UNIVERSITÀ DEGLI STUDI DI UDINE

Prof. Gianluca Tell
Full Professor of Molecular Biology
Head of the Laboratory of Molecular Biology and DNA repair
Deputy Head of the Department of Medicine
Department of Medicine
University of Udine - Italy

Prof. Gianluca Tell, Curriculum Vitae as on January 2023

Gianluca Tell was born in Udine on 06.03.1968 got his Biology degree cum laude on 13 March 1993 (Academic Year 1991/92) at the University of Trieste, Italy.

A. Personal Statement

His prevailing interests is the study of molecular mechanisms of gene expression particularly in the field of redox signalling and cell oxidative stress. Now, he is focusing on some aspects linking gene expression and DNA repair and its relevance in molecular oncology and cancer. In particular, from 1998, he contributed to the understanding of the molecular mechanisms, involving the main mammalian Apurinic/Apyrimidinic Endonuclease, i.e. APE1, in coordinating cellular responses to oxidative stress in different cell models. His background includes molecular and cellular biology as well as biochemistry techniques and –OMICS technologies to characterize the relationship between structure and function of proteins involved in gene expression and DNA repair. He coordinated several research projects granted from Telethon, AIRC, FIRB, FISR, NIH, PRIN, ASI and worked as a Referee for several different International Journals, including: Oncogene, Nucleic Acids Research, Proteomics, Cancer Research, Clinical Cancer Research, etc. Actually, from 2010, his research activity is focused on characterizing the non-canonical roles of DNA repair enzymes of the Base Excision Repair pathway in association with RNA metabolism. He is currently head of the Laboratory of Molecular Biology and DNA repair of the Department of Medicine at the University of Udine, Italy, coordinating the work of three Post-Doctoral fellows and two PhD students.

Prof. G. Tell authored more than 150 publications in international peer reviewed journals and several international congress communications, concerning control of gene expression and DNA damage response during response to oxidative stress and genotoxic treatments. In 55% of these publications Prof. Tell gave a central contribution, acting as a first or last name. Total Impact Factor >500. The value of citation index (h-index) according to Scopus is 46 with a mean citation value of 39.50.

MAJOR ACHIEVEMENTS IN SCIENCE. Prof Tell has contributed to the understanding of the molecular mechanisms, involving the main mammalian Apurinic/Apyrimidinic Endonuclease APE1, in coordinating cellular responses to oxidative stress using different cancer cell models. He discovered one of the most important non-canonical roles of this protein in miRNA processing highly relevant in cancer biology.

A. Positions and Honors

- Academic Years 1988-1992 Laurea in Biological Sciences at the University of Trieste, Italy, Magna cum Laude on March 13th 1993.
- 1993 – 1994 Research Scientist (Postgraduate fellow) supported by Oncological Research Center (C.R.O.) Aviano, PN, Italy
- Research assistant (tenure track), April 1995-March 2000, Department of Biomedical Sciences and Technologies, School of Medicine, University of Udine, Italy;
- 1996, visiting scientist in the lab of Dr. David Segal, Experimental Immunology Branch, Division of Basic Sciences, NCI, NIH, Bethesda (MD) USA;

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- March 2000-September 2003, Assistant Professor (tenure track) of Molecular Biology, Department of Biochemistry, Biophysics and Macromolecular Chemistry, School of Medicine, University of Trieste, Italy;
- September 2003-October 2005, Assistant Professor (tenure track) of Molecular Biology, Department of Biomedical Sciences and Technologies, School of Medicine, University of Udine, Italy;
- June-August 2006, Visiting Professor in the lab of Prof. Sankar Mitra. School of Medicine-Sealy Center For Molecular Science And Department Of Human Biological Chemistry And Genetics. University of Texas, Galveston, TX, USA;
- July 2009, Visiting Professor in the lab of Prof. Pablo Radicella. CEA, Institut de Radiobiologie Cellulaire et Moléculaire, UMR217 CNRS, F-92265 Fontenay-aux-Roses, France;
- From 2010-present, Head of the Laboratory of Molecular Biology and DNA repair of the Department of Medicine at the University of Udine, Italy (**Web site: https://gianlucatell.wixsite.com/labtell**);
- July-September 2011, Visiting Research Scholar in the lab of Prof. Bruce Demple. Department of Pharmacological Sciences, Stony Brook University, Stony Brook, NY, USA;
- From November 2012-September 2018, he is Director of the B.Sc. of Biotechnology at the University of Udine, Italy;
- From November 2005-December 2010, he is Associate Professor (tenure track) of Molecular Biology, at the Department of Biomedical Sciences and Technologies, School of Medicine, University of Udine, Udine, Italy;
- from January 2011-December 2016 he is Associate Professor (tenure track) of Molecular Biology, at the Department of Medical and Biological Sciences, School of Medicine, University of Udine, Udine, Italy;
- 12/02/2014, winner of the national habilitation competition as Full Professor in Biochemistry (BIO/10) and in Molecular Biology (BIO/11);
- From 25th October 2015 to 30th September 2019, he is member of the Technology Transfer Commission of the University of Udine, Italy;
- from January 2017- November 2018 he is Associate Professor (tenure track) of Molecular Biology, at the Department of Medicine, University of Udine, Udine, Italy;
- From October 2017-present he is Deputy of the Head of the Department of Medicine for Research, at the Department of Medicine, University of Udine, Udine, Italy;
- From December 2018-present he is Full Professor (tenure track) of Molecular Biology, at the Department of Medicine, University of Udine, Udine, Italy.

