Bio Data

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Education

Ph. D. (Drug Design & Synthesis) University of New Brunswick, Canada 1980, Supervisor: Prof. Karel Wiesner, FRS; D. Phil (Chemistry) Allahabad University 1978, Supervisor: Prof. Nil Ratan Dhar, FRS

Career

2006-2007, Founder Dean, School of Biotechnology, Jawaharlal Nehru University; 2005-2006, Chairman, Centre for Biotechnology; 2002, Professor; 1999 – 2001, Chairman, Centre for Biotechnology, Jawaharlal Nehru University; 1998, Acting Director, Genetic Engineering Unit, Jawaharlal Nehru University 1994-2002, Associate Professor, Centre for Biotechnology Jawaharlal Nehru University; 1991-1994, Assistant Professor of Medicine & Molecular Biology, School of Medicine, Augusta, Georgia, USA; 1986-1991, Associate Research Scientist, Yale University School of Medicine, CT, USA; 1983-1985, Research Associate, Yale University, CT, USA; 1982-1983; Research Associate, Massachusetts Inst. of Technology, Cambridge, USA; 1981-1982, Post doctoral Research Fellow, Max-Planck Inst, Germany; 1976-1978, Lecturer in Chemistry, Regional College of Education, Bhubaneswar.

Contributions

Synthesis of cardioactive drugs, PhD Thesis, 1980, Patent, Hoffman La Roche; Cloning of human RNA polymerase II subunits, 1989; Hypothesis of mammalian polymerase II assembly, 1994; Establishing of CHIP as a molecular chaperone of p53, 2007; Role of p53 in genetic programming of necrotic death & gold nanoparticle-mediated hypoxic tumor regression 2011; Discovery of p53 as a molecular chaperone & p53-chaperone therapy 2011; Oxygen Therapy for hypoxic tumor, 2012. Discovery of SCO2, a new tumor Suppressor, 2013

Honors and Awards

American Cancer Society Award, 1992-95; MCG (Georgia) Institutional Award, 1991-92; Swebilus Cancer Research Award, 1990; American Cancer Society Grant Award, 1991; American Cancer Society Travel Award, 1990; Yale Research Fellowship, 1983-85; MIT Research Fellowship, 1982-83; Max-Planck Fellowship, 1981-82; University of New Brunswick Teaching Assistantship 1978-81; CSIR Junior Fellowship, 1975-78.

Research Interests

Cancer Biology, Gene regulation in hypoxia, Re-oxygenation, p53 and HIF1a and their role in hypoxic tumor, Molecular chaperones and gene regulation

Other Interests

Dimensions and interpretation of Consciousness, Comparative Religion, Education and society, Social Ethics, Public health and education, Welfare of Disabled and Old

Teaching Experience

28 year experience in post graduate teaching at the M.Sc and PhD level

Students Supervised

M.Sc: **68**; PhD: **16**; PhD student registered at present: **8** Summer students (M. Sc) from other Institutes: **50**

Selected International Publications

1. Esha Madan1, Rajan Gogna, Bernhard Keppler, **U Pati**, p53 Increases Intra-cellular calcium release by transcriptional regulation of calcium channel TRPC6 in GaQ3-treated cancer cells, ***PloS* One** (2013) (In press)
2. Rajan Gogna, Esha Madan, Mahmood Khan, **Uttam Pati**, Periannan Kuppusamy. p53's choice of myocardial death or survival: Oxygen protects infarct myocardium by recruiting p53 on NOS3 promoter through regulation of p53Lys^{162}acetylation. ***EMBO Report*** (2013)(In press)
3. E Madan, R Gogna, P Kuppusamy, M Bhatt, A Ali Mahdi, **U Pati**. SCO2 Induces p53-Mediated Apoptosis by Thr^{845} Phosphorylation of ASK-1 and Dissociation of ASK-1-TRX Complex 2012 ***Mol Cell Biol*** (2013) 33, No 7, 1285-1302
4. Mohammad Azam, Saud I. Al-Resayesa, Agata Trzesowska-Kruszynskab, Rafal Kruszynsk, Ambarish Verma, **Uttam Pati.** Apoptosis induction by chiral anionic binuclear Zn(II) complexes based on (*1S*,*2S*)-(+)-Cyclohexanediamine in HCT cells with different p53 status. ***Inorganic Chemistry*** (2013) (In press)
5. E Madan , R Gogna , **U Pati**. p53^{Ser15} Phosphorylation disrupts p53-RPA70 complex and induces RPA70- mediated DNA repair in hypoxia, ***Biochem Jour*** (2012) 443 (3) 811-820
6. R Gogna, E Madan, P Kuppusamy, **U Pati**. Re-oxygenation causes hypoxic tumor regression through restoration of p53 wild type

conformation and post-translational modifications, ***Cell Death & Disease,*** Cell Death and Disease (2012) 3, eK; doi:10.1038/cddis.2012.15

