## Dr. Sanjeev Shukla, Ph.D.

**Assistant Professor** 

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#### Research Interests

My long-term goal is to study how alternative pre-mRNA splicing modulates and is modulated by higher order chromatin structure and signal transduction pathways during tumorigenesis, with an initial focus on CTCF/CTCFL mediated regulation of alternative splicing in cancer. Because there is aberrant CTCF expression and DNA methylation in several different cancers, it is likely that change in methylation sensitive DNA binding of CTCF in cancer cells may cause generation of cancer specific transcripts and protein isoforms. The study on methylation mediated cancer specific alternative splicing will shed more light on the mechanism of tumorigenesis and might help in cancer management.

#### **Education**

**Ph.D., Biochemistry,** February 2009, Cancer Research Institute, ACTREC, Tata Memorial Centre, Mumbai University, India. Thesis: "Study of tumor antigens eliciting humoral immune response in oral cancer"

M. Sc., Biotechnology, 2002, Jiwaji University, Gwalior, India. [First Division]
Thesis: "Molecular phylogeny of fish using 12S mitochondrial DNA as a molecular marker"
B. Sc., Chemistry, Zoology and Botany, 2000, Jiwaji University, Gwalior, India. [Ist Division, Gold medal]

## Research and Teaching Experience

May 2013-present: Assistant Professor, Indian Institute of Science Education and Research Bhopal (IISERB), Madhya Pradesh, India

Pathological consequences of epigenetic changes on alternative pre-mRNA splicing in cancer biology

March 2010- March 2013: Postdoctoral Fellow, National Institutes of Health, National Cancer Institute, Frederick, MD

Study of mechanism and regulation of alternative splicing during lymphocyte development.

- ➤ Role of DNA methylation sensitive CTCF binding in regulation of alternative splicing.
- > Role of higher order chromatin structure in regulation of alternative splicing.

May 2009- Feb 2010: Postdoctoral Fellow, Georgetown University School of Medicine, Washington, DC.

#### TGF-β signaling in gastrointestinal cancer, and the regulation of Telomerase Reverse Transcriptase.

- > β2-Spectrin(β2SP) as an adaptor molecule in TGF-β signaling. Studied structure and functional analysis of β2-Spectrin(β2SP)-smad3 and β2SP-TβRI interaction in Hepatocellular carcinoma.
- $\triangleright$  Role of  $\beta$ 2-SP in the TGF- $\beta$  mediated regulation of hTERT gene.
- $\triangleright$  Identification of  $\beta$ 2SP-interacting proteins using immunoprecipitation and mass spectrometry.

# October 2008-March 2009: Lecturer at Pillai's Institute of Management Studies & Research (PIMSR), Navi Mumbai, India.

➤ Courses taught- Immunology and Molecular biology to M.Sc. Biotechnology Students and various topics on application of Biotechnology to post graduate students in Biotechnology Management students.

# Nov 2003- Feb 2009: Research Fellow and Ph.D. student, Cancer Research Institute, ACTREC, Tata Memorial Centre, Mumbai University, India.

Thesis: "Study of tumor antigens eliciting humoral immune response in oral cancer".

- ➤ Identified autoantibody response against 12 new tumor antigens in oral cancers using Proteomics, biochemical and molecular approaches.
- > Studied the implication of autoantibody response as biomarkers in prognosis of oral cancer.
- > Studied the sub-site specific autoantibody response in cancer of oral cavity.
- Established a platform to develop a multiplex protein array/ ELISA to help in early detection and prognosis of oral cancer.

#### February 2003- Nov 2003: Scientist at Torrent Research Centre, Ahmedabad, India.

Expression and purification of recombinant insulin and screening of phosphatase inhibitors for Diabetes treatment.

#### Academic Service

- 1. Chairman and Funds Organizer (for two consecutive years) of a conference "*Graduate Students Meet*" on *Trends in life sciences* held at ACTREC, New Mumbai in 2005 and 2006.
- 2. Reviewed two manuscripts for *Journal of Oncology* in 2010 (Hindawi publications).

#### Awards and Academic Achievements

- 1. NIH Postdoctoral Mentor Award 2012.
- 2. Awarded Senior Research Fellowship from Lady Tata Memorial Trust (LTMT), Nov 2007-July 2008.
- 3. Awarded Junior and Senior Research Fellowship from ACTREC, Tata Memorial Centre, 2003-2007.
- 4. Qualified in GATE (Graduate Aptitude test in Engineering) 2003
- 5. Gold medalist in B.Sc. 2000 (Jiwaji university).
- 6. Silver medalist in General Knowledge and Intelligence Test held by Central Institute of General Knowledge Learning, New Delhi.