Others:

- 1994 (January) -1995 (May) Second lieutenant, Italian Army, anti-aircraft artillery, Sabaudia (Rome) and 5th Regiment "A. Pe. Cam. Superga" of Artillery in Udine, Italy
- 1997 – 1998 Teaching assistant, Biochemical and Molecular Gene Expression Techniques, Department of Biomedical Sciences and Technologies, Udine University Medical School, Udine – Italy

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- 1997 – 1999 Teaching assistant, Molecular Immunology, Department of Biomedical Sciences and Technologies, Udine University Medical School, Udine – Italy
- 1998 – 1999 Deputy Associate Professor, General Pathology, Department of Biomedical Sciences and Technologies, Udine University Medical School, Udine – Italy

Professional memberships

- From 2000-present American Association for Biochemistry and Molecular Biology (ASBMB)
- From 2000-present Italian Society for Biochemistry and Molecular Biology (SIB)
- 2003-2008 American Society for Bone and Mineral Research (ASBMR)
- 2004 Human Proteome Organization (HUPO)
- From 2004-present Italian Human Proteome Organization (IHUPO)
- 2011-2015 Visiting Research Scholar at Stonybrook University, Stonybrook, NY-USA
- From 2014-2020, Member of the Scientific Board of the Italian Research Cancer Association (AIRC)
- From 2015-preent, Member of the Scientific Board of the Fondazione Italiana Fegato, FIF-ONLUS, Trieste, Italy

Honors and Awards including invitations as speaker in International Congresses

- 2008-2012 Consultant, Ministry of Science (Georgia)
- 2008 Invited Speaker at "Anticancer Research Congress" in Kos, Greece;
- 2009 Invited Speaker at "3rd US/EU-DNA repair meeting" in Galveston, TX-USA;
- 2010 Invited Speaker at INBB meeting in Rome, Italy;
- 2011 UICC Yamagiwa-Yoshida Memorial International Cancer Study Grant funded by the Kyowa Hakko Kogyo Company Ltd., Tokyo and the Japan National Committee for UICC
- 2011-present Consultant, Ministry of University and Research (Italy);
- March 2018, Inviter Speaker at EEMGS International Conference, Potsdam, Germany;
- August 2018, Invited Speaker by the Institute of Chemical Biology and Fundamental Medicine, SB, RAS, NSU Novosibirsk Russia, to give a lecture at the 11th International Multiconference BGRS/SB-2018 "Bioinformatics of Genome Regulation and Structure/Systems Biology", at Novosibirsk, Russia.

B. Contributions to Science and publication performances

Prof Tell has more than 180 scientific publications. Peer reviewed Publications and citations parameters:

- First author publications: 25
- Last/corresponding author publications: 60
- Total publications in peer reviewed international journals: 166
- Peer-reviewed publications at this link: ORCID ID: https://orcid.org/0000-0001-8845-6448.
- Scopus Author ID: 7005032283
- Sum of the Times Cited (Scopus): 7111
- Average Citations per Item (Scopus): 39.50
- **h-index (Scopus): 46**

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Most cited paper: The intracellular localization of APE1/Ref-1: More than a passive phenomenon? Tell, G; Damante, G; Caldwell, D; et al. ANTIOXIDANTS & REDOX SIGNALING (2005), 7, 367-384. **Number of citations:** 264 with a mean of 21.82/year.

Paper with highest Impact Factor: Antoniali G, Serra F, Lirussi L, Tanaka M, D'Ambrosio C, Zhang S, Radovic S, Dalla E, Ciani Y, Scaloni A, Li M, Piazza S, **Tell G**. *Mammalian APE1 controls miRNA processing and its interactome is linked to cancer RNA metabolism.* **Nature Communications (2017) Oct 6;8(1):797**. doi: 10.1038/s41467-017-00842-8. PubMed PMID: 28986522; PubMed Central PMCID: PMC5630600. **Impact Factor:** 12.1

Journals with mid-high Impact Factor in which Prof. G. Tell published as first or as corresponding author:
1. Nature Communications
2. Nucleic Acids Research
3. Molecular and Cellular Biology
4. Oncogene
5. Genome Biology
6. Antioxidants and Redox Signalling
7. Journal of Biological Chemistry
8. Molecular Biology of the Cell

Referee for the following granting agencies:
1. NSERC (Canada)
2. Wellcome Trust (UK)
3. Cancer Research (UK)
4. Georgia Ministry of Science
5. National Medical Research Council (NMRC), Singapore
6. Italian MIUR
7. Italian Association for Cancer Research (AIRC)
8. National Academy of Sciences of Poland

C. Research Support

In the Last 10 years, Prof. Tell received grants in support of his research activities, for an overall budget of more than 2 MEuros from different granting agencies including: the National Institutes of Health (NIH), MIUR, MAE, Telethon, AIRC, Regione FVG, Private Companies.

Ongoing Research Support

- 2021-2022 Research Grant MUR, FISR2020IP_01563 (D.D. n.562 del 5.5.2020), dal titolo: "*A system approach platform, based on Artificial Intelligence (AI) / Machine Learning (ML), for serum proteomics, radiomics and clinical data analysis to identify diagnostic and prognostic biomarkers in SARS-CoV-2 (SCV2) infection*". Project location: University of Udine, Italy. Total funding to Dr Tell: € 52.967,91.