7. R Gogna, E Madan, P Kuppusamy, **U Pati**. Chaperoning of Mt p53 by Wt p53 causes hypoxic tumor regression. ***Jour Biol Chem,*** (2012) 287, No.4, 2907-2914, 2012 Published on December 6, 2011 as Manuscript M111.317354
8. E Madan, R Gogna , P Kuppusamy , M Bhatt , **U Pati** *, A Ali Mahdi * TIGAR Induces p53-Mediated Cell-Cycle Arrest by Regulation of RB-E2F1 Complex. ***British Jour Cancer*** (2012), 1–12
9. E Madan, R Gogna, M Bhatt, **U Pati**, P Kuppusamy, A Ali Mahdi. Regulation of glucose metabolism by p53: Emerging new roles for the tumor suppressor. ***Oncotarget*** (2012) 2, No 12, 948-957
10. R Gogna, E Madan, P Kuppusamy, **U Pati**. P53 core domain modifications determine apoptotic and necrotic death in cancer cells. ***Antioxidant & Redox Signaling***, (2012) 16, 400-412
11. R Gogna, E Madan, B Keppler, **U Pati**. Gallium compound GaQ3-induced Ca2+ signaling triggers p53-dependent and independent apoptosis in cancer cells, ***British Jour Pharmacology*** (2012) 166 617–636; 2011
12. M Shrivastava, S. Vivekanandhan, **U Pati**, M Behari, and T K. Das. Mitochondrial Perturbance and Execution of Apoptosis in Platelet Mitochondria of Patients with Amyotrophic Lateral Sclerosis. ***International Journal of Neuroscience***, 121, 149–158, 2011
13. M Shrivastava, T K. Das, M Behari, **U Pati**, Vivekanandhan. Ultrastructural Variations in Platelets and Platelet Mitochondria: A Novel Feature in Amyotrophic Lateral Sclerosis. ***Ultrastruct Pathol***, 35(2), 52–59, 2011
14. A Sharma, A Ali, R Gogna, A Singh, **U pati**. The role of p53 amino terminus domain in displaying chaperone like function. ***PloS One*** 4 (10), 2009, 7159-
15. S. Subhankar ,**U Pati**, S. Chandna, U. Stress response of a p53 homologue in the Radioresistant Sf9 insect cells, ***Int Jour Rad Biol*** 85 (3), 2009, 238-249
16. SK Dubey, A K Sharma, U Narain, K Mishra, **U Pati**. Design, synthesis, and characterization of some bioactive conjugates of curcumin with glycine, glutamic acid, valine, and demethylenated piperic acid and study of their antimicrobial and anti-proliferative properties. ***Eur j Med Chem***. 43,2008, 837-449
17. V tripathi, A Ali, R Bhat, **U Pati**. CHIP chaperones wild type p53 tumor suppressor protein. ***Jour Biol Chem,*** 282, 39, 2007, 28441-454
18. N Kapoor, A K Sharma, V Dwivedi, A Kumar, **U Pati**, K Mishra. Telomerase-targeted anti cancer bioactive prodrug by antisense-based approach. ***Cancer Lett***. 248, 2007, 245-250
19. R.Chauhan, R. Handa, Trinath P. Das, and **U. Pati**. Over expression of TATA-binding protein (TBP) and p53 and autoantibodies to these

antigens are features of systemic sclerosis, systemic lupus erythematosus, overlap syndromes. ***Clin Exp Immunol***136, 2004, 574-584

