

PROF. DR. SC. KRESIMIR PAVELIC



MODIFIED ZEOLITE IN MEDICINE: DETOXIFICATION AND OTHE EFFECTS

Zeolites are aluminosilicates known for their ion-exchange properties. Properties of zeolites such as ion-exchange, intercrystalline pores that discriminate between molecules of different dimension, strong acidic sites, and active reservoirs for metal-catalyzed reactions have promoted their extensive use and fundamental zeolite research has become an area of great interest. Zeolites have high cation exchange selectivity, good resistance to temperature and ionizing radiations, and excellent compatibility with the environment, for which reasons they have been widely used in modern technology as selective adsorbents, molecular sieves, and particularly as catalysts. It is obvious that the ion sieving and other remarkable properties of

zeolites will be utilized in the near future for the environmental and health care industries for several reasons: (a) their known biological properties accompanied with their long-term chemical and biological stability; (b) zeolites reversibly bind small molecules such as oxygen and nitric oxide ; (c) they possess size and shape selectivity; (d) and the possibility of metalloenzyme mimicry. Zeolite used for medical applications in animals and humans is clinoptilolite. For example the type of clinoptilolite PMA has a similar, but finer structure which makes its active surface larger in comparison with natural raw clinoptilolite. PMA is for example, a strong inorganic cation exchanger as many other zeolites. This effect is due to negatively charged aluminosilicate structure that attracts cations. These cations consequently reside inside the empty spaces (pores and channels). As these spaces or cages are large, they easily accommodate large cations such as Na^+ , K^+ , Br^+ , and Ca^{2+} and even relatively large molecules and cationic groups such as water, ammonia, carbonate ions and nitrate ions. The basic structure of PMA is biologically neutral. The ion exchange process is reversible, allowing adsorption of ions and molecules which makes it useful in toxin removal from the body. This effect on body detoxification has already been documented in many studies on dietary inclusion of clinoptilolite in animal production, *i.e.* pigs fed with clinoptilolite experience weight gains and are less susceptible to disease than pigs fed normal which can be partially attributed to a lower toxin burden on the animal body. Moreover, addition of clinoptilolite to the aflatoxin diet reduced the adverse effects of aflatoxin. Similarly, clinoptilolite incorporated into the diet reduces deleterious effects of aflatoxin in growing chicks from 10 to 45 days of age, as it significantly reduced the negative aflatoxin effects on food consumption ratio. Heavy metals released in waste water are among the most worrisome pollution problems due to their cumulative effects along the food chain. The natural zeolites clinoptilolite, phillipsite and chabazite proved particularly useful in selectively eliminating ammonia and heavy metals such as Cd^{2+} , Pb^{2+} , Zn^{2+} , Cu^{2+} and, partially Cr^{3+} . For example, mercury is a well-known poison to human and animal health, but still widely used in many industrial processes and products (e.g. catalysis, pigments, batteries, saving lighting bulbs) and even in agriculture (e.g. antifungals). This creates serious environmental problems, pollution of aquatic systems, which leads to mercury accumulation in human body as well. Remarkable

removal rates of mercury from aqueous solutions by NaCl-pretreated pure heulandite crystals and NaCl-pretreated clinoptilolite-containing rock samples have been observed showing that natural zeolite materials could be used to remove heavy metals from aqueous solutions. The same mechanism occurs in human body upon intake of PMA. It moves through the intestine and removes toxins or heavy metals by the ion-exchange mechanism. It is not subject to intestinal uptake and is very stable. This prolongs its effect within the body and enforces the intestinal barrier, known to play a pivotal role in immunity. Moreover, double activated clinoptilolite® may exert preventive effects on the intoxication of organophosphate poisoning as zeolite tuff containing 61% clinoptilolite has already been shown to prevent and eliminate organophosphate poisoning. The organophosphate poison substance can strongly inhibit enzyme cholinesterase in erythrocytes, and in the stomach, brain and liver. This effect can be strongly diminished after pre-treatment with zeolite (1 g/kg 5 min before intoxication). The duodenum and colon are exceptions, where the cholinesterase activity was not significantly restored. Detoxification effect of PMA is therefore of great importance in patients subject to different poisoning, i.e. organic metals, heavy metals or toxic drugs. In particular, patients undergoing anti-infectious therapy with nucleoside analogues or chemotherapy often develop painful neuropathies due to increased levels of toxins and free radicals in the body. This simultaneous malfunction of peripheral nerves in the body cannot be cured at the moment and the condition is treated by palliative approach. PMA may be used in these cases as an adjuvant drug of choice either for acute states as for chronic conditions as it might substantially decrease the level of toxins and free radicals thus preventing the damage of nerves and/or increase the body natural capability of tissue recovery. In particular, polyneuropathic pain caused by ammonia has been observed in patients suffering from cancer. For example, ammonia/ammonium concentrations increase in the gastric mucosa due to infection with *H. pylori*, Ammonia acts as a promoter in a rat model of gastric cancer induced by *N*-methyl-*N*-nitro-*N*-nitrosoguanidine (MNNG). Similarly, colon cancer has been associated with high-protein diets poor in fibres and carbohydrates when undigested proteins reach the colon and are fermented by microflora into toxic compounds such as phenol compounds, indoles, cresol, amines and ammonia.