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- 2018-2022 Research grant AIRC #IG19862 (Unveiling the role of Ape1 in regulating tumor cell resistance to chemotherapy through miRNAs processing in HCC and NSCL). The goal of this proposal is to characterize new Ape1 functions in cancer resistance associated with miRNAs and gene expression regulation. This project will evaluate the roles of Ape1 and Ape1-regulated miRNAs as predictive biomarkers in NCSLC and HCC. Project location: University of Udine, Italy. Total funding to Dr Tell: € 454.000
- 2016-2021 Research Grant R01 NIH (1R01ES026243-01), National Institutes of Health agency: National Cancer Institute Special Emphasis Panel (Ribose-seq profile and analysis of ribonucleotides in DNA of oxidatively-stressed and cancer cells). PI: Prof. Francesca Storici, Georgia Technology Institute, Atlanta, GA, USA. Co-PI: Prof. Gianluca Tell Project. The goal of this project is to map ribonucleotides embedded in DNA in normal and cancer cells and identify the mechanisms for their repair. Project location: Georgia Technology Institute, Atlanta, GA, USA and University of Udine, Italy. Total fundings to Dr. Tell: $388,190.
- 2017-2019 Crossborder cooperation program Interreg V Italia Austria Bando 2016 funded by the European Regional Development Fund (ERDF) and the National Funds, implemented by the Autonomous Region Friuli Venezia Giulia, in quality of Managing Authority (PreCanMed: Generation of a Precision Cancer Medicine platform). Total funding to Dr Tell: € 205.450

Completed Research Support

- 2015-2017 Research Grant R21 NIH, National Institutes of Health agency: National Cancer Institute Special Emphasis Panel (The Ape1-NPM1 Axis and Telomere Maintenance). PI: Prof. Bruce Demple, Stony Brook University, NY, USA. Co-PI: Prof. Gianluca Tell Project. Total fundings: $429,642. The goal of this project is to unveil the role of the Ape1-NPM1 axis in telomere maintenance for development of new anticancer drugs. Project location: Stony Brook University, NY, USA and University of Udine, Italy
- 2014-2016 Research grant AIRC #IG14038 (Base Excision Repair dysregulation and cancer: Ape1 as a therapeutic target) € 169.604,0. The goal of this proposal is to identify the Ape1 regulated genes in cancer cells through RIP and ChipSeq gene analysis through NGS strategies and to identify small compounds able to interfere with the Ape1 functional network to sensitize tumor cells to anticancer therapy. Project location: University of Udine, Italy
- 2012-2015 Crossborder cooperation program Italy- Slovenia 2007- 2013 funded by the European Regional Development Fund (ERDF) and the National Funds, implemented by the Autonomous Region Friuli Venezia Giulia, in quality of Managing Authority (Environmental pollutants and neurodegenerative diseases).
- 2010-12 Research grant AIRC #IG10269 – three years (Understanding the functional regulation of APE1 for development of new specific inhibitors) € 201.930,00
- 2010-12 Telethon, Grant # GGP10051B (New diagnostic and therapeutic approaches for the Crigler−Najjar Syndrome Type I)
- 2010-12 Research grant PRIN_2008CCPKRP_003 (Molecular networks involving APE1 and role of post-translational modifications in fine-tuning the APE1 different functions for development of new drugs for cancer treatment). Co-PI, €34.857
- 2009-2010 ITALY/FRANCE 'Galileo' exchange grant from the Università Italo-Francese.

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- 2008-11 Grant FIRB-National Proteomics Network RBRN07BMCT_008 (Italian Human ProteomeNet) €1.006.000
- 2008-10 EU/USA Exchange Grant by Ministry from Foreign Affairs: Role of Ape1 in Neurotoxicity of Cancer Treatments
- 2006-08 Telethon, Grant #GGP06208 (DJ-1 in neurodegeneration)
- 2005-09 Private grants from Procter & Gamble and Abiogen
- 2005-07 AIRC, (New approaches for studying genetics, early molecular diagnosis and prognostic factors relevant for HCC)
- 2005-07 Telethon, Grant #GGP05062 (Genetic determinants of bilirubin encephalopathy)
- 2005-07 National coordinator grant PRIN2005051307 (Molecular mechanisms of cell response to oxidative stress) €182900

