

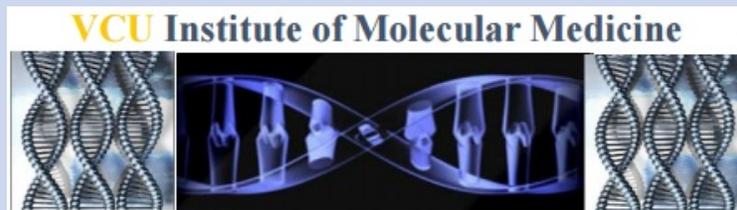
**VCU**

VIRGINIA COMMONWEALTH UNIVERSITY

Institute of Molecular Medicine

VIMM NEWS & VIEWS

The VCU Institute of Molecular Medicine (VIMM), established in 2008 by Paul B. Fisher, M.Ph., Ph.D., the Founding Director, is comprised of outstanding scientists/clinicians from VCU School of Medicine focusing on important medical-related research in cancer, neurodegeneration and infectious diseases. The purpose of this NEWS & VIEWS is to highlight the exciting research being performed by the VIMM members.



A Potential Path to Enhanced Therapy of Pancreatic and Other Cancers

- Pancreatic cancer is one of the most aggressive and frequently fatal cancers, emphasizing the need for improved therapies.
- A unique approach permitting targeting of pancreatic cancer cells with therapeutic agents is described in this report.
- Pancreatic and other cancers express elevated levels of the EphA2 receptor and conjugating a peptide agonist with Gemcitabine increases chemotherapy in pre-clinical animal models.
- This novel strategy holds promise for more effectively using chemotherapy, with reduced toxicity, to treat pancreatic and other cancers.

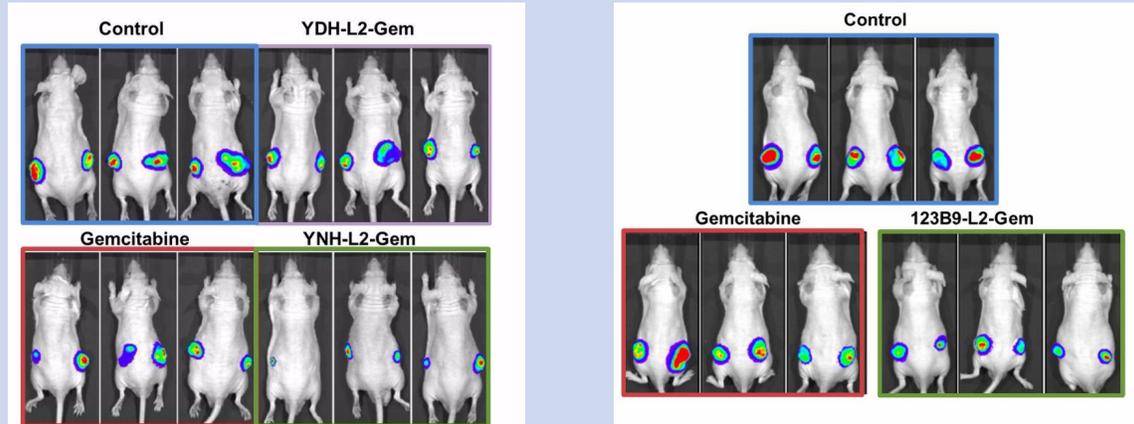
Enhancing Chemotherapy of Pancreatic Cancer: Targeted Delivery

Pancreatic cancer is a devastating disease with few patients surviving as long as 1 year after diagnosis. In this study, a novel method for targeted therapy of pancreatic cancer was explored using mouse models. The EphA2 receptor, which binds ephrinA1 as its ligand, is a highly expressed biomarker on many cancer cells. EphA2 was targeted using a new peptide agonist called 123B9, which has improved stability in plasma compared to previously studied peptides. 123B9 binds to the EphA2 receptor at its ligand-binding domain, and the authors hypothesized this would reduce the amount of un-activated EphA2 and thereby its oncogenic activity. The peptide agonist was conjugated to Gemcitabine, the current first-line treatment for pancreatic cancer. Although Gemcitabine alone does not offer great therapeutic benefit to most pancreatic cancer patients, this work showed that

conjugation of Gemcitabine with the 123B9 EphA2 targeting agent increases Gemcitabine efficacy in pre-clinical animal models.