Double activated clinoptilolite eliminates very efficiently ammonia by ion exchange process. Such mechanism might act preventively and contribute to the therapeutic effect in such patients. The ultimate mechanisms of PMA action in states such as polyneuropathies thus, involve direct detoxification effects (it is a 'scavenger' for toxic compounds and free radicals) and increase of cellular antioxidant capacities, i.e. superoxide dismutase enzymes activity (SOD). Indeed, it is known that the activity of SOD1 and SOD2 are completely dependent on minerals (Cu, Zn and Mn). Moreover, activated clinoptilolite protected the cells by radical oxygen species (ROS)-induced cell death. The mechanism underlying this effect included reduction of the mitochondrial ROS production following a pro-oxidant stimulation. Indeed, they observed increased activity of SOD enzymes in the hippocampus of treated mice involved in the study. This study is important as it confirms previous data on detoxification effects of PMA. The detox-mechanism involves reduction of oxidative stress which enables physiological regeneration of each cell and prevents damage of biological structures. Altogether, PMA positively influences the mineral metabolism, adds to the antioxidant status of cells, lowers the levels of ROS and increase the activity of SOD enzyme. This effect synergistically contributes to lowering of cellular damage (i.e. those of neural cells) and consequently prevents and alleviates neuropathic pain. Decrease in ROS levels was also documented for PMA and it proved efficient to lower the damage of neurons in other diseases, *i.e.* Alzheimer disease. Indeed, on an Alzheimer mice model the authors showed that a reduction in amyloid levels and plaque load Alzheimer were observed in animals treated with activated clinoptilolite in comparison with control mice. Moreover, PMA has antimicrobial effects as reported previously. This effect might be attributable to adsorption of microbes on the mineral surface. It proved efficient for various urological patients who needed long-term use of indwelling balloon catheter for lower urinary tract obstruction and for neurogenic bladder. Moreover, PMA might have a positive impact in Diabetes Mellitus patients as well. Our previous, unpublished data brings out results on clinoptilolite effects on alloxan-induced diabetic mice model. Results proved that natural clinoptilolite might prevent or alleviate some late complications of diabetes, including development of polyneuropathies. Although natural, finely ground clinoptilolite did not significantly

decrease the blood glucose levels in studied animals, there were some indications that clinoptilolite managed to adsorb small amounts of glucose, as it was already proven that natural purified clinoptilolite hydrothermally transformed by use of FeSO_4 causes selectivity for glucose adsorption. Clinoptilolite showed positive effects on many diabetic symptoms. For example, non-treated diabetic mice had 1.92 mM/L Ca^{2+} in sera, whereas clinoptilolite-treated diabetic mice had higher Ca^{2+} concentration in sera ranging from 2.15 to 2.3 mM/L. Furthermore, Fe_2^+ -containing natural clinoptilolite interacts with glucose forming an iron-glucose complex in the clinoptilolite. The mechanism of action of the Fe_2^+ -clinoptilolite-glucose interaction is a strong adsorption governed by the reactive characteristics of glucose.

