MBI Department January/February 2016 Faculty Accolades

Publications:

Dr. Kapur, Dr. Mir, Dr. Clark, Dr. Beech and Dr. Shailesh Singh (Professor, II) for their recent publication accepted by the British Journal of Cancer.

British Journal of Cancer 2016
Higher CCR6 in colon cancer is associated with advanced disease and supports epithelial to mesenchymal transition.

Kapur et al show clinical and biological significance of CCR6 in colon cancer in both patient samples and colon cancer cell lines. The authors show a positive correlation of CCR6 expression and colon cancer progression, and comparable human colon cancer cell lines. In vitro experiment suggests CCR6-CCL20 axis mediates EMT and increased migration and invasion. The data provided in this manuscript show a role of CCR6 in etiopathogenesis of colon cancer and a molecular signature of colon cancer, in addition to TNM, has the potential to improve therapeutics and patient outcome.

Dr. Rajesh Singh (Assistant Professor) and Dr. Shailesh Singh (Professor II) publication

CXCR6-CXCL16 axis promotes prostate cancer by mediating cytoskeleton rearrangement via Ezrin activation and αvβ3 integrin clustering.

Abstract
Cytoskeletal rearrangement is required for migration and invasion, which are the key steps of cancer metastasis. Ezrin and integrin co-ordinate these processes by regulating cellular adhesion and cytoskeletal polymerization-depolymerization. It is also well established that chemokine-chemokine receptor axis plays a crucial role in regulating cancer cell migration and invasion. In this study, we show involvement of CXC chemokine receptor 6 (CXCR6) and its only natural ligand CXCL16 in pathobiology of prostate cancer (PCa). CXCR6 is highly expressed in PCa tissues and cell lines (LNCaP and PC3), relative to normal tissue and cells. CXCR6 expression in PCa tissues correlated with higher Gleason score. Similarly, aggressive PCa cells (PC3) show high CXCR6 compared to less aggressive LNCaP. Besides, PC3 cells show higher MMPs expression compared to LNCaP cells following CXCL16 stimulation. Intriguingly, CXCR6-CXCL16 interaction in PCa cells promotes Ezrin activation, αvβ3 integrin clustering and capping at the leading edge in FAK/PI3K/PKC dependent manner, thereby modifying cellular adhesion as well as motility. Together these results demonstrate that CXCL16 stimulation changes cytoskeletal dynamics resulting in enhanced migration, invasion and adhesion to endothelial cells, ultimately enabling PCa cells to achieve their metastatic goal.

Dr. Hina Mir (Postdoctoral Fellow) and Dr. Shailesh Singh (Professor, II) recent publication
Cell Cycle 2016
Andrographolide inhibits prostate cancer by targeting cell cycle regulators, CXCR3 and CXCR7


Despite the state of art cancer diagnostics and therapies offered in clinic, prostate cancer (PCa) remains the second leading cause of cancer-related deaths. Hence, more robust therapeutic/preventive regimes are required to combat this lethal disease. In the current study, we have tested the efficacy of Andrographolide (AG), a bioactive diterpenoid isolated from Andrographis paniculata, against PCa. This natural agent selectively affects PCa cell viability in a dose and time-dependent manner, without affecting primary prostate epithelial cells. Furthermore, AG showed differential effect on cell cycle phases in LNCaP, C4-2b and PC3 cells compared to retinoblastoma protein (RB)/ and CDKN2A lacking DU-145 cells. G2/M transition was blocked in LNCaP, C4-2b and PC3 after AG treatment whereas DU-145 cells failed to transit G1/S phase. This difference was primarily due to differential activation of cell cycle regulators in these cell lines. Levels of cyclin A2 after AG treatment increased in all PCa cells line. Cyclin B1 levels increased in LNCaP and PC3, decreased in C4-2b and showed no difference in DU-145 cells after AG treatment. AG decreased cyclin E2 levels only in PC3 and DU-145 cells. It also altered Rb, H3, Wee1 and CDC2 phosphorylation in PCa cells. Intriguingly, AG reduced cell viability and the ability of PCa cells to migrate via modulating CXCL11 and CXCR3 and CXCR7 expression. The significant impact of AG on cellular and molecular processes involved in PCa progression suggests its potential use as a therapeutic and/or preventive agent for PCa.