20. S. Negi, S. Singh, N. Pati, V. Handa, R. Chauhan, and **U. Pati**. A proximal tissue-specific and a distal negative regulatory module control apo(a) gene transcription. ***Biochem Jour* 378**, 2004, 1-9
21. V. Handa, Mahboob-ul-Hussain, N. Pati, and **U. Pati**. Multiple liver-specific factors bind to a 64 bp element and activate apo(a) gene. ***Biphy. Biochem. Res. Comm***. 292, 2002, 243-249
22. **U. Pati**. Atherosclerosis and the genetic switch. ***Biotechnology in Health Care.*** Eds. T. Lazzar Mathew. Delhi, 2001
23. **U Pati** and N Pati Lipoprotein(a), Atherosclerosis, and Apolipoprotein(a) Gene Polymorphism. ***Mol Genet Met* 71**, 2000, 87 – 92.
24. **U Pati** and J.K.Gambhir. Apolipoprotein(a) Polymorphism and Plasma Lipoprotein(a) levels. ***Indian Heart Journal*** 52, 2000, 171-172.
25. N. Pati, A. Rouf and **U. Pati**. Simultaneous mutations (A/G-418 and C/T-384) in the apo(a) promoter of individuals with low LP(a) levels, ***Mol. Genet. Met.*** 69 ,2000, 165–67.
26. N. Pati and **U. Pati**. Paraoxanase gene polymorphism and coronary artery disease in Indian subjects, ***Int. Jour. Cardiol***. 66, 1998, 165-168.
27. **U.K. Pati**. Human RNA polymerase II subunit hRPB14 is homologous to yeast RNA polymerase I, II and III subunit (AC19 and RPB11) and is similar to a portion of the bacterial RNA pol II subunit**.** ***Gene*** 145, 1994, 289-292.
28. M. Hirakata, Y. Okano, **U. Pati**, A. Suwa, J. Hardin and J. Craft Identification of autoantibodies to RNA polII: Occurance in systemic sclerosis and association with autoantibodies to RNA polI, III. ***J. Clin. Invest***. 91, 1993, 2665-2672.
29. **U.K. Pati**. Novel vectors for expression of cDNA encoding the epitope-tagged proteins in mammalian cells. ***Gene*** 114, 1992, 285-288.
30. M. Hirakata, J. Kanungo, **U.K. Pati**, A. Suwa, Y. Okano, and J.A. Hardin. The auto-antigenic domain of RNA polymerase II resides at the carboxyl terminal. ***Arthritis Rheum***. 35, 1992, 38-40.
31. L. Denner, J. Hongjun, R.D. Owen, G.L. Kato, C.L. Clarke, and **U.K. Pati**. Steroid receptors, transcription factors, and gene expression ***Cancer. Res.*** 50, 1990, 6430-6436.
32. **U.K. Pati** and S. Weissman. The amino acid sequence of human RNA polII subunit hRPB33 is highly conserved in eukaryotes ***J. Biol. Chem***. 265, 1990, 8400-8403
33. **U.K. Pati** and K. Wiesner. Synthesis of 17β- (3'-thiphenyl) 15β-androstane-3β, 14-β-diol 3-βD glucopyranoside, an-antitropic cardiac glucoside. ***Steroid****s* 55, 1990, 65-68.
34. **U.K. Pati** and S.M. Weissman. Converted domains of mammalial RNA polymerase II. ***Cold Spring Harbor Journal of Cancer Cells*** 65, 1989, 157.

35. **U.K. Pati** and S. Weissman. Isolation and molecular characterization of cDNA encoding the 23 K subunit of human RNA polymerase II complex. ***J. Biol. Chem***. 264, 1989, 13114-13121.
36. **U.K. Pati** and K. Wiesner Synthesis of 5β-androstane-17β-(oxocyclohex-2'-en-3'-yl)-3β, 14β-diol 3β-D-glucopyranosdie, a potent cardiac glucoside with high safety margin. ***Heterocycles*** 29, 1989, 1275-1282.
37. **U.K.Pati** and S.M. Weissmn.Molecular characterization of mammalian RNA polymerase II complex**.** ***Cold Spring Harbor Journal of Cancer Cells***. 64, 1988, 121- 24.
38. K. Stone, **U. Pati**, S. Weissman, S. Sebti, J. Lazo and K. Williams. Isolation and re-purification of picomole amounts of peptides on microbore HPLC columns **ASBMB *Journal of Protein Purification***, 37, 1987, 180-81.
39. F. E. Ziegler, S. I. Klein, **U.K. Pati**, and T.F. Wang. Acylic Diastereoselection as a synthetic route to quassinoids : A claisen F.E. Ziegler, U.K. Pati, S.C rearrangment based strategy for bruceantin. ***Jour. Am. Chem. Soc***. 107, No. 9, 1985, 2730-2737.
40. F. E. Ziegler, K. J. Hwang, J. F. Kadow, S. I. Klein, **U. K. Pati**, T. F. Wang. Practical Routes to 2 functionilized decalones for the synthesis of quassinoids. ***Jour. Org. Chem***. 51(24), 1986, 4573-4579.