CURRICULUM VITAE PROF. KRESIMIR PAVELIC

Personal Data

Born July 19, 1952. in Slavonski Brod, Croatia -Croatian citizen

Krešimir Pavelić (1952) medical doctor, professor of molecular biology, Head, Department of Biotechnology, University of Rijeka, former director and establisher of Division of Molecular Medicine, Ruđer Bošković Institute, Former Secretary General of the European Molecular Biology Conference (EMBC), EMBO member, member of Croatian Academy of Sciences and Arts and many others international scientific organisations, former vice-president of European Molecular Biology Conference, EMBC, Delegate of Croatian Academy of Sciences and Arts in European Science Foundation, Former President of the National Scientific Council, Republic of Croatia, former member of the parliamentarian committee for national scientific awards, expert for molecular medicine of the Trans radical party in the European Parliament. Krešimir Pavelić is *ex officio* member of the Council of the European Molecular Biology Laboratory. He has published 280 scientific papers in world top scientific journals and several invited review papers and chapters in prestigious journals and book published by American and European publishers. He significantly contributed to the understanding of biology of the transformed cell.

Degrees

M.D. School of Medicine, University of Zagreb, Croatia - july 1975.

M.Sc. Thesis "Effect of immunosuppression on the growth of six murine tumors", Center for Postgraduate Studies, University of Zagreb 1977.

Ph.D. Thesis "Combined chemotherapy and immunotherapy of mice with malignant tumors". School of Medicine, University of Zagreb, 1979.

Assistant Professor (Research Associate) Ruđer Bošković Institute, Zagreb, april, 1980.

Associate Professor (Senior Research Associate), Ruđer Bošković Institute, Zagreb, october, 1981.

Full Professor (Senior Scientist), Ruđer Bošković Institute, Zagreb, march, 1985.

Teaching and Research Experience

Research Assistant, Ruđer Bošković Institute, Department of Biology and Medicine, University of Zagreb 1975-1979.

Research on the tumor immunology and experimental cancer chemotherapy.

Assistant Professor, Ruđer Bošković Institute, April 1980.

Elucidation of the physiological and cellular mechanisms underlying induction of tumor associated hormonally active substances which are involved in regulation of tumor growth.

Senior Research Associate, Ruđer Bošković Institute, October 1981.

Growth factors and positive feed back mechanism of tumor growth. Autocrine tumor growth regulation.

Full Professor, Ruđer Bošković Institute, 1985.

Growth factors and oncogenes in embryonal and tumor growth, cancer genetic.

Professor of Anatomy and Physiology, School of Pharmacy and Biochemistry, University of Zagreb 1982-1989.

Professor of Molecular Biology, School of Pharmacy and Biochemistry, University of Zagreb, 1990-2007.

Professor of Molecular Biology, Department of biotechnology, University of Rijeka, 2007-present.

Teaching - Postgraduate Studies

Postgraduate Study in Oncology, School of Medicine, University of Zagreb, 1977-present

Hormones and cancer, growth factors, oncogenes, new approaches in anticancer therapy, new diagnostic procedures

Postgraduate Study in Predclinical and Experimental Pharmacology and Clinical Pharmacology. School of Medicine, University of Zagreb, 1987-1989

Molecular pharmacology

Postgraduate Study in Endocrinology, School of Medicine, University of Zagreb, 1988-1989

Growth factors

International Postgraduate Study in Diabetology, School of Medicine, University of Zagreb, 1988-1989

Growth factors, hormones and cancer

Postgraduate Study in Neurology, School of Medicine, University of Zagreb, 1993-1994

Cancer genetics

Postgraduate Study in Medical Genetics, School of Medicine, University of Zagreb, 1994-present

Molecular genetic, cancer genetic

Postgraduate Study in Cytology, School of Medicine, University of Zagreb, 1994-present

Molecular genetic of cancer

Postgraduate Study in Medical Microbiology, School of Medicine, University of Zagreb, 1994/1995

Principles and application of recombinant DNA technology in medical microbiology

Postgraduate Study Biomedicine, School of Medicine University of Rijeka, 1996-present

Molecular oncology

Postgraduate and Postdoctoral Study, School of Medicine, University of Zagreb, 1998-present

Molecular Oncology

Selected Executive and Administrative International Functions

Secretary General, European Molecular Biology Conference (EMBC), 2008-2013.

Ex Officio Member, EMBO Council 2008-2013.