D. Invited seminars

Invited seminars and International teaching courses

- October 11th, 1997; Udine University - Medical School, Department of Biomedical Sciences and Technologies, Udine – Italy;
- April 5th, 1998; Udine University - Medical School, Department of Biomedical Sciences and Technologies, Udine – Italy;
- February 20th, 1999; Naples University - Medical School, Department of Molecular and Cellular Pathology 'L. Califano', Naples - Italy;
- March 7th, 2001; Florence University - Chemistry School, CERM and Department of Chemistry, Title: "Role of APE/Ref-1 in the transcriptional control of eukaryotic cells", Florence – Italy;
- October 1st, 2004; Trieste, AREA Science Park – EASL International Workshop 'The Molecular Basis of Bilirubin Encephalopathy and Neurotoxicity' – Title: "Redox regulation of cellular functions: new perspectives for the antioxidant role of bilirubin", Trieste – Italy;
- July 20th, 2007; Trieste, AREA Science Park – Summer School in Molecular Medicine – Title: "Proteomics in the new post-genomic era", Trieste – Italy;
- November 14th, 2007, Indiana University Melvin and Bren Simon Cancer Center; Title: "The many faces of APE1/Ref-1: molecular journey to unveil the secrets of this multifunctional protein", Indianapolis, IN (USA);
- November 23rd (2010); Department of Molecular Embriology, DKFZ, Heidelberg, D, Title: 'New insights into the unusual DNA repair protein APE1 and implications for cancer";
- April 7th, 2011; Naples University - Medical School, Department of Molecular and Cellular Pathology 'L. Califano', Naples - Italy; Title: 'New insights into the unusual DNA repair protein APE1 and implications for cancer";
- September 17th, 2012; College of Medicine, Graduate Center for Toxicology, University of Kentucky, Lexington, KY 40536-0305, USA –Title: "New insights into the unusual DNA repair protein Ape1 and relevance for Base Excision Repair and cancer";
- June 13th, 2018; Fondazione Istituto Italiano di Tecnologia (IIT), Genova Italy; Title: 'Non canonical roles of BER enzymes in RNA processing: novel perspectives in cancer biology through the study of APE1 RNA- and protein-interactomes' **(Host: Stefano Gustincich)**;
- September 24-29, 2018; Savitribai Phule, Pune University, Pune, INDIA; Teaching course of 15 hours: "Genome integrity and DNA repair in cancer" under the GIAN scheme of

MHRD, Government of India.
- September 25th, 2018; National Centre for Cell Science S.P. Pune University Campus, Pune, INDIA; Title: "Non canonical roles of BER enzymes in RNA processing: novel perspectives in cancer biology through the study of APE1 protein - and RNA –interactomes"
- September 27th, 2018; Indian Institute of Science Education and Research, Pune, India; Title: "Non canonical roles of BER enzymes in RNA processing: novel perspectives in cancer biology through the study of APE1 protein - and RNA –interactomes"
- April 3rd, 2019; School of Biological Sciences, Georgia Institute of Technology, Atlanta (GA), USA (Host. Prof. Francesca Storici);
- April 5th, 2019; Department of Biochemistry, St Louis University, St Louis (MO) USA, (Host: Prof. Alessandro Vindigni);
- April 9th, 2019; NIEHS/NIH, Triangle Park (VA), USA (Host. Prof. Samuel Wilson)
- May 11th, 2019; Opening Lecture at the '5th Liangjiang Meeting on the tumor and transformation research', Chongqing, China;
- September 24th, 2019; Istituto Superiore di Sanità, Rome, Italy (Host: Dr. Eugenia Dogliotti)

E. Meeting/Courses organization and invited chairman

- September 8th-11th 2003. European Science Foundation Programme on integrated approaches for functional genomics. *Biocrystallography course: from gene to drug*, Trieste, Italy. Chairman and course organizer in collaboration with Prof. Silvano Geremia
- February 29th-March 1st 2012. EASL Basic School of Hepatology, course 7: *Hepatocyte damage and Liver metabolism*, Trieste, Italy. Chairman and course organizer in collaboration with Prof. Claudio Tiribelli.
- September 24th-28th 2017, 6th EU-US International Meeting on Endogenous DNA Damages, Udine, Italy. Chairman and Congress organizer in collaboration with Prof. Robert Sobol, Alexander Buerckle, Eugenia Dogliotti;
- March 21st 2018, Chairman and invited speaker at EEMGS International Conference, Potsdam, Germany.

F. Referee for the following journals

- Analytical Chemistry
- Antioxid. Redox. Signal.
- Biochemical Journal
- Biochimica and Biophysica Acta
- Biotechnology Progress
- Biochimie
- Cancer Research
- Cell Biology International
- Cell Death and Differentiation
- DNA Repair
- European Journal of Pharmacology
- Experimental Cell Research
- Gastroenterology
- Gene

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- Hepatology
- International Journal of Biochemistry & Cell Biology
- International Journal of Cancer
- J. Proteome Res.
- Molecular and Cellular Endocrinology
- Molecular Biosystems
- Mutation Research
- Nucleic Acids Research
- Nucleic Acids Research-Cancer
- Nucleic Acids Research-Methods
- Nature Metabolism
- Oncogene
- Oncology
- PlosONE
- PNAS
- Proteomics
- RNA

G. Associate Editor of the following Journals

- Biomolecules
- BMC Research Notes
- BMC Biochemistry
- Proceedings of the National Academy of Sciences (PNAS)
- Scientific Reports

H. Institutional assignments

- Academic Years 2010-2012: Representative of Associate Professors in Academic Senate of the University of Udine;
- Academic Years 2009-2012: Member of the Teaching Commission for the Degree in Biotechnologies of the University of Udine;
- Academic Years 2012-2018: Director of the B.Sc. in Biotechnologies of the University of Udine;
- From 2010-present, Head of the Laboratory of Molecular Biology and DNA repair of the Department of Medicine at the University of Udine, Italy;
- From October 2015-October 2019, member of the Technology Transfer Commission of the University of Udine, Italy;
- Academic Years: 2014-present: Representative of the Rector of the University of Udine within the "Consortium of Molecular Biomedicine" of the Regione Friuli Venezia Giulia (CBM S.c.r.l. http://www.cbm.fvg.it);
- From 2017-present: Deputy of Research of the Department of Medicine, University of Udine;
- From January 2018-present: member of the Scientific Committee for the organization of ESOF2020 (https://www.euroscience.org/tag/esof-2020/ and http://www.proesof2020.eu/).
- From October 2019-present: Deputy Director of the Department of Medicine of the University of Udine

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I. Research topics developed by Prof. G. Tell

The scientific activity of Prof. G. Tell is fully developed within the themes of the BIO / 11 Disciplinary Scientific Sector.