7. Passed in National Talent search Contest (Mathematics) held by Central Institute of General Knowledge Learning, New Delhi.

#### **Publications**

- 1 Pranay A, Shukla S et al. Prognostic utility of autoantibodies to α-enolase and Hsp70 for cancer of the gingivo-buccal complex using immunoproteomics. Proteomics Clinical Applications 2012; DOI: 10.1002/prca.201200081.
- 2 **Shukla S.**, Oberdoerffer S. Co-transcriptional regulation of alternative pre-mRNA splicing. **BBA-Gene Regulatory Mechanism** July 2012, 1819 (7), 673-683.
- 3 **Shukla S**, Kavak E, Gregory M, Imashimizu M, Shutinoski B, Kashlev M, Oberdoerffer P, Sandberg R, Oberdoerffer S. "CTCF-promoted RNA polymerase II pausing links DNA methylation to splicing". **Nature** 479, 74–79 (03 November 2011).
  - This article was highlighted in Cell Research- Kornblihtt A. "CTCF: from insulators to alternative splicing regulation", *Cell Research* advance online publication 7 February 2012; doi:10.1038/cr.2012.22
     http://www.nature.com/cr/journal/vaop/ncurrent/full/cr201222a.html
  - This article was also highlighted in CCR connections Vol 6 (1), 2012 "CTCF, a
    Novel Regulator of Alternative Splicing"
     <a href="http://home.ccr.cancer.gov/connections/dev/2012/Vol6\_No1/news\_7.asp">http://home.ccr.cancer.gov/connections/dev/2012/Vol6\_No1/news\_7.asp</a>
  - Received F1000 article factor (FFa) -17 (exceptional rating) from Faculty of 1000 based on following 4 evaluations. http://f1000.com/13371987
    - 1. Exceptional evaluation by Faculty of 1000 (http://f1000.com/14742098) Ge W, Sun Y: "This is the first study to show that CCCTC-binding factor (CTCF), RNA polymerase II (pol..." Evaluation of: [Shukla S et al. CTCF-promoted RNA polymerase II pausing links DNA methylation to splicing. Nature. 2011 Nov 3; 479(7371):74-9; doi: 10.1038/nature10442]. Faculty of 1000, 22 Nov 2011. F1000.com/13371987#eval14742098
    - 2. Must read evaluation by Faculty of 1000 (<a href="http://f1000.com/14742097">http://f1000.com/14742097</a>) Valcárcel J: "This paper is important because it documents a mechanistic link between DNA methylation and the..." Evaluation of: [Shukla S et al. CTCF-promoted RNA polymerase II pausing links DNA methylation to splicing. Nature. 2011 Nov 3; 479(7371):74-9; doi: 10.1038/nature10442]. Faculty of 1000, 22 Nov 2011. F1000.com/13371987#eval14742097
    - 3. Exceptional evaluation by faculty of 1000 (<a href="http://f1000.com/15281056">http://f1000.com/15281056</a>)
      Guo J, Song H: "This elegant series of experiments demonstrate a long-speculated

role for intragenic DNA methylation in regulating..." Evaluation of: [Shukla S et al. CTCF-promoted RNA polymerase II pausing links DNA methylation to splicing. Nature. 2011 Nov 3; 479(7371):74-9; doi: 10.1038/nature10442]. Faculty of 1000, 20 Feb 2012. F1000.com/13371987#eval15281056

- 4. Must read evaluation by faculty of 1000 (http://f1000.com/15372056)

  Beck S: "This study is interesting because it functionally links a chromatin modifier, CCCTC-binding factor (CTCF), and..." Evaluation of: [Shukla S et al. CTCF-promoted RNA polymerase II pausing links DNA methylation to splicing. Nature. 2011 Nov 3; 479(7371):74-9; doi: 10.1038/nature10442]. Faculty of 1000, 23 Feb 2012. F1000.com/13371987#eval15372056
- 4 **Shukla S**, Pranay A, D'Cruz AK, Chaturvedi P, Kane SV, Zingde SM "Immunoproteomics reveals that cancer of the tongue and the gingivo buccal complex exhibit differential autoantibody response." *Cancer Biomarkers* 2009, 5(3): 127-35.
- 5 **Shukla S**, Govekar RB, Sirdeshmukh R, Sundaram CS, D'Cruz A, Pathak KA, Kane SV, Zingde SM Tumor antigens eliciting autoantibody response in cancer of gingivo-buccal complex. *Proteomics Clinical Applications* 2007, 1(12): 1592-1604.