Vicepresident European Molecular Biology Conference (EMBC), 2004 – 2008.

Member, Standing Committee, European Medical Research Council, European Science Foundation 2004-present

Delegate, European Molecular Biology Conference, 2001-present

Delegate, European Molecular Biology Laboratory, 2006-present

Member, Strategic Working Party EMBC/EMBO, 2004-present

Member, Nahrstoff Akademie Salzburg, scientific board, 2003-present

Member of Executive Committee, European Association for Cancer Research 1999-2003

Selected Executive and Administrative Domestic Functions

Member, Senat, University of Rijeka, 2016-present

President, National Scientific Board Republic of Croatia, 2007-2012.

Head, Department of Biotechnology, University of Rijeka, 2008-present

Director, Division of Molecular Medicine, Ruđer Bošković Institute, 1993-2009.

President Governing Council, Institute for Medical Research and Occupational Health 2005-2011.

Director, National Cancer Research Program, Ministry of Science and Technology, Republic of Croatia, 1997-2001.

President, Executive board of the Workers Council, Ruđer Bošković Institute, 1981-1982.

President, Scientific Council, Department of Experimental Biology and Medicine, Ruđer Bošković Institute, 1986-1988.

Dean (President), Scientific Council of the Ruđer Bošković Institute, 1987-1992.

Member, Senat, University of Zagreb, 1987-1992.

Member, Scientific Council of the University of Zagreb (Board of deans) 1987-1992.

Member, National Board for Scientific Awards, Republic of Croatia, 1988.

Head, Laboratory of Molecular Oncology, Division of Molecular Medicine, Ruđer Bošković Institute, 1991-1997.

Member, Council of the School of Medicine, University of Zagreb, 1991-1992

Member, National Board for Biomedicine, Ministry of Science and Technology, Republic of Croatia, 1995-1998.

President, Section of Molecular Genetic, Croatian Society of Human Genetic, 1995-1997.

Member, Croatian Association of the Club of Rome, 1995-present.

Assistant Director General, Ruđer Bošković Institute, 1999-present

Member and vicepresident, National Board for Scientific Awards, Biomedicine, 2001-2005.

Member, Gouverning Board, Agency for Science and High Education, Ministry of Sciences, Education and Sports, 2005-present

Member, National Scientific Board, 2004-2012.

President, Gouverning Board, Institute for Medical Research and Occupational Medicine, Zagreb, 2005-2011.

Evaluator and panel member European Science Foundation

Evaluator and panel member Portugese Foundation for Science and Technology (2014-present)

Current Membership in Scientific Societies

Croatian Immunological Society

Croatian Cancer Society

Croatian Genetical Society

Croatian Physiological Society

Croatian Association of Human Genetics

Croatian Endocrinological Society

European Association for Cancer Research

International Stress Management Association

European Society of Human Genetics

Croatian Bioethical Society

Visiting Research Fellow

Roswell Park Memorial Institute, Buffalo, N.Y. U.S.A. November 1978.

Visiting Professor, Roswell Park Memorial Institute, Grace Cancer Drug Center, Buffalo, N.Y. U.S.A. 1984-1986.

Visiting Professor, University of Hamburg, University Clinic Eppendorf, Institute for Physiological Chemistry, Hamburg, Germany, (three months) 1988.

Visiting Professor, University of Cincinnati, College of Medicine, Department of Pathology and Laboratory Medicine, Cincinnati, OH, U.S.A.(6 months) 1990.

.Visiting Professor, Mayo Clinic and Foundation, Division of Developmental Oncology Research Rochester, MN. U.S.A. (3 months) 1991.

Honors and Awards

University of Zagreb May Prize for research performed by students for 1972. and 1973.

Drago Perović Prize for students of the School of Medicine, University of Zagreb for 1973.

Federal Prize for Young Scientists (under 30) for 1978.

Vuk Vrhovac Prize for research in diabetology (Diabetology Section of Croatian Medical Association) for 1982.

Roswell Park Memorial Institute Fellowship 1984-1986.

University of Hamburg Fellowship 1988.

Fullbright Fellowship of U.S. Government 1990 and 1991.

Yamagiwa-Yoshida Memorial Award, International Union Against Cancer, 1993.