Scientific activity in recent years has developed according to the following three major lines of research:

A. Gene expression and molecular mechanisms controlling cellular responses to oxidative stress.
A.1 Molecular mechanisms involved, role and regulation of the Ape1/Ref-1 coactivator in the cellular response to oxidative stress;
A.2 Structure/function relationship of the Transcription Factors.

B. Innovative approaches in the characterization of the complexity of biological systems applied to Molecular Medicine.
B.1 New Proteomics approaches applied to: i) ischemia / reperfusion injury in liver transplantation; ii) identification of biomarkers in pre-eclampsia; iii) identification of transcriptional targets of NF-kB in the neoplastic transformation process in thyroid carcinoma; iv) identification of molecular targets of the action of bisphosphonates in osteoblastic cell lines.

C. Non-canonical roles of DNA repair pathways in RNA metabolism

Specific description of the research themes developed by Prof. G. Tell

A. Gene expression and molecular mechanisms controlling cellular responses to oxidative stress.
A.1 Molecular mechanisms involved, role and regulation of the Ape1/Ref-1 coactivator in the cellular response to oxidative stress.

This topic has been the main interest of all the scientific activity of Prof. Gianluca Tell. Reactive oxygen species (ROS), such as H_2O_2, and OH° and O_2° radicals, play important physiological functions but can also cause cell damage and DNA mutations. The balance between physiological functions and damage is determined by the relative relationship between production and removal of ROS. Normally, these species are quickly removed before they can interfere with the functioning of the cell or bring it to death. Oxidative stress, an imbalance between the production of ROS and the antioxidant defense capabilities of the cell, can affect the main cellular components such as lipids, proteins, carbohydrates and DNA. This is closely associated with a number of human diseases such as many degenerative diseases, cardiovascular diseases, diabetes, cancer, neurodegenerative diseases and inflammatory processes. Various experimental evidences indicate that the redox state (oxidation / reduction) of the cell may affect growth and other cellular functions through the modulation of signal transduction pathways that start from the membrane receptors (such as the purinergic receptors) and arrive at conditioning cell specific gene expression. These pathways include the activation of gene expression mediated by various transcription factors (FT) such as Egr-1, Pax8, NF-kB, AP-1, HIF-1α, p53, c-Myc. The redox activation of these FT controls, in turn, a series of cellular responses to a

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variety of environmental stimuli. These responses include cell cycle control and differentiation, programmed cell death, cytokine gene expression, and growth factors. The emergence of these pathways of activation is mediated by the presence/production of ROS, which are therefore considered, in sublethal doses, as signalling molecules. Experimental observations, in which antioxidants are able to block signal transduction, provide further evidence that ROS can act as second messengers. In numerous models of human pathology (such as Gaucher's disease, fatty liver disease, estrogen-deficient osteoporosis, kernicterus, Parkinson's disease, liver cancer) and in physiological conditions (in ischemia/reperfusion during liver transplantation) there is a process of alteration of cellular redox homeostasis. These models have been studied by Prof. G. Tell in the perspective described above. From the molecular point of view, an important role in the cellular adaptive response to oxidative stress is that played by Ape1/Ref-1, a protein involved in the processes of DNA oxidative damage repair and in the regulation of gene expression acting as a transcriptional co-activator of numerous FTs such as: p53, AP-1, NF-kB, Myb, HIF-1α. Little is known about the ways in which Ape1 can perform, in a specific way, its multiple functions but it is now certain its involvement in processes of tumorigenesis and chemioresistance. The work carried out by Prof. Tell, has allowed to elucidate some aspects related to the regulation of the different functions of Ape1, in different models both in vitro and in vivo, as well as the biological role of these functions in particular associated with pathological events. The group coordinated by Prof. G. Tell has recently identified a new function, associated with the metabolism of RNA, which would explain the involvement of this protein in tumor transformation. In collaboration with the Cancer Genomic Center of the National Institutes of Health in Bethesda (MD, USA), Prof. Tell's group has selected specific inhibitors for this function in order to develop new anti-tumor strategies. The scientific value of these projects has been recognized by several fundings received from AIRC, MIUR and Friuli Venezia Giulia Region.

A.2 Structure/function relationship of Transcription Factors

This topic, which in the early phases of his career has characterized the scientific activity of Prof. Gianluca Tell, has also been dealt with. The main model, in which these topics were studied, was the thyroid cell, in which differentiation and proliferative events are modulated, in particular, by hormonal stimulation by TSH (thyrotropin). Pax-8 is one of the main transcription factors responsible for the expression of thyroid-specific genes encoding Thyroglobulin (Tg) and for the enzyme Thyroperoxidase (TPO). In particular, the role of DNA binding domain of Pax-8, called Paired domain, was studied in the promoter sequence of the aforementioned genes. The type of approach used was of a structural type (X-ray and NMR crystallography) as well as biochemical characterization *'in vitro'* (recognition of DNA sequences). The data obtained have made a significant contribution to the understanding of how these classes of proteins may recognize specific DNA sequences and have allowed to extend the observations also to another transcription factor (Pax6) belonging to the same family but to a different subclass of which it is been characterized the role of a human mutation.