Scientific Articles

Management of Plagiarism and Misconduct in USA Ivy League and other Schools Society for Scientific values News & Views, 2012, 10, No 1. 28-33

Research Projects

PI:Role of p53 tumor suppressor as a molecular sensor of oxygen in inducing apoptosis in hypoxic cancer cells, ICMR, 2013-16, 25 lakh; PI: Role of triplex DNA in transcriptional regulation of cardio-protective NOS2 gene, ICMR, 2012-2015, 48 lakh; Role of pentanucleotide repeat sequence (PNR) in triplex formation and apo(a) gene regulation, ICMR, 2008-11 , 29 lakhs; Role of CHIP and p53 in prevention of amyloid-b fibrils, UGC, 10 lakh; 2008- 2011, CVD biomarkers profiling in acute coronary events by antibodies and antigen array, ICMR, 32 lakh; 2008-2011, Suppression of oral cancer-specific p53 mutant by SiRNA, DBT, 38 lakh; 2006- Correlation of p53 levels and its functional domains to apoptotic response of oral carcinoma cells. University with Potential for Excellence, 15 lakhs; 2002 – 2007, Anti polII and anti-TBP antibodies as markers for scleroderma and mixed connective tissue diseases (MCTD), ICMR, 20 lakh; 2001-2004, Immunodeficiency virus: Isolation, molecular characterization, and development of diagnostics. CGP-NATP, 37 lakhs; 2001–2004, The role of Pentanucleotide repeat (PNR) and Kringle IV Polymorphism in Atheosclerosis, ICMR, 16 lakhs; 2000 – 2003, A transgenic mice model of Homozygous deletion of Tumor suppressor gene p53 for gene therapy, Department of Biotechnology, 1997 - 2000, 35 lakhs; Structure and Function Human RNA polII, Department of Science and Technology, 1996-99, 15 lakhs; Interaction of RNA pol II with BTF3 and TFIID, American Cancer Society, 1992-95, $250,000. Genetic and Environmental determinants of

lipoproteins(a), American Heart Association, 1993-94, $30000; Interaction of RNA pol II with transcription factors MCGRI (Georgia) Grant, 1992-94, $15000.00; (Co-PI) Structure and Function of Ku Proteins, American Arthritis Foundation, 1993-98, $900,000;

Invited Lectures

Ravenshaw University, Odisha, February 2013; 32nd Convention of Indian Association for Cancer Research, February 13-16, 2013, New Delhi; International Conference on "Recent Advances in Molecular Mechanisms of Neurological Disorders", 21 -23 February, 2013, AIIMS;Chairman, Neurobiology & Consciousness, "Nalanda Dialogue", Nalanda University, January, 2013; Vishakhapatnam University, 2012; IACR Symposium, AIIMS, 2012; Chairman, Consciousness & Reality, Pune University, 2012; Chairman, Consciousness & Yoga Praxis, JNU, 2012; Global Hypoxia Summit, New Delhi 2012; Leh Hypoxia Summit, Leh, Aug 2012; RNT Medical College, Udaipur, 2012; Vivekananda Institute of Technology, Jaipur; National University of Hongkong, 2010; Ambedkar University, 2010; DIPAS, New Delhi, 2010; University of Mumbai, 2010; University of Pune, 2010; World Cancer Congress, Singapore, 2009; University of Fudan, Shanghai, 2009; University of Vienna, 2009; University of Vienna, 2008; Hissar University, 2008; KITT University, 2008; Madhava Rao Scindia Memorial Lecture, Gwalior, 2008; Tribhuban University, Nepal, 2006; Transcription Assembly, Hyderabad, 2005; Indo-U.K Seminar on Biomarkers of ecotoxicity, cancer, and prevention, 2004, New Delhi; Transcription Assembly, Jawaharlal Nehru Center for Advancement of Science, Bangalore, 2003; Transcription Assembly, Centre for DNA Fingerprinting, Hyderabad, 2001; Transcription assembly, JNU, New Delhi, 2002; Human Genome Organizaion Dynamics and Disease, Mahabalwswar, March 2002; BioTech 2000, New Delhi, Session Chair (Molecular Diagnostics); Utkal University, Bhubaneswar, 2001; Annual conference of International Society for Heart Research, New Delhi, 2001; Institute of Nuclear Medicine, New Delhi, Feb 2001; Cancer Research Institute, Mumbai, 2000; Indo-Cuba Workshop on Biotechnology, 2000; Academic Conference on Indian Medical association, 2000; Center for Biochemical technology, New Delhi, 1999; Institute of Microbial Technology, Chandigarh, 1999; Institute of Life Sciences, Bhubaneswar, 1999; National Institute of Immunology, New Delhi, 1998; ASBS Conference, New Delhi, 1998; DRDO, Gowalior, 1996; National Pharmaceutical Assocation of India, Vishakapatnam, 1996.