Croatian Academy of Medical Sciences, Annual award "*Ante Šercer*" for best scientific paper published in 1996.

Croatian Government State Award for 1998.

Membership in Academies

Member of European Molecular Biology Organization (EMBO), 2002.

Member of Croatian Academy of Sciences and Arts, 1992.

Member of Croatian Academy of Medical Sciences, 1994.

Membership in the Editorial Boards in Scientific Journals

Libri Oncologici, Zagreb, Croatia, member of editorial board, since 1992.

Pathology Oncology Research, Budapest, Hungary, member of editorial board, since 1996.

Medical Science Monitor, member of editorial board since 2002.

Balkan Journal of Medical Genetics, member of editorial board since 2002.

Journal of Oncology, Hindawi publishing Group, member of editorial board, May 2008.

MD - Medical Data, Mostart, Zemun, Serbia, June 2011.

Acta Medica Academica, Journal of Department of Medical Sciences of Academy of Sciences and Arts of Bosnia & Herzegovina, Sarajevo.

Archives of Industrial Hygiene and Toxicology, Zagreb, Croatia

Advances in Genetic Engineering and Biotechnology, Boston, MA, USA member of editorial board since July 2014

External Reviewer for International Scientific Organizations

European Science Foundation

ESF-EMBO Symposia Review Panel

Portuguese Foundation for Science and Technology, periodic evaluation of R&D Units

Grants Awarded (Principal Investigator)

1. *Development of Technology for Radioimmunoassay Components for Measuring Hormone Levels in Blood.* Ministry of Science, Technology and Information, Republic of Croatia, Zagreb, 1982., Grant No. V-683/1-82

2. *Development of Technology for Production of Fetal Calf and Newborn Calf Serum for Cell Culture System.* Ministry of Science, Technology and Information, Republic of Croatia, Zagreb, 1983. Grant No. V-511/1-83

3. *Isolation and Characterization of Tumor Produced Substance Immunologically Cross Reactive with Insulin.* BRSG Grant Committee, Roswell Park Memorial Institute, Buffalo, Department of Health, State of New York, 1984-1985.

4. *Differentiation and Growth Control of Normal and Tumor Cells*. Ministry of Science, Technology and Information, Republic of Croatia, Zagreb, 1986-1990. Grant No. 2.04.01.02.01

5. *Substance Immunologically Cross Reactive with Insulin*. Commission of the European Communities. 1989 - 1992. Grant No. I1-0334-YU/A

6. *Growth Factors*. Yugoslav Government. 1990- 1995. Grant No. P-354/6

7. *Expression and Role of Oncogenes and Growth Factors in Malignant Tumors*. Ministry of Science, Technology and Information, Republic of Croatia, Zagreb, 1991-1993. Grant No.1/08/144

8. *Automatic synthesis of DNA*. Institute Open Society Croatia (Soros Foundation), Zagreb, 1993.

9. *Establishment of the Eastern and Central European Human Tumor Bank Network*. Institute Open Society Croatia (Soros Foundation), Zagreb, 1994.

10. *National Cancer Research Program*, Ministry of Science and Technology, Republic of Croatia, 1997- present, Grant No. P-9811

11. *Molecular Genetic Basis of Metastasis*, Ministry of Science and Technology, Republic of Croatia, 1997- present, Grant No. P-1104

12. *Establishing of toxicological and antitumoral effects of potential agents against tumors*. Ministry of Science and Technology, Republic of Croatia, 2001- present, Grant No. 00981499

13. *Effect of transduction of genes/proteins on signal transduction in tumor cells*. Ministry of Science and Technology, Republic of Croatia, Zagreb, Project No.. 0098093, 2001-2006

14. Center for Integrative Genomics. Technology Related Research and Development Projects (TEST). Program Core, Ministry of Science, Education and Sports, Republic of Croatia, Zagreb, Project No J-1/2004.

15. *Molecular characteristics of miofibroblasts in Dupuytren disease*. Ministry of Science, Education and Sports, Republic of Croatia, Zagreb, Project No 098-0982464-2393.

16. *Development of drug against Dupuytren contracture*. National Fund for Development and Employment, Zagreb, Croatia, Project No 450-05/06-01/0003.

