FWF Der Wissenschaftsfonds.

Doctoral College
Metabolic & Cardiovascular Disease

Medical University of Graz

UNI GRAZ TU Graz Graz University of Technology

REVEALING VULNERABILITIES IN KRAS-DEPENDENT CANCERS BY GENOMIC PROFILING OF MOLECULAR SUBTYPES

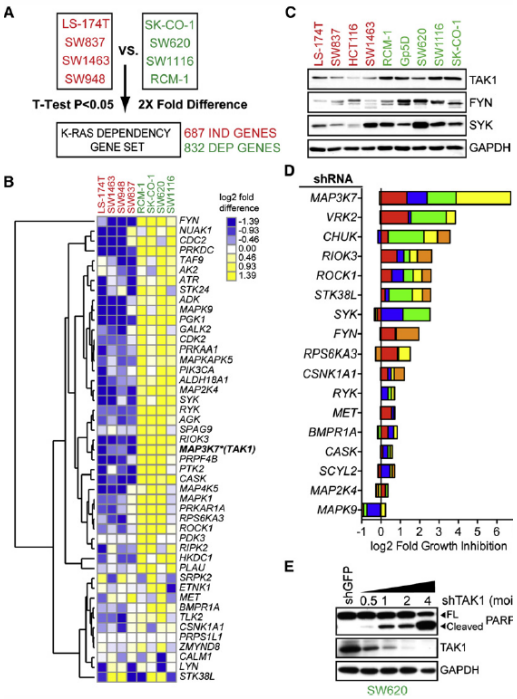
GUEST LECTURE by

Prof. Anurag Singh, PhD

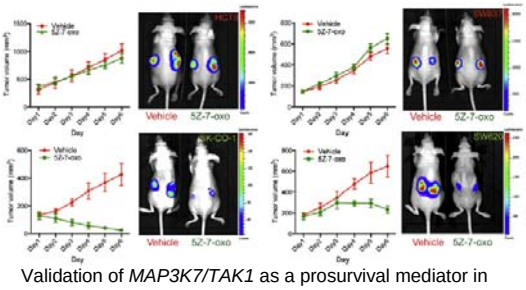
Dept. of Pharmacology & Experimental Therapeutics, Div. of Medical Oncology & Hematology, The Cancer Center, Boston University School of Medicine, USA

Monday, 26.05.2014
17:00

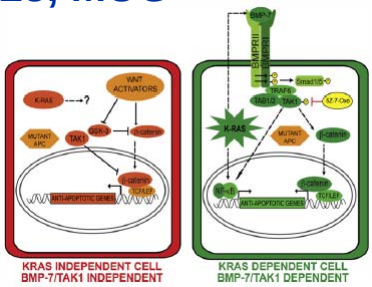
Lecture Hall, Department of Pathology, Auenbruggerplatz 25, MUG



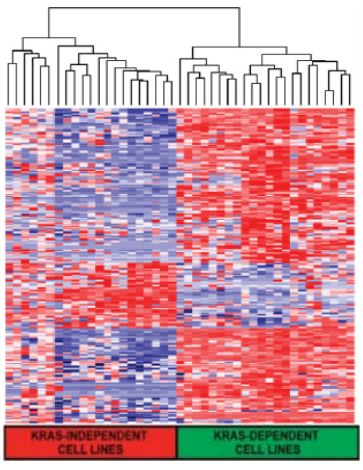
Analysis of kinases from a „KRAS dependency signature“ in colon cancer cell lines
Singh et al. (2012) Cell 148:639-650



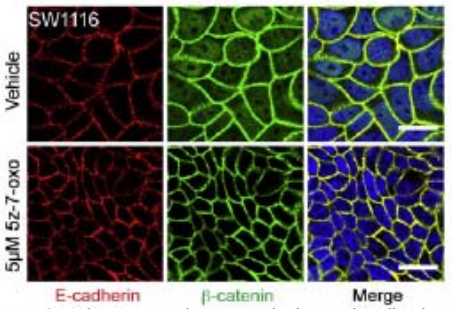
Validation of *MAP3K7/TAK1* as a prosurvival mediator in KRAS-dependent colon cancers
Singh et al. (2012) Cell 148:639-650



A model for context-specific KRAS dependency in colon cancers
Singh et al. (2012) Cell 148:639-650



Heat-map showing hierarchical clustering of K-Ras dependency signature gene expression in a cross-tissue panel of *K-ras* mutant cell lines
Singh et al. (2009) Cancer Cell 15:489-500



KRAS and TAK1 regulate canonical Wnt signaling in KRAS-dependent cancer cells
Singh et al. (2012) Cell 148:639-650

Curriculum Vitae

Anurag Singh, Ph.D.
asingh3@bu.edu

Department of Pharmacology & Experimental Therapeutics
Boston University School of Medicine
72 East Concord Street, K-712B, Boston, MA 02118
617-638-4175 (Phone)
617-638-4176 (Fax)

ACADEMIC TRAINING:

1999 B.S.	State University of New York at Stony Brook, NY; Cum Laude, Pharmacology
2005 Ph.D.	University of North Carolina at Chapel Hill, NC; Pharmacology

POSTDOCTORAL TRAINING:

2005 - 2005	Postdoctoral Fellow in the Laboratory of Dr. Channing Der, Department of Pharmacology, University of North Carolina at Chapel Hill, NC
2005 – 2010	Postdoctoral Fellow in the Laboratory of Dr. Jeffrey Settleman. Massachusetts General Hospital Cancer Research Center/Harvard Medical School, Charlestown/Boston, MA

ACADEMIC APPOINTMENTS:

2010 - 2011	Instructor in Medicine, Harvard Medical School/Massachusetts General Hospital Cancer Research Center, Laboratory of Dr. Daniel A. Haber, Charlestown, MA
9/2011- Present	Assistant Professor, Department of Pharmacology & Experimental Therapeutics, Division of Hematology/Oncology, Boston University School of Medicine, Boston, MA

HONORS AND AWARDS:

1994 - 1999	Dean's List Student every semester, State University of New York, Stony Brook, NY
1999	Cum Laude, State University of New York, Stony Brook, NY
2010	AACR Bristol-Myers Squibb Scholar-in-Training Award
2009	Howard Temin Award (K99/R00 NIH/NCI)
2013	American Lung Association, Lung Cancer Discovery Award

Bibliography: ORIGINAL, PEER REVIEWED ARTICLES:

1 Luquain C., **Singh A.,** Wang L., Natarajan V., Morris A.J. Role of phospholipase D in agonist-stimulated lysophophatidic acid synthesis by ovarian cancer cells. J. Lipid Res. 2003 Oct;44(10): 1963-75.

2 **Singh A.**, Karnoub A.E., Palmby T.R., Lengyel E., Sondek J., Der C.J. Rac1b, a tumor associated, constitutively active Rac1 splice variant, promotes cellular transformation. Oncogene. 2004 Dec 16;23(58):9369-80.

3 Campbell P.M., **Singh A.**, William F.J., Frantz K., Ulkü A.S., Kelley G.G., Der C.J. Genetic and pharmacologic dissection of Ras effector utilization in oncogenesis. Methods Enzymol. 2006;407:195-217.

4 Montagut C., Sharma S.V., Shioda T., McDermott U., Ulman M., Ulkus L.E., Dias-Santagata D., Stubbs H., Lee D.Y., **Singh A.,** Drew L., Haber D.A., Settleman J. Elevated CRAF as a potential mechanism of acquired resistance to BRAF inhibition in melanoma. Cancer Res. 2008 Jun 15;68(12):4853061.

5 Chin T.M., Quinlan M.P., **Singh A.**, Sequist L.V., Lynch T.J., Haber D.A., Sharma S.V., Settleman J. Reduced Erlotinib sensitivity of epidermal growth factor receptor-mutant non-small cell lung cancer

following cisplatin exposure: a cell culture model of second-line erlotinib treatment. Clin. Cancer Res. 2008 Nov 1; 14(21):6867-76.

6 **Singh A.**, Greninger P., Rhodes D., Koopman L., Violette S., Bardeesy N., Settleman J. A gene expression signature associated with "K-Ras addiction" reveals regulators of EMT and tumor cell survival. Cancer Cell. 2009 Jun 2;15(6):489-500.

7 **Singh A.**, Settleman J. Oncogenic K-ras "addiction" and synthetic lethality. Cell Cycle. 2009 Sep 1;8(17):2676-7.

8 **Singh A.**, Boyer J.L., Der C.J., Zohn I.E., Transformaton by a nucleotide-activated P2Y receptor is mediated by activation of Galphai, Galphaq and Rho-dependent signaling pathways. J. Mol. Signal. 2010 Jul 23;5:11.

9 **Singh A**., Settleman J. EMT, cancer stem cells and drug resistance: an emerging axis of evil in the war on cancer. Oncogene. 2010 Aug 26.;29(34):4741-51.

10 Ebi H, Corcoran RB, **Singh A**, Chen Z, Song Y, Lifshits E, Ryan DP, Meyerhardt JA, Benes C, Settleman J, Wong KK, Cantley LC, Engelman JA. Receptor tyrosine kinases exert dominant control over PI3K signaling in human KRAS mutant colorectal cancers. J Clin. Invest. 2011 Nov 1; 121(11):4311-21.

11 **Singh A**, Sweeney M, Burger A, Yu M, Greninger P, Peterson R, Haber DA, Settleman J. Inhibition of TAK1 inhibition promotes apoptosis in KRAS dependent colon cancers. Cell. 2012 Feb 17; 148(4):639-50.

12 Corcoran RB, Cheng KA, Hata AN, Faber AC, Ebi H, Coffee EM, Greninger P, Brown RD, Godfrey JT, Cohoon TJ, Song Y, Lifshits E, Hung KE, Shioda T, Dias-Santagata D, **Singh A**, Settleman J, Benes CH, Mino-Kenudson M, Wong KK, Engelman JA. Synthetic Lethal Interaction of Combined BCL-XL and MEK Inhibition Promotes Tumor Regressions in KRAS Mutant Cancer Models. Cancer Cell. 2013 Jan 14; 23(1):121-128.

13 Wang M, Kern AM, Hülskötter M, Greninger P, **Singh A**, Pan Y, Chowdhury D, Krause M, Baumann M, Benes CH, Efstathiou JA, Settleman J, Willers H. EGFR-Mediated Chromatin Condensation Protects KRAS-Mutant Cancer Cells Against Ionizing Radiation. Cancer Research. 2014. *Manuscript accepted and in press.*

CASE REPORTS, REVIEWS, CHAPTERS AND EDITORIALS

Textbook Chapters:

1 **Singh A.**, Sharma S.V., Settleman J. Epidermal Growth Factor Receptor mutations and sensitivity to selective kinase inhibitors in human lung cancer. Genomics and Pharmacogenomics in Anticancer Drug Development and Clinical Response. Chapter 8. pp. 103-126. Oct 23, 2008. Humana Press.

2 **Singh A.** Deregulated Signaling Networks in Lung Cancer. Systems Biology of Cancer, edited by Sam Thiagalingam. Cambridge University Press 2013. *In press*.