The benefits of targeting approaches as documented in this work are becoming more and more apparent in cancer therapy. The promise of this approach is that it has dual negative effects on oncogenicity, which may represent a more effective strategy for treatment. Future studies to direct chemotherapy to pancreatic cancers is therefore warranted to attempt to develop more effective therapies for this invariably fatal and aggressive cancer.

This study represents a unique collaborative effort between the laboratories and colleagues of Paul B. Fisher, MPh, PhD and Maurizio Pellecchia, PhD. Dr. Fisher is Director of the VIMM and a Visiting Professor at the Sanford-Burnham-Prebys Medical Discovery Institute (SBPDI) in La Jolla, CA. Dr. Pellecchia is a Professor at the SBPDI and at the University of California in Riverside, CA. Drs. Fisher and Pellecchia are co-senior authors on this work. This research was supported in part by a NIH/NCI R01 grant awarded to Drs. Pellecchia and Fisher and an NIH/NCI R21 grant awarded to Dr. Fisher. Bridget A. Quinn an MD/PhD student in Dr. Fisher's laboratory at VCU and co-first author of this paper performed much of the biological and animal work, while the chemistry was performed predominantly by co-first author Si Wang, PhD in Dr. Pellecchia's group at the SBPDI and at the University of California Riverside, School of Medicine. This important type of collaborative effort between biologists and chemists holds promise for future advances in the treatment of cancer. The study was published in the journal *Oncotarget* on March 5, 2016*.



[*Bridget A. Quinn, Si Wang, Elisa Barile, Swadesh K. Das, Luni Emdad, Devanand Sarkar, Surya K. De, Susan Morvaridi Kharagh, John L. Stebbins, Stephen J. Pandol, Paul B. Fisher, Maurizio Pellecchia. Therapy of pancreatic cancer via an EphA2 receptor-targeted delivery of gemcitabine. *Oncotarget*. 2016 Mar 5. doi: 10.18632/oncotarget.7931. PMID: 26959746, PMCID PMC4941374]

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About the Investigators: Paul B. Fisher, MPh, PhD, is Professor and Chair of Human and Molecular Genetics, Director of the VCU Institute of Molecular Medicine (VIMM) and Thelma Newmeyer Corman Chair in Cancer Research in the VCU Massey Cancer Center (MCC), Virginia Commonwealth University, School of Medicine, Richmond, VA. Maurizio Pellecchia, PhD, is Adjunct Professor at the SBPDI and Professor of Biomedical Sciences, Daniel Hays Endowed Chair in Cancer Research, University of California Riverside, School of Medicine, Riverside, CA. Ms. Bridget Quinn is an MD/PhD student in Dr. Fisher's laboratory. Si Wang, PhD, Elisa Barile, PhD, Surya K. De, PhD and John Stebbins, PhD are research scientists working in the Pellecchia Laboratory at the SBPDI and UCR. Swadesh K. Das, PhD, is an Assistant Professor in HMG and a Member of the VIMM. Luni Emdad, MBBS, PhD, is an Assistant Professor in HMG and a Member of the VIMM. Devanand Sarkar is an Associate Professor in HMG, Associate Scientific Director of Therapeutics in the VIMM and a Harrison Foundation Distinguished Professor in Cancer Research in the MCC. Susan Morvaridi Kharagh, PhD, and Stephen J. Pandol, MD, are collaborating research scientists in Cedars-Sinai Medical Center, Los Angeles, CA.

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