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B. Innovative approaches in the characterization of the complexity of biological systems applied to Molecular Medicine.

B.1 New Proteomics approaches applied to: i) ischemia / reperfusion injury in liver transplantation; ii) identification of biomarkers in pre-eclampsia; iii) identification of transcriptional targets of NF-kB in the neoplastic transformation process in thyroid carcinoma; iv) identification of molecular targets of the action of bisphosphonates.

One of the modern challenges of Molecular Medicine is to characterize and study biological systems and pathology models in their complexity, rather than as a multitude of individual components through –OMICS approaches. To this end, technologies for the definition of cellular and tissue proteome, highly processive and of high resolution have recently been developed. Through the use of two-dimensional gel analysis techniques (2D-PAGE) and high sensitivity mass spectrometry (MS) (MALDI-TOF), applied both to samples of tissue and cellular protein extracts and to the analysis of conditioned culture and amniotic fluid from patients with preeclampsia, Prof. G. Tell has contributed to the identification of new protein markers of tissue damage as a result of the ischemia / reperfusion process during liver transplantation, of a new marker of early damage of preeclampsia and some proteins involved in the processes of neoplastic transformation in thyroid carcinoma. In the very recent years, also Functional Genomics approaches based on NGS strategies have been coupled with Proteomics strategies described. The unbiased and high-throughput techniques in the Genomic and Proteomic field developed, were also applied for the identification of the molecular mechanisms in the antitumor effects of the amino-bisphosphonate drugs (currently used in antitumor therapy for the treatment of breast carcinoma metastasis and for the treatment of osteoporosis, in a project developed in collaboration with Procter & Gamble, USA). These projects have been developed with the contribution of different structures both at national and international level. Currently, the laboratory of Prof. Tell has developed a series of functional proteomic and genomics methodologies and cellular models for the study and characterization of the interactome of Ape1 in order to develop specific inhibitors for the different activities of this protein in the optics of antitumor therapy and neurodegenerative diseases.

C. Non-canonical roles of DNA repair pathways in RNA metabolism

This is the most recent Topic developed by Prof. Tell and is largely based on previous research experiences. The Base Excision Repair (BER) pathway, initially studied as a mere DNA repair pathway, has been later found to be implicated in the expression of cancer related genes in human also thanks to the pioneeristic work leaded by Prof. Gianluca Tell who was the first demonstrating a role for Ape1 in RNA metabolism in 2009. A seminal paper has been recently published by Tell's group in *Nature Communications* demonstrating, for the first time, a role for Ape1 in miRNA processing important for cancer development. The BER handles simple alkylation and oxidative lesions arising from both endogenous and exogenous sources, including cancer therapy agents. Surprisingly, and largely thanks to the work carried out by Prof. G. Tell in the last decade, BER pathway involvement in transcriptional regulation, immunoglobulin variability and switch

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recombination, RNA metabolism and nucleolar function is astonishingly consolidating. An emerging evidence in tumor biology is that RNA processing pathways may participate in DNA Damage Response (DDR) and that defects in these regulatory connections are associated with genomic instability of cancers. In fact, many BER proteins are associated with those involved in RNA metabolism, ncRNA processing and transcriptional regulation, including within the nucleolus, proving a substantial role of the interactome network in determining their non-canonical functions in tumor cells. Maybe these new insights of BER enzymes, along with their emerging function in RNA-decay, may explain BER essential role in tumor development and chemoresistance and may explain the long-time mystery. The actual work leaded by Prof. G. Tell and his research group point to these potential new roles of BER in gene expression and RNA metabolism, as well as on the recent identification for a role of BER in recognition and repair of abasic and oxidized ribonucleotides embedded in DNA. This field of studies is very promising as also confirmed by a 5-years project recently granted, in 2017, by the Associazione Italiana per la Ricerca sul Cancro.

L. Teaching and services to students

Teaching

Medical School of the University of Trieste

1. Molecular Biology (4 CFU), B.Sc. Degree in Medical Biotechnologies, Academical Years 2000/2001, 2001/2002, undergraduate students;
2. Molecular Biology 2 (4 CFU), B.Sc. Degree in Medical Biotechnologies, Academical Years 2001/2002, 2002/2003, 2003/2004, undergraduate students;
3. Molecular Biology (1 CFU), Degree in Medical Dentistry, Academical Years 2001/2002, 2002/2003, undergraduate students;
4. Recombinant technologies (2 CFU), B.Sc. Degree in Medical Biotechnologies, Academical Years 2001/2002, 2002/2003, undergraduate students;
5. Functional Genomics and Proteomics (3 CFU), M.Sc. Degree in Medical Biotechnologies, Academical Years 2001/2002, 2002/2003, 2003/2004, 2004/2005, undergraduate students;
6. Techniques in Molecular Biology (9 CFU), B.Sc. Degree in Medical Biotechnologies, Academical Years 2001/2002, 2002/2003, 2003/2004, undergraduate students;
7. Molecular Genetics 2 (2 CFU), Master School in Medical Genetics, Academical Years 2001/2002, 2002/2003, graduated students.