### Patent

1. Zingde, **Shukla**, Sirdeshmukh, Sundaram D'Cruz, Pathak, Kane [Inventors] Autoantibodies for protein antigens as markers for cancer of the ginigivo –buccal complex:

**CSIR: Ref No**: 0187NF 2006/1N, filed on Feb 14, 2007; 290DEL **2007 European Patent Application** EP2126578 (Published: Feb 12, **2009**) **US application**- US 2011/0189699A1 (published: date Aug 04, **2011**)

#### In conversation

CCR Connections, Centre for Cancer Research, vol 6, No. 1, 2012 <a href="http://home.ccr.cancer.gov/Connections/2012/Vol6\_No1/news\_8.asp">http://home.ccr.cancer.gov/Connections/2012/Vol6\_No1/news\_8.asp</a>

# Abstracts presented in Conference

#### **Oral presentations:**

- **1. Shukla S** "Epigenetic regulation of alternative pre-mRNA splicing" at Young Investigators Meeting (YIM) at Boston on Oct 7, 2012.
- **2. Shukla S**, Haque N, Kavak E, Gregory M, Imashimizu M, Shutinoski B, Kashlev M, Oberdoerffer P, Sandberg R, Oberdoerffer S. "Epigenetic regulation of alternative premRNA splicing" at Fellows and Young Investigator Seminars of Centre for Cancer Research,

- NCI June 27, 2012.
- **3. Shukla S**, Kavak E, Gregory M, Imashimizu M, Shutinoski B, Kashlev M, Oberdoerffer P, Sandberg R, Oberdoerffer S. "CTCF-promoted RNA polymerase II pausing links DNA methylation to splicing" at Chromatin-DECODE meeting, NIH, Oct 11, 2011.
- **4. Shukla S**, Pranay A, Govekar RB, Sundaram CS, Sirdeshmukh R, Zingde SM. "Immunoproteomics for identification of autoantibodies in oral cancer" *27<sup>th</sup> Ann. Conv. of Indian Asso. for Cancer Research*, Feb 2008, Ahmedabad, India
- **5. Shukla S,** Zingde SM. "Immunoproteomics for identification of biomarkers in oral cancer" *29th All India Cell Biology Conference*, Jan 2006, Lucknow, India.

### **Poster presentations:**

- Shukla S et al, "Regulation of alternative pre-mRNA splicing by epigenetic alterations" Gordon Research Conference on Post-transcriptional gene regulation at Rhode Island, Newport 2012.
- 2. **Shukla S** et al "Role of the DNA-binding protein CTCF in CD45 pre-mRNA alternative splicing" Cold Spring harbor lab conference 2011.
- 3. **Shukla S, et al** "Role of DNA binding protein CTCF in CD45 pre-mRNA alternative splicing" in 5<sup>th</sup> Annual Centre for Excellence in Chromosome Biology: Postdoctoral Fellows Retreat, NIH Bethesda on 12.17.2010.
- 4. Yao Z, Jogunoori W.S., Shukla S., Yao W., Mishra B., Mishra L. "Epigenetic Silencing of TGF-β/β-2 Spectrin Signaling in a Human Cancer Stem Cell Disorder: Beckwith-Wiedemann Syndrome-Implication for GI Cancers". Gastroenterology 2010, 138 (5), Supplement 1, Pages S-43.
- 5. Jiao Z., **Shukla S.**, Kumar G., Yao Z., Jogunoori W.S., Yao W., Mishra L., Mishra B. "The 2 Spectrin Suppresses Telomerase Reverse Transcriptase in Normal Cells. Its Loss May Lead to Hepatocellular Cancer Progression". **Gastroenterology** 2010, 138 (5), Supplement 1, Pages S-250.
- 6. **Shukla S**, et al "Tumor antigens eliciting autoantibody response in oral cancer" *International symposium on Current Trends in Proteomics*, CCMB, Hyderabad, India.
- 7. Zingde SM, Govekar RB, **Shukla S**, et al. "Proteomics analysis of cancer of buccal mucosa: Tissue profile and antibody response to tumor antigens" *HUPO 5<sup>th</sup> Annual world congress* at Long Beach, CA, USA. (Published in the form of abstract in *Mol Cell Prot* 2006, vol 5, issue 10, S160, poster no. 627) (3<sup>rd</sup> best poster award)
- 8. **Shukla S,** Zingde SM. "Identification of tumor antigens eliciting humoral immune response in oral cancer using proteomics." 24<sup>th</sup> Annual Convention of Indian Association for Cancer Research Feb 2005, Delhi, India. (Published in the form of abstract in Indian Journal of medical Research, Feb 2005 W-23)
- Attended Gordon research conference on "Post-transcriptional gene regulation" at Salve Regina University Newport, RI in 2010.