Manuscripts:

Article title: Sustained Effectiveness of Monovalent and Pentavalent Rotavirus Vaccines in Children
Reference: YMPD8110
Journal title: The Journal of Pediatrics
Corresponding author: Dr. Lilly C. Immergluck (Associate Professor)
First author: Dr. Lilly C. Immergluck (Associate Professor)

Roth WW1, Huang MB2, Addae Konadu K3, Powell MD4, Bond VC5.
KEYWORDS: HIV-1; exosomes; microRNA; microarray; qPCR

Huang MB1, Ye L2, Liang BY3, Ning CY4, Roth WW5, Jiang J6, Huang J7, Zhou B8, Zang N9, Powell MD10, Liang H11,12, Bond VC13.
KEYWORDS: China; HIV/AIDS epidemic; the United States

Konadu KA1, Huang MB1, Roth W1, Armstrong W2, Powell M1, Villinger F3, Bond V4.
PMID: 26780239 [PubMed - in process]

J Neurovirol. 2015 Sep 25. [Epub ahead of print]
Nef exosomes isolated from the plasma of individuals with HIV-associated dementia (HAD) can induce Aβ1-42 secretion in SH-SY5Y neural cells.

**Khan MB1, Lang MJ1, Huang MB1, Raymond A2, Bond VC1, Shiramizu B3, Powell MD4.**

**KEYWORDS:** Amyloid; Combination antiretroviral therapy; HIV; HIV-associated neurocognitive disorders; Nef

PMID: 26407718 [PubMed - as supplied by publisher]


Nef-M1, a peptide antagonist of CXCR4, inhibits tumor angiogenesis and epithelial-to-mesenchymal transition in colon and breast cancers.

Katkoori VR1, Basson MD1, Bond VC2, Manne U3, Bumpers HL1.

**KEYWORDS:** CXCR4; Nef-M1 peptide; breast cancer; colorectal cancer; epithelial-to-mesenchymal transition; tumor angiogenesis

PMID: 26318034 [PubMed - in process] PMCID: PMC4695024


Heme-Mediated Induction of CXCL10 and Depletion of CD34+ Progenitor Cells Is Toll-Like Receptor 4 Dependent.

**Dickinson-Copeland CM1, Wilson NO1, Liu M1, Driss A1, Salifu H1, Adjei AA2,3, Wilson M3, Gyan B3, Oduro D3, Badu K4, Botchway F2, Anderson W5, Bond V1, Bacanamwo M6, Singh S1, Stiles JK1.**


**Patent:**

Dr. Gale Newman (Associate Professor) along with Dr. Barbara A. Jacob-Mungin and Dr. Chamberlain Obialo received a United States Patent on Method and Compositions for the Treatment and Detection of Endothelin-1 related Kidney Diseases (Patent No: US 9,255,931 B2). She also received a patent from South Africa entitled: “Method and Compositions Use for Endothelin-1 Related Kidney Diseases.” (South Africa Patent No. 2013/01126) from Andrews Kurth Attorneys LLP, (Ping Wang, M.D., Esq.)

**Grant Awards:**

Dr. Anisia Silva-Benitez (Associate Professor II) has just been awarded a R21 - “Molecular basis of the differential expression of the VieSAB regulatory system in Vibrio cholerae biotypes”. This work builds on her previous R-funded research into the mechanisms underlying cholera pathogenicity. She received a perfect score (100) for the R21.

Dr. Jonathan Stiles has been awarded R01 “PROTECTIVE ROLE OF NEUREGULIN-1 AGAINST CEREBRAL MALARIA PATHOGENESIS AND MORTALITY. Dr. Stiles has been working on cerebral malaria at Morehouse School of Medicine for many years. In the last half year or so, he has been on extended fieldwork, gathering data that should lead to additional, exciting translational outcomes targeting this major global disease and health disparity (Malaria).