For all the above-indicated courses, Prof. G. Tell acted as member or President of the evaluation commission. For all the courses held by Prof. G. Tell, the overall judgment of the students was always completely satisfactory.

Medical School and Biotechnology School of the University of Udine, Italy

1. General Pathology Degree in Rehabilitation Physiotherapy (4 CFU), Academical Year 1998/1999, undergraduate students;
3. Techniques in Molecular Biology (9 CFU), B.Sc. Degree in Medical Biotechnologies, Department of Medicine, Academical Years: 2001/2002, 2002/2003, 2003/2004, 2004/2005, 2005/2006, 2006/2007, 2007/2008, 2008/2009, 2009/2010, 2017/18, undergraduate students;

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4. Molecular Methodologies in Proteomics (3 CFU), Department of Medicine, M.Sc. Degree in Medical Biotechnologies, Academical Years: 2005/2006, 2006/2007, 2007/2008, 2008/2009, 2009/2010, 2010/2011, 2016/17, undergraduate students;
5. DNA repair mechanisms in mammalian cells (1 CFU), Department of Medicine, M.Sc. Degree in Medical Biotechnologies, Academical Years: 2007/2008, 2008/2009, 2009/2010, undergraduate students;
6. Molecular Biology (1 CFU, 16 hours), Department of Medicine, M.Sc. Degree in Sports Medicine, Academical Year 2011/2012, 2012/13, 2013/14, undergraduate students;
7. Molecular Biology (7 CFU), Department of Medicine, B.Sc. Degree in Biotechnologies, Academical Years: 2011/2012, 2012/13, 2013/14, 2014/15, 2015/16, 2016/17, 2017/18, undergraduate student;
8. Molecular Biology (5 CFU), Department of Medicine, Degree in Medicine, Academical Years: 2011/2012, 2012/13, 2013/14, 2014/15, 2015/16, 2016/17, 2017/18, undergraduate students.

For all the above indicated courses, Prof. G. Tell acted as member or President of the evaluation commission. For all the courses held by Prof. G. Tell, the overall judgment of the students was always completely satisfactory.

PhD Program in "Biomedical Sciences and Biotechnologies" of the University of Udine

From 2005-present Prof. G. Tell acted as teaching member of the PhD Program in "Biomedical Sciences and Biotechnologies" of the University of Udine.

Supervisor of Graduated Students (years 1998-2018): 77 students

7 in Biology, University of Trieste
1 in Chemistry, University of Trieste
24 in Medical Biotechnologies, University of Trieste
42 in Biotechnologies, Department of Medicine, University of Udine
2 in Biomedical Laboratory, Department of Medicine, University of Udine
1 in Medicine, Department of Medicine, University of Udine

Supervisor of Post-graduated students (years 2005-2018): 19 students

2 in Biochemistry, University of Trieste
17 in Biomedical Technologies, Department of Medicine, University of Udine

Supervisor of PhD students (years 2005-2021): 15

2 in Biomedical Sciences at the University of Trieste
13 in Biomedical Sciences and Biotechnologies at the Department of Medicine, University of Udine

Supervisor of PostDoctoral fellows (years 2005-2018): 18 Fellows

2 At the University of Trieste
16 At the Department of Medicine, University of Udine

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Participation to the Laurea Commission for the Degrees in Medicine and Biotechnology and for PhD Degrees

- From 2000-present: member or President of the evaluation commission for the '*Laurea*' Degrees in Medicine or in Biotechnologies both at the University of Trieste and Udine;
- From 2005-present Prof. G. Tell acted as member of the PhD Program in "Biomedical Sciences and Biotechnologies" of the University of Udine;
- From Academic Year 2016-2017-present: member of the evaluation committee for the PhD Program in "Molecular Biomedicine " of the University of Trieste;
- Academic Year 2016-2017: member of the evaluation committee for the PhD Program in "Molecular Medicine and Medical Biotechnologies-XXIX Cycle" of the University of Napoli.

M. Dissemination of Science and students orienteering activities

- From 2014-present: Organizer or collaborator to several orienteering events for college students, such as the "Open Day" and the "Moduli Formativi" (https://www.uniud.it/it/servizi/servizi-orientamento-scuole/servizi-scuole/moduli-formativi) of the University of Udine. These activities involve about 400 students/year;
- Academic Years 2015-2018: Coordinator for the University of Udine of the dissemination initiative in the field of Biology and Biotechnologies to students of the Primary and Secondary Schools within the Project titled '*Piano Lauree Scientifiche-PLS-Biotecnologie*', granted by the MIUR. These activities involve about 600 students/year.

LIST OF PUBLICATIONS

A. Full papers in peer reviewed international journals

1. **Tell, G.**, Leonardi, A., Damante, G., Di Lauro, R. and Formisano, S. "*Circular Dichroism as Preliminary Approach on the Study of Secondary Structure of Homeodomains*". (1993) Minerva Biotec. 5, 220-223.
2. Damante G, **Tell G**, Formisano S, Fabbro D, Pellizzari L, Di Lauro R. *Effect of salt concentration on TTF-1 HD binding to specific and non-specific DNA sequences.* Biochem Biophys Res Commun. 1993 Dec 15;197(2):632-8. PubMed PMID: 8267599.
3. Damante G, **Tell G**, Leonardi A, Fogolari F, Bortolotti N, Di Lauro R, Formisano S. *Analysis of the conformation and stability of rat TTF-1 homeodomain by circular dichroism.* FEBS Lett. 1994 Nov 14;354(3):293-6. PubMed PMID: 7957942.
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5. Bearz A, Tolazzi G, Leonardi A, Pucillo C, **Tell G**, Colombatti A, Formisano S. *Expression, purification and functional characterisation of a Kunitz-type module from chicken type VI collagen*. Biochem Biophys Res Commun. 1995 Oct 24;215(3):1050-5. PubMed PMID: 7488030.