Membership Elected and nominated

Editorial Board Member, International Journal of Pharma & Biological Sciences; Member, International Advisory Committe, Amity University; Member, Technical Advisory Committe, Delhi Cancer Institue, Member, Project Review Committe, 2013-; Neuorbiology, ICMR, 2013; Member, Selection Committe, Naitional Brain Research Center, 2013; Life member, Microvita Society, Udaipur, 2012; Member, Faculty Selection Committee, Visva-Bharati, 2012; Chairman, National Board Accreditation Committee, Integral University, Lucknow, 2012; Executive Council member, Society for

Scientific Value, New Delhi 2011-; Member, Selection Committee, Guru Indraprastha Govind Singh Indraprastha University, 2011**-;** Expert Member, Ambedkar Center, Delhi University 2012-; Expert member, North Odisha University 2012; Member, JNU Court, Member, Academic Council, Jawaharlal Nehru University, 2011; Member, JNU Court, 2011-; Chairman, NBA Team, Mumbai, 2011; Member, UGC Project Review Committe 2010-; Member, Neurobiology Task Force ICMR 2010-; Member, Cardiovascular Disease Task Force ICMR 2010-; Chairman, NBA Team for BIT 2010; Member, National Project Implementation Unit (NPIU), Govt of India 2010-; Member, NBA Accreditation Implementation (Under Graduate Engineering Programmes) 2010-; Member, NBA Accreditation of (Post Graduate Engineering Programmes) 2010-; Member, National Advisory Committee, Guru Nanak Dev Unv 2010-; Academic Council JNU 2010-; JNU Court 2010-; Member, World Business University 2009-; Member, Society for Scientific Values2009-; Advisor, Genome India Internationl,2009-; Advisor, Amritsar University 2009-; National Expert ENVIS Centre 2009-; Member, National Board of Accreditation (NBA) 2008-; Member, NBA, AICTE, 2000-; Member, JNU Ethics Committee, 2008; Member, Sectoral Committee, AICTE, 2008; Member, Editorial Review, Oncogene, 2008; Secretary, Genome INDIA International, 2008-; Member, Sub-Committee, 11th Planning Commission, Disability, 2007-08; Member, DBT Biotechnology Curriculum, 2008; Chairman, DBT Environment Biotechnology Curriculum, 2008; Advisor, Biotechnology Park, Orissa Govt, 2003-; Member, Review Committee, Clinica Chimica Acta, 2007-; Member, Review Committee, Clinical genetics, 2005, 2007; Member, Industrial Award Committee, CSIR, 2007-08; Member, Review Committee, AICTE, 2007-; Member, Review Committee, ICMR, 2007; Member, Review Committee, UGC, 2008; Member, Selection Committee, DRDO, 2007; Member, Selection Committee, AICTE Nomineee, 2001, 2005, 2007; Member, Selection Committee, Assam University, 2007; Member, Technical Committee, JNU; Member, Selection Committee, Orissa Agricultural University, 2007; Advisor, Academic Committee, Tribhuban University, Nepal, 2005; Member, Cancer Biology, DBT, 2005-06; Life Member, Indian Biotech. Association, 2000; Member, Academic Council, JNU, 2005; Member, New York Academy of Sciences, 1999; Member, American Association of Advancement of Science, 1999; Member, Academic Advisory Committee, 2000; Member, Executive Council, Institute of Microbial Technology, Chandigarh, 1999-2001; Member, Graduate Admission Committee, National Institute of Immunology, Delhi, 1998-99; Member, Task Force, Buffalo Genome DBT, 2001; Member, Academic Council, JNU, 1995-97; Principal Investigator Radiation Safety Committee School of Medicine, Univ. of Georgia, 1991-94; Leader, Mol. Biology Group, Division of Oncology Yale University School of Medicine, 1991.