SR&D contracts with international industrial partners (2009-2014)

Coorganizer of International Conferences

- 1st International Conference on Signal Transduction
8-11 October 1998, Cavtat-Dubrovnik, Croatia

- 2nd International Conference on Signal Transduction
26-31 May 2000, Cavtat-Dubrovnik, Croatia
- 3rd International Conference on Signal Transduction
May 2002, Cavtat-Dubrovnik, Croatia
- 4th International Conference on Signal Transduction
May 2004, Cavtat-Dubrovnik, Croatia
- 1st International Conference on Mechanisms of Action of Nutraceuticals
14-19 October, 2001, Cavtat-Dubrovnik, Croatia
- 2nd International Conference on Mechanisms of Action of Nutraceuticals. October,
2002, Krems, Austria
- 3rd International Conference on Mechanisms of Action of Nutraceuticals
November, 2004, Maggie Walley, North Carolina, USA
- 2nd EMBO Sectoral Meeting on Molecular Medicine
19-22. June, 2003, Cavtat-Dubrovnik, Croatia
- 2nd International conference on regenerative orthopaedics and tissue
engineering. 20-22, 09. 2012, Opatija, Croatia. (Co-president).

Books

Author

- Pavelić K., *Kako pobijediti rak*, Globus, Zagreb, 1989
- Pavelić K., *Kako spriječiti rak*, Globus/ Ministarstvo zdravstva Republike Hrvatske/ Hrvatska liga protiv raka, Zagreb, 1996.
- Pavelić K., Schimpf S., Meyer-Wegener J.: *Zeolites: Energy from the Earth's Primary Rock*. VIP Sante, Luxemburg, 2002, English edition;
- Pavelić K., Schimpf S., Meyer-Wegener J.: *Zeolithe: Die Kraft aus dem Urgestein der Erde*. VIP Sante, Luxemburg, 2002, German edition;
- Pavelić K., Schimpf S., Meyer-Wegener J.: *La Zeolite: La force de la roche primitive terrestre..* VIP Sante, Luxemburg, 2002, French edition;
- Pavelić K., Schimpf S., Meyer-Wegener J.: *As Zeolitas: A força que provem da rocha primitiva da Terra*. VIP Sante, Luxemburg, 2002, Portuguese edition;
- Pavelić K., Schimpf S., Meyer-Wegener J.: *Le Zeoliti: Forza dalla pietra primigenia della terra*. VIP Sante, Luxemburg, 2002, Italian edition.
- Pavelić K.: *Čuda moderne medicine. Nadanja i strepnje*, Globus, Zagreb, 2004.
- Pavelić K.: *Wunder der modernen Medizin. Hoffnungen und Bedenken*. Globus, Zagreb, 2004. German edition.

Editor

- Ikić D, Pavelić K, Spaventi R: Onkogeni i faktori rasta, JAZU/Globus, Zagreb, 1989.
- Pavelić K, Spaventi R: Molekularna onkologija, HAZU/Globus, Zagreb, 1992.
- Polšek D, Pavelić K: Društveni značaj genske tehnologije, Institut društvenih znanosti Ivo Pilar, Zagreb, 1999.
- Kurjak A, Stavljenić-Rukavina A., Pavelić K.: Prenatalna dijagnostika i terapija. Tonimir, Varaždinske Toplice, 2000.
- Bodiroga N, Pavelić K, Rukavina D, Sanger GC eds.: Personalized medicine, a new medical and social challenge. Springer, Dordrecht, Heidelberg, London, New York, 2016.
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International Initiatives