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6. Fabbro D, **Tell G**, Leonardi A, Pellizzari L, Pucillo C, Lonigro R, Formisano S, Damante G. *In the TTF-1 homeodomain the contribution of several amino acids to DNA recognition depends on the bound sequence.* Nucleic Acids Res. 1996 Sep 1;24(17):3283-8. PubMed PMID: 8811078; PubMed Central PMCID: PMC146104.

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8. Esposito G, Fogolari F, Damante G, Formisano S, **Tell G**, Leonardi A, Di Lauro R, Viglino P. *Analysis of the solution structure of the homeodomain of rat thyroid transcription factor 1 by 1H-NMR spectroscopy and restrained molecular mechanics.* Eur J Biochem. 1996 Oct 1;241(1):101-13. PubMed PMID: 8898894.

9. Leonardi A, Altomonte M, Maio M, **Tell G**, Bearz A, Formisano S, Pucillo C. *Biphasic control of NF-kappa B activation induced by the triggering of HLA-DR antigens expressed on B cells*. Cytokine. 1997 May;9(5):295-9. PubMed PMID: 9195127.

10. Pellizzari L, **Tell G**, Fabbro D, Pucillo C, Damante G. *Functional interference between contacting amino acids of homeodomains.* FEBS Lett. 1997 May 5;407(3):320-4. PubMed PMID: 9175876.

11. Esposito G, Fogolari F, Damante G, Formisano S, **Tell G**, Leonardi A, Di Lauro R, Viglino P. *Hydrogen-deuterium exchange studies of the rat thyroid transcription factor 1 homeodomain.* J Biomol NMR. 1997 Jun;9(4):397-407. PubMed PMID: 9255944.

12. Moro M, Ceriello A, Mercuri F, **Tell G**, Pellizzari L, Damante G. *Glyceraldehyde 3-phosphate-induced DNA or protein modifications severely inhibit the protein/DNA interaction*. Horm Metab Res. 1997 Jul;29(7):347-50. PubMed PMID: 9288567.

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15. Bearz A, **Tell G**, Colombatti A, Formisano S, Pucillo C. *Fibronectin binding promotes a PKC-dependent modulation of NF-kappa B in human T cells.* Biochem Biophys Res Commun. 1998 Feb 24;243(3):732-7. PubMed PMID: 9500973.

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19. Scaloni A, Monti M, Acquaviva R, **Tell G**, Damante G, Formisano S, Pucci P. *Topology of the thyroid transcription factor 1 homeodomain-DNA complex.* Biochemistry. 1999 Jan 5;38(1):64-72. PubMed PMID: 9890883.

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33. Marsich E, Bandiera A, **Tell G**, Scaloni A, Manzini G. *A chicken hnRNP of the A/B family recognizes the single-stranded d(CCCTAA)(n) telomeric repeated motif*. Eur J Biochem. 2001 Jan;268(1):139-48. PubMed PMID: 11121114.

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36. Puglisi F, Barbone F, **Tell G**, Aprile G, Pertoldi B, Raiti C, Kelley MR, Damante G, Sobrero A, Beltrami CA, Di Loreto C. *Prognostic role of Ape/Ref-1 subcellular expression in stage I-III breast carcinomas*. Oncol Rep. 2002 Jan-Feb;9(1):11-7. PubMed PMID: 11748448.

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38. D'Elia AV, **Tell G**, Russo D, Arturi F, Puglisi F, Manfioletti G, Gattei V, Mack DL, Cataldi P, Filetti S, Di Loreto C, Damante G. *Expression and localization of the homeodomain-containing protein HEX in human thyroid tumors.* J Clin Endocrinol Metab. 2002 Mar;87(3):1376-83. PubMed PMID: 11889211.

39. Puglisi F, Aprile G, Minisini AM, Barbone F, Cataldi P, **Tell G**, Kelley MR, Damante G, Beltrami CA, Di Loreto C. *Prognostic significance of Ape1/ref-1 subcellular localization in non-small cell lung carcinomas.* Anticancer Res. 2001 Nov-Dec;21(6A):4041-9. PubMed PMID: 11911289.

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44. Paron I, Scaloni A, Pines A, Bachi A, Liu FT, Puppin C, Pandolfi M, Ledda L, Di Loreto C, Damante G, **Tell G**. *Nuclear localization of Galectin-3 in transformed thyroid cells: a role in transcriptional regulation.* Biochem Biophys Res Commun. 2003 Mar 14;302(3):545-53. PubMed PMID: 12615069.

45. D'Ambrosio C, Talamo F, Vitale RM, Amodeo P, **Tell G**, Ferrara L, Scaloni A. *Probing the dimeric structure of porcine aminoacylase 1 by mass spectrometric and modeling procedures.* Biochemistry. 2003 Apr 22;42(15):4430-43. PubMed PMID: 12693939.

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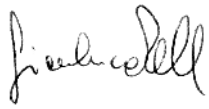

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