Conferences/Workshops Organized

6th Indo-US Flow cytometry Workshop, February 2007

Convenor, 8th Society for Scientific Values Paintal Memorial Lecture by Dr. APJ Abdul Kalam, JNU, May 2013

News Paper Highlights on Discoveries

doi:10.1038/nindia.2013.7; Published online 18 January 2013

Research highlight

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Novel protein for cancer gene therapy

In a discovery that could result in gene therapy for cancer, researchers in New Delhi have identified synthesis of cytochrome-c oxidase — otherwise known as SCO2 — as a potential tumour suppressor gene.[1]

"Our study established SCO2 as an apoptotic protein which has potential to function as an anti-cancer gene therapy molecule," Uttam Pati, who led the research told Nature India.

Apoptosis, or programmed cell death, is a natural process that allows old cells to die so that new cells can replace them. In cancer, too little apoptosis occurs resulting in malignant cells not dying. So, there is an imbalance between cell division and cell death. Cells that should die fail to receive signals to do so. This results in uncontrolled cell growth. Apoptosis is a popular target of treatment in cancer. Pati and co-workers have shown in mice that SCO2 behaves as an apoptotic protein and can be a potential molecule for gene therapy.

"The SCO2 gene therapy conducted by exogenous addition of SCO2 gene into both breast and colon tumours resulted in the consistent regression of these tumour xenografts in mice," the researchers reported. They found that combining their SCO2 gene therapy with known anti cancer drugs cisplatin or tamoxifen resulted in more than 85% tumour regression in four weeks.

SCO2 regressed the tumour in mice by increasing the generation of 'reactive oxygen species'(ROS), toxic to cancer cells, and by activating the 'Apoptosis Signal-regulating Kinase 1 (ASK1)', a

pathway to apoptosis.
"The cancer cell normally consumes oxygen in a glycolysis pathway in contrast to normal tissue that gets oxygen supply through oxidative phosphorylation pathway," Pati explains. "The role of this SCO2 gene in helping the cancer cell to reverse the glycolytic pathway will be very useful in future gene therapy protocol", he says.

The authors of this work are from: Jawaharlal Nehru Univeristy, New Delhi and Chhatrapati Shahuji Maharaj Medical University, Lucknow, India; and Ohio State University Medical Centre, Columbus, Ohio, USA.

References

1. Madan, E.et. al. SCO2 induces p53-mediated apoptosis by Thr^{845} phosphorylation of ASK-1 and dissociation of ASK-1-TRX complex. Mol. Cell. Biol. doi: 10.1128/MCB.06798-11 (2013)

JNU decoding answer to cancer

Jayashree Nandi, TNN Jan 16, 2013, 02.18AM IST (**Times of India**)

NEW DELHI: There is great excitement at Jawaharlal Nehru University's School of Biotechnology. Scientists here claim to have found that the SCO2 gene has potential tumour-suppressing qualities and that it can be a treatment for different kinds of cancer. Their research paper has been published in the current issue of the journal, Molecular and Cellular Biology.

Till now, it was known that p53 gene is a tumour suppressor protein and is involved in preventing cancer. But according to research studies conducted by the JNU School of Biotechnology along with Ohio State University Medical Centre and other universities, p53 recruits SCO2 gene and gives it this quality.

"We injected SCO2 protein encoded in SCO2 gene in both breast and colon tumour xenografts in mice. It resulted in consistent regression of these tumours. A combination of SCO2 along with cancer drugs like cisplatin and tamoxifen resulted in more than 85% hypoxic tumour regression in four weeks," Professor Uttam Pati, the lead researcher, said.

SCO2 enhances reactive oxygen species (ROS) production to activate apoptosis signal-regulating kinase 1 (ASK1) which then regresses tumour growth rate. ROS is a type of unstable molecule that contains oxygen and that easily reacts with other molecules in a cell. A build-up of ROS in cells may cause damage to DNA, RNA, and proteins and may cause cell death. But SCO2 promotes ROS for a good purpose which is to activate cell death and shrinking of tumours.

But translating the finding into actual therapy may take time. "The finding that SCO2 is a potential tumour suppressor is an important step in our continued effort to understand the mechanistic causes of cancer. Gene therapy has not yet matured in clinical practice and needs work," head of research and healthcare innovations at Mazumdar-Shaw Cancer Center in Bangalore Dr Biju Jacob said.

"All genes involved in cancer cell metabolism are important and need to be discovered and understood. With advanced therapies in near future, cancer will hopefully no longer be a disease that will scare people," Dr S J Patil, consultant, Clinical Genetics Centre for Molecular and Metabolic Diagnostics & Research, Narayana Hrudayalaya Health City, said.