- K. Pavelic: Initiator of Croatian membership to European Molecular Biology Laboratory as organization's 19th Member State, 29.06.2006.
- K. Pavelic: Science Policy Briefing: **Human stem cell research and regenerative medicine**. European Medical Research Council, European Science Foundation, 52nd plenary meeting, London, United Kingdom, 22.-23. April, 2008.
- K. Pavelic: Forward Look: **Personalized medicine for the European citizen – towards more precise medicine for the diagnosis, treatment and prevention of disease**. European Medical Research Council, European Science Foundation, 55th plenary meeting, Copenhagen, Denmark, 13.-14. October, 2009.
- **Invited speakers at international meetings**
 1. Pavelić K.: Growth of tumors in diabetic hosts. *First International Symposium on Basic Diabetology*, 22.-28.01.1984. Porlamar, Venezuela
 2. Pavelić K.: Extracellular matrix: A new in vitro system. *Roswell Park Memorial Institute*, 5.11.1985, Buffalo, New York, USA
 3. Pavelić K.: Nerve growth factor (NGF) induced differentiation of human neuroblastoma cells biochemical properties of methionine 5-enkephalin and its receptors. *Conference Embryonic Origins and Control of Neoplasia*, 13.-14.10.1986., Dubrovnik
 4. Pavelić K., Čabrijan T., Levanat S.: Autocrine tumor growth regulation by the IGF I and the EGF. *Third International Congress on Hormones and Cancer*, 9. 1987., Hamburg, Germany
 5. Pavelić K.: Induction of tumor cell differentiation in different human cell lines. *Institut for Physiological Chemistry, University Clinic Eppendorf, University of Hamburg*, 11.2.1988., Hamburg, Germany
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 6. Pavelić K.: A new method for tumor cell cultivation on artificial basement membrane. *Department for Molecular Endocrinology, University Clinic Eppendorf, University of Hamburg*, 23.8.1988., Hamburg, Germany
 7. Pavelić K.: A substance immunologically cross reactive with insulin, *University Clinic Eppendorf, University of Hamburg*, 24.8.1988., Hamburg, Germany
 8. Pavelić K.: Extracellular matrix: A new model for the in vitro cultivation of primary human tumor explants. *Mayo Clinic*, 11.5.1990., Rochester, Minnesota, USA
 9. Pavelić K.: Immunohistochemical detection of C-MYC oncoprotein in paraffin-embedded tissue. *University of Cincinnati, College of Medicine*, 17.8.1990., Cincinnati, Ohio, USA
 10. Pavelić K.: Molecular mechanism of cell activation. 35. *Congresso Nazionale Societa Italiana di Biochemica*, 29.09.- 3.10.1990., Bari, Italy
 11. Pavelić K.: Oncogene and growth factors in autocrine control of tumor proliferation. *Molekularna genetika v medicini*, 22. *Memorijalni sastanak profesora Janeza Plečnika* 12. - 13.12.1991., Ljubljana, Slovenia

