy. At the heart of tumour suppression is p53, which was [...] Read more.

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p53-Related Transcription Targets of TAp73 in Cancer Cells—Bona Fide or Distorted Reality?

by Chao Wang,Cui Rong Teo andKanaga Sabapathy

Int. J. Mol. Sci. 2020, 21(4), 1346; https://doi.org/10.3390/ijms21041346 - 17 Feb 2020

Cited by 1

Abstract Identification of p73 as a structural homolog of p53 fueled early studies aimed at determining if it was capable of performing p53-like functions. This led to a conundrum as p73 was discovered to be hardly mutated in cancers, and yet, TAp73, the full-length [...] Read more.

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Gain-of-Function Mutations in p53 in Cancer Invasiveness and Metastasis

by Katarzyna A. Roszkowska,Slawomir Gizinski,Maria Sady,Zdzislaw Gajewski andMaciej B. Olszewski

Int. J. Mol. Sci. 2020, 21(4), 1334; https://doi.org/10.3390/ijms21041334 - 17 Feb 2020

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Abstract Forty years of research has proven beyond any doubt that p53 is a key regulator of many aspects of cellular physiology. It is best known for its tumor suppressor function, but it is also a regulator of processes important for maintenance of homeostasis [...] Read more.

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How p53 Molecules Solve the Target DNA Search Problem: A Review

by Kiyoto Kamagata,Yuji Itoh andDwiky Rendra Graha Subekti

Int. J. Mol. Sci. 2020, 21(3), 1031; https://doi.org/10.3390/ijms21031031 - 04 Feb 2020

Cited by 3

Abstract Interactions between DNA and DNA-binding proteins play an important role in many essential cellular processes. A key function of the DNA-binding protein p53 is to search for and bind to target sites incorporated in genomic DNA, which triggers transcriptional regulation. How do p53 [...] Read more.

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P53 and The Immune Response: 40 Years of Exploration—A Plan for the Future

by Arnold J. Levine

Int. J. Mol. Sci. 2020, 21(2), 541; https://doi.org/10.3390/ijms21020541 - 15 Jan 2020

Cited by 10

Abstract The p53 field was born from a marriage of the techniques of cancer virus research and immunology. Over the past 40 years, it has followed the path of cancer research. Now cancer treatments are turning to immunotherapy, and there are many hints of [...] Read more.

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Regulation of the p53 Family Proteins by the Ubiquitin Proteasomal Pathway

by Scott Bang,Sandeep Kaur andManabu Kurokawa

Int. J. Mol. Sci. 2020, 21(1), 261; https://doi.org/10.3390/ijms21010261 - 30 Dec 2019

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Abstract The tumor suppressor p53 and its homologues, p63 and p73, play a pivotal role in the regulation of the DNA damage response, cellular homeostasis, development, aging, and metabolism. A number of mouse studies have shown that a genetic defect in the p53 family [...] Read more.

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How the Other Half Lives: What p53 Does When It Is Not Being a Transcription Factor

by Teresa Ho,Ban Xiong Tan andDavid Lane

Int. J. Mol. Sci. 2020, 21(1), 13; https://doi.org/10.3390/ijms21010013 - 18 Dec 2019

Cited by 10

Abstract It has been four decades since the discovery of p53, the designated ‘Guardian of the Genome’. P53 is primarily known as a master transcription factor and critical tumor suppressor, with countless studies detailing the mechanisms by which it regulates a host of gene [...] Read more.

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The Emerging Landscape of p53 Isoforms in Physiology, Cancer and Degenerative Diseases

by Thineskrishna Anbarasan andJean-Christophe Bourdon

Int. J. Mol. Sci. 2019, 20(24), 6257; https://doi.org/10.3390/ijms20246257 - 11 Dec 2019

Cited by 4

Abstract p53, first described four decades ago, is now established as a master regulator of cellular stress response, the “guardian of the genome”. p53 contributes to biological robustness by behaving in a cellular-context dependent manner, influenced by several factors (e.g., cell type, active signalling [...] Read more.

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Do Mutations Turn p53 into an Oncogene?

by Consuelo Pitolli,Ying Wang,Mara Mancini,Yufang Shi,Gerry Melino andIvano Amelio

Int. J. Mol. Sci. 2019, 20(24), 6241; https://doi.org/10.3390/ijms20246241 - 11 Dec 2019

Cited by 14

Abstract The key role of p53 as a tumor suppressor became clear when it was realized that this gene is mutated in 50% of human sporadic cancers, and germline mutations expose carriers to cancer risk throughout their lifespan. Mutations in this gene not only [...] Read more.