Oxygen may fight cancerous tumours: Study

Jayashree Nandi, TNN Jun 9, 2012, 04.18AM IST(**Times of India**)

NEW DELHI: Oxygen therapy may be the answer to cancer, scientists from JNU have found. A research study carried out by JNU's school of biotechnology has revealed that exposing cancerous tumours to pure oxygen can help shrink them drastically.

The JNU team, in collaboration with department of internal medicine, Davis Heart and Lung Research Institute, Ohio State University, tried the method on mice with hypoxic (lacking oxygen) tumours. The researchers — for the first time — measured the oxygen concentration in these tumours and found it to be 1.8 % in core cells as against 21.8% in normal cells. Repeated oxygenation at normal resulted in an eight-fold increase in cell death and significant regression of tumours. The research paper has been published in the Journal of Cell Death and Disease.

The degree of hypoxia in tumours is variable. "We grew tumour xenografts in mice and the tumours were treated with cisplatin (breast cancer drug) for 20 days. These tumours were then exposed to 30-50% oxygen for three hours per day. The results showed that re-oxygenation induced around 77% regression in breast and colon tumours. Interestingly, re-oxygenation also activated genes that cause cell death," said lead scientist from JNU, Uttam Pati. Hypoxic tumours are resistant to radiation and chemotherapy. "Hypoxia is a survival technique for cancer cell to progress. ", he said.

However, scientists say it may take some time before the remedy can be tried on humans. First, a mechanism to deliver pure oxygen to human tumours has to be devised. Since the tumours in mice were smaller, it was easier to expose them to oxygen. Also, getting the approval for human trials will take time. "It has been established that oxygen is very useful in treating hypoxic tumours that are usually resistant to other treatment. But the problem is that the oxygen has to reach the hypoxic region. An efficient method to deliver oxygen has not yet been established. That's a challenge." said Dr Moni Abraham Kuriakose, an oncologist.

Oxygen therapy is not unknown to doctors in western countries. Oxygen bars in these places can be compared with our age-old pranayam system where a synchronized breathing process helps boost immunity. The technique was tried in the 1980s. It involved the use of pressurized oxygen to shrink the tumour but the process had various side effects. Patients often suffered toxic seizures and radiation injuries. However, in the current study, non-pressurized oxygen is being used to avoid side effects.

doi:10.1038/nindia.2012.83; Published online 4 June 2012 (Nature India)

Research highlight

Oxygen therapy for breast cancer

Researchers report a new approach to shrink cancerous breast tumours with pure oxygen[1].

Mice carrying breast tumors when subjected to 30% pure oxygen showed significant reduction of tumor (64%) in 2-3 days without any side effects. The researchers say this is a significant considering that the widely used tumour drug cisplatin failed to show any result in shrinking hypoxic tumours.

Hypoxic tumors contain a core that is deprived of oxygen. The researchers have, for the first time, measured the oxygen concentration to be 1.8 % in the core of breast tumors (against 21.8% in normal cells). Repeated oxygenation at normal atmospheric pressure resulted in an eight-fold increase in cell death and significant regression of tumour in the mice without any adverse effect.

The scientists from New-Delhi based Jawaharlal Nehru University (JNU) have found that the re-oxygenation activates the tumour suppressor protein p53, which remains 'non-functional' in the hypoxic core because of lack of oxygen. Oxygen therapy without pressure, as opposed to hyperbaric oxygen therapy, may be ideal for hypoxic tumour regression, they conclude. The discovery might have far reaching consequences in translational research.

The authors of this work are from: *School of Biotechnology, Jawaharlal Nehru University, New Delhi, India and Davis Heart and Lung Research Institute, The Ohio State University, Columbus, Ohio, USA.*

References

1. Gogna, R. *et al*. Re-oxygenation causes hypoxic tumor regression through restoration of p53 wild-type conformation and post-translational modifications. *Cell Death Dis.* doi: 10.1038/cddis.2012.15 (2012)

THE HINDU
Online edition of India's National Newspaper
Tuesday, August 08, 2000

Some heart-warming research at JNU

By Pranab Dhal Samanta

NEW DELHI, AUG. 7. An obscure gene could have the best news for heart patients the world over thanks to researchers at the Centre of Biotechnology in Jawaharlal Nehru University here. They have plotted the gene responsible for regulating fluids that block arteries leading to heart attacks.

Based on the concept of treating ailments by replacing genes that regulate a particular metabolic activity, researchers at JNU studied the behaviour of numerous genes before discovering the one responsible for blocking arteries. They named it ``Apo (a)''. The behaviour of this gene, researchers say, is directly related to formation of plaque in arteries leading to heart attacks.