- 12. Pavelić K.: c-erb B-2/neu oncogene: A potencial prognostic value. *University of Cincinnati, College of Medicine*, , 28.10.1992. Cincinnati, Ohio, USA
- 13. Pavelić K.: New aspects in molecular medicine, uvodno predavanje. *New Aspects in Molecular Medicine 2*, Hrvatska akademija znanosti i umjetnosti, Zagreb, 5.11.1993., Cincinnati, Ohio, USA
- 14. Pavelić K.: Multiple genetical changes in malignant insulinoma. *Cancer Research Institute, Slovak Academy of Sciences*, 20.3.1995., Bratislava, Slovakia
- 15. Pavelić K.: Expression of nm23 gene in human tumors. *College of Medicine, University of Cincinnati*, 30.3.1994., Cincinnati, Ohio, USA
- 16. Pavelić K.: Multiple genetical alterations in malignant insulinomas. *Dnevi medicinske genetike z mednarodno udeležbo*. 19.-20.12. 1995., Ljubljana, Slovenia
- 17. Pavelić K.: Multiple genetical changes in neuroendocrine tumors. *Oncogenes and Tumor-Suppressor Genes*. 2.-7.12.1996., Cincinnati, Ohio, USA
- 18. Pavelić K.: Tumor suppressor gene NM23-H1 - A potential new tumor marker. *15th International Conference on Tumor Markers "Clinical Cancer Genetics and Biological Therapies"*. 14-17. 6. 1998, Lugano Switzerland
- 19. Pavelić K.: Metastasis repressor gene nm23-H1 - a potential new genetical marker. *The International Congress on Malformations and Rare Tumors of the Head and Neck*., 24.-27. 11. 1998. Zagreb, Croatia
- 20. Pavelić K.: Metastasis repressor gene nm23-H1 – a potential new genetical marker. *Österreichische Biochemische Gesellschaft, Österreichische Gesellschaft f. Genetik und Gentechnik, Österreichische Gesellschaft f. Klinische Chemie*, 29.04.1999., Graz, Aust
- 21. Pavelić K.: Molecular genetics of malignant insulinomas. *International Conference on Disease of Pancreas, Biliary Tract and Duodenum*, 07.05.1999., Ljubljana, Slovenia
- 22. Pavelić K.: Zeolites in Medicine. *Gesellschaft fur Biologische Krebsabwehr E.V., Krebserkrankungen im Jahr 2000.*, 04.03.2000., Chemnitz, Germany
- 23. Pavelić K.: Breast cancer genetics and biology. *Second Central European Oncology Congress*. 27.-30.06. 2000. Opatija, Croatia
- 24. Pavelić K.: Molecular genetics of breast cancer. *2nd Congress of the Slovenian Genetic Society*. 13.-17.09. 2000. Bled, Slovenia
- 25. Pavelić K.: Increased activity of nm23-H1 gene in squamous cell carcinoma of the head and neck is associated with advanced disease and poor prognosis. *31st Memorial Meeting for Professor Janez Plečnik*. 7.-8.12. 2000. Ljubljana, Slovenia
- 26. Pavelić K.: New break-throug in gastrointestinal cancer. *Conference on "Current Perspectives on Biomolecular Indicators and Clinical Management of Bladder, Breast, Colorectal and Lung Cancer"*. 18.-22. 04. 2001. Erice, Italy
- 27. Pavelić K.: Biomedical applications of zeolites. *13th International Zeolite Conference*. 8.-13.07. 2001. Montpellier, France
- 28. Pavelić K.: Arguments for human therapeutic cloning. *Conference on Stem Cells: for the Freedom of Research in Europe*. *European Parliament*, 18.-19.09. 2001. Bruxelles, Belgium
- 29. Pavelić K.: Molecular genetics in oncology. *SEE – Conference on Molecular Medicine*, 6-8,12. 2001., Skopje, Macedonia
- 30. Pavelić K.: Globalization and scientific freedom in molecular medicine. *38th Congress of the Transnational Radical Party*, 4. - 7. 4. 2002. Geneva, Switzerland
- 31. Pavelić K.: Adjuvant effect of natural clinoptilolite in anticancer therapy. *6th International Conference on the Occurrence, Properties and Utilization of Natural Zeolites*. Thessaloniki, 31.5. – 3.6. 2002. Greece
- 32. Pavelić K.: New developments in molecular oncology. *3rd Central European Oncology Congress*. Opatija 19.06-22.6. 2002.
- 33. Pavelić K.: Could medicine benefit from zeolites: Molecular mechanisms of clinoptilolite activity. *2nd International Conferenc on Mechanisms and Actions of Nutraceuticals*. Krems 6.10.-9.10, 2002. Austria
- 34. Pavelić K.: Involvement of insulin-like growth factor family of genes in human cancer. *EMBO Conference Frontiers of Molecular Biology*. Oslo 11.10.-14-10. 2002, Norway.
- 35. Pavelić K.: Molecular genetics of breast cancer. *2nd Meeting of the Molecular Medicine Network in SE Europe*. *University Hamburg and DAAD Stability Pact for SE Europe*. Skopje, 18. 10. 2002. Macedonia.

- 36. Pavelić K.: Molecular mechanisms of clinoptilolite action at cellular level. Institute of Mineralogy, University of Salzburg, Salzburg, 23. 10. 2002. Austria.
- 37. Pavelić Kresimir: International Conference on Bioethics in Central and Eastern Europe. Lithuanian National Commission for UNESCO. Vilnius, 11.-12. 11. 2002. Lithuania
- 38. Pavelić K.: The role of insulin-like growth factor family in cancer development and growth. Technical University Dresden, Institute for Zoology, Faculty of Science, Department of Biology, Dresden, 19.11. 2002. Germany.
- 39. Pavelić K.: Arguments for and against human reproductive and therapeutic cloning. Scientific, ethical, religious dilemmas on the embryo status and its cloning, Sarajevo, 15.02. 2003. Bosnia and Herzegovina.
- 40. Pavelić K.: Functional genomics in perinatal medicine. Scientific, ethical, religious dilemmas on the embryo status and its cloning, Sarajevo, 15.02. 2003. Bosnia and Herzegovina.
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See under list of publication:

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