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Gain-of-Function Mutant p53: All the Roads Lead to Tumorigenesis

by Yan Stein,Varda Rotter andRonit Aloni-Grinstein

Int. J. Mol. Sci. 2019, 20(24), 6197; https://doi.org/10.3390/ijms20246197 - 08 Dec 2019

Cited by 15

Abstract The p53 protein is mutated in about 50% of human cancers. Aside from losing the tumor-suppressive functions of the wild-type form, mutant p53 proteins often acquire inherent, novel oncogenic functions, a phenomenon termed mutant p53 gain-of-function (GOF). A growing body of evidence suggests [...] Read more.

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The Diverse Functions of Mutant 53, Its Family Members and Isoforms in Cancer

by Callum Hall andPatricia A.J. Muller

Int. J. Mol. Sci. 2019, 20(24), 6188; https://doi.org/10.3390/ijms20246188 - 07 Dec 2019

Cited by 2

Abstract The p53 family of proteins has grown substantially over the last 40 years. It started with p53, then p63, p73, isoforms and mutants of these proteins. The function of p53 as a tumour suppressor has been thoroughly investigated, but the functions of all [...] Read more.

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p53 Isoforms in Cellular Senescence- and Ageing-Associated Biological and Physiological Functions

by Kaori Fujita

Int. J. Mol. Sci. 2019, 20(23), 6023; https://doi.org/10.3390/ijms20236023 - 29 Nov 2019

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Abstract Cellular senescence, a term originally used to define the characteristics of normal human fibroblasts that reached their replicative limit, is an important factor for ageing, age-related diseases including cancer, and cell reprogramming. These outcomes are mediated by senescence-associated changes in gene expressions, which [...] Read more.

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The Rich World of p53 DNA Binding Targets: The Role of DNA Structure

by Václav Brázda andMiroslav Fojta

Int. J. Mol. Sci. 2019, 20(22), 5605; https://doi.org/10.3390/ijms20225605 - 09 Nov 2019

Cited by 10

Abstract The tumor suppressor functions of p53 and its roles in regulating the cell cycle, apoptosis, senescence, and metabolism are accomplished mainly by its interactions with DNA. p53 works as a transcription factor for a significant number of genes. Most p53 target genes contain [...] Read more.

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The Association and Significance of p53 in Gynecologic Cancers: The Potential of Targeted Therapy

by Mitsuhiro Nakamura,Takeshi Obata,Takiko Daikoku andHiroshi Fujiwara

Int. J. Mol. Sci. 2019, 20(21), 5482; https://doi.org/10.3390/ijms20215482 - 04 Nov 2019

Cited by 5

Abstract Dysfunction of p53 is observed in the many malignant tumors. In cervical cancer, p53 is inactivated by degradation through the complex with human papilloma virus (HPV) oncoprotein E6 and E6-associated protein (E6AP), an E3 ubiquitin protein ligase. In endometrial cancer, overexpression of p53 [...] Read more.

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Translational Control in p53 Expression: The Role of 5′-Terminal Region of p53 mRNA

by Agata Swiatkowska,Mariola Dutkiewicz,Paulina Zydowicz-Machtel,Joanna Szpotkowska,Damian M. Janecki andJerzy Ciesiołka

Int. J. Mol. Sci. 2019, 20(21), 5382; https://doi.org/10.3390/ijms20215382 - 29 Oct 2019

Abstract In this review, the latest research concerning the structure and function of the 5′-terminal region of p53 mRNA was discussed. Special attention was focused on defined structural motifs which are present in this region, as well as their conservation and plausible functional role [...] Read more.

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Roles of p53 Family Structure and Function in Non-Canonical Response Element Binding and Activation

by Bi-He Cai,Chung-Faye Chao,Hsiang-Chi Huang,Hsueh-Yi Lee,Reiji Kannagi andJang-Yi Chen

Int. J. Mol. Sci. 2019, 20(15), 3681; https://doi.org/10.3390/ijms20153681 - 27 Jul 2019

Cited by 4

Abstract The p53 canonical consensus sequence is a 10-bp repeat of PuPuPuC(A/T)(A/T)GPyPyPy, separated by a spacer with up to 13 bases. C(A/T)(A/T)G is the core sequence and purine (Pu) and pyrimidine (Py) bases comprise the flanking sequence. However, in the p53 noncanonical sequences, there [...] Read more.

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Amniotic Fluid Cells, Stem Cells, and p53: Can We Stereotype p53 Functions?

by Melissa Rodrigues,Christine Blattner andLiborio Stuppia

Int. J. Mol. Sci. 2019, 20(9), 2236; https://doi.org/10.3390/ijms20092236 - 07 May 2019

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Abstract In recent years, great interest has been devoted to finding alternative sources for human stem cells which can be easily isolated, ideally without raising ethical objections. These stem cells should furthermore have a high proliferation rate and the ability to differentiate into all [...] Read more.

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