Explaining the discovery, the research head, Dr. Uttam Pati, says while tremendous genetic research on cardiac diseases is going on the world over, this is the first effort in applying gene regulation therapy to find a cure for arteriosclerosis --

blocking of arteries.

Research has shown that Apo (a) is universally present among different racial stocks including Asians, Afro-Asians and Caucasians. Studying samples collected from 400 heart patients from India and other countries, Dr. Pati's team found that mutations in Apo (a) are related to increasing levels of lipoprotein (a), the plasmic fluid which blocks arteries.

``We then took samples of a person without any history of cardiac diseases and found no mutations in the Apo gene. Thus it became clear that this particular gene regulates the plasma fluid and if it is not active, it can prevent arteriosclerosis,'' says Dr. Pati.

On this hypothesis, researchers began studying more samples. Since research institutions are not linked with hospitals in India, direct contact with patients became an irritant. Moreover, most government hospitals did not have a data bank, and those with one had not done DNA sampling. Finally, researchers parked themselves at Escorts Heart Institute where they collected samples to confirm their hypothesis. Parts of the research were subsequently published in scientific journals like Molecular Genetics and Metabolism as well as the International Journal of Cardiology.

Experiments showed that the gene is present in Chromosome No. 6 of the 23 pairs present in a human DNA. Like every gene, Apo (a) has a transcribed portion carrying hereditary traits and a regulator that controls its activity depending on the environment. It is in the regulator -- which has an activator and a repressor element -- of the gene that the distinguishing factor was finally identified after three years of research. In people with cardiac diseases, the gene is controlled by the activator while those without a heart disease have the repressor variety.

Now whether replacing the activator with the repressor variety in cardiac patients will lead to a permanent cure defines the next stage of research as Dr. Pati's team will shortly be experimenting this with ``new generation monkeys'' like apes, particularly chimpanzees, who have the same gene. ``We have also entered into an agreement with Escorts Institute to study more samples,'' Dr. Pati adds. ``Collecting more data is crucial for our investigations. Once our experiment with animals is successful, we will be

ready to try it on humans."

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They catch con jobs in science

The writer has posted comments on this articleJayashree NandiJayashree Nandi, TNN | May 14, 2013, 02.27 AM IST

NEW DELHI: A plagiarism charge against an IIT academic is shocking news but for the Society for Scientific Values it is just another shameful statistic. On average, this volunteer 'watchdog' investigates around 200 new complaints of plagiarism and corruption against scientists every month.

In the latest one, a well-known Indian scientist is accused of lifting entire paragraphs from a plant biology paper by a scientist at the University of Heidelberg. Earlier, an international journal had retracted three papers of an acclaimed scientist from the chemical engineering department of IIT Kanpur.

While complaints against faculty at little known universities and other organizations pour in daily, 'prestigious' institutions too have their share of scandals. "We get complaints against scientists from the IITs and central universities," says Professor KL Chopra, former director of IIT Kharagpur and president of the society. Once, he says, a US based journal retracted the paper of an IIT Delhi scientist who used data from Wikipedia and other online documents about the impact of radiation from mobile phones. "Despite several letters to the IIT Delhi director, we have received no response and no action has been taken against the scientist," adds Chopra.

The 25-year-old society has seen the malaise grow. "Plagiarism cases have increased because scientists want to publish as many papers as possible in a short time. Their promotions are linked to the number of papers they publish," says Professor Uttam Pati of the School of Biotechnology at JNU who is an SSV member.

The society, formed in 1987 "to uphold the spirit of science and original research", now has more than 500 members. It can proudly look back on the cheating it has exposed. For example, a prominent scientist, an adviser to the PM, had

lifted sentences verbatim from a journal for a paper on infrared photodetectors. Chopra recalls the case of a scientist from Tirupati University who plagiarized 75 research papers.

Still, the society feels powerless in its crusade for values. "We don't have legal powers. Our cases move forward only if the university acknowledges them or the scientist accepts misconduct," says Pati.

Although cases are taken up only after verifying the background of the complainant and much deliberation, progress is slow. "Many times, it has taken us years to investigate a case. People don't respond easily. They want to cover up," says Chopra.

With new journals promising to review scientific papers in two weeks, plagiarism is bound to become more rampant, Chopra and Pati say. But the society is determined to expose every con. "Science has to be honest and we want more young members to take this cause forward," says Pati.