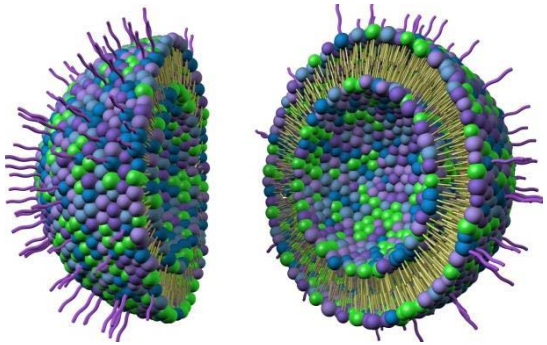

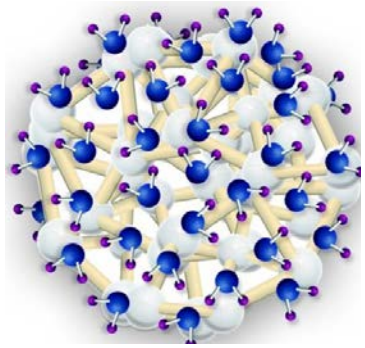

Mark Kester is a Professor of Pharmacology, Molecular Physiology/Biophysics, Biomedical Engineering and the Director of the NanoSTAR Institute at the University of Virginia. He was previously the G. Thomas Passananti Professor of Pharmacology at Penn State Hershey College of Medicine and the inaugural Director of the Penn State Center for NanoMedicine and Materials. Dr. Kester's research interests include the design, characterization and validation of nanotechnologies for targeted drug delivery in cancer. His laboratory has evaluated nanoliposomes, nanodendrimers and nanocolloids as effective drug delivery vehicles for pharmacological and molecular agents. Recent work focuses on nontoxic nanoscale systemic delivery systems for hydrophobic pro-apoptotic lipids as well as siRNAs that target mutated tumorigenic proteins. Dr. Kester has consulted with, or founded, several companies that have the license to his nano"Solutions". In addition, Dr.Kester is a co-author of Integrated Pharmacology, published by Elsevier, Ltd., which was recognized as a "highly commended textbook" by the British Medical Society.

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Research Description

Nanotechnologies for targeted drug delivery. Dr. Kester has research interests that include the design, characterization and validation of nanotechnologies for targeted drug delivery. His laboratory has evaluated nanoliposomes, nanodendrimers and nanocolloids as effective drug delivery vehicles for pharmacological and molecular agents. Recent work focuses on nontoxic nanoscale systemic delivery systems for hydrophobic pro-apoptotic lipids as well as siRNAs that target mutated tumorigenic proteins. Dr. Kester has consulted with, or helped found, several companies that have the license to his "nano Solutions". In addition, Dr.Kester is a co-author of Integrated Pharmacology, published by Elsevier, Ltd., which was just recognized as a "highly commended textbook" by the British Medical Society.

Using nanotechnology to take ceramide from the bench to the clinic

We, and others, have published that ceramide is a sphingolipid metabolites that is selectively apoptotic for cancer cells. Unfortunately, the therapeutic utility of ceramide is severely limited by its inherent hydrophobicity and impermeability. We have engineered a nanoliposomal formulation that delivers short chain bioactive ceramide nontoxically and efficaciously in multiple in vivo models. The ceramide nanoliposome is presently being developed by Keystone Nano, Inc. and human clinical trials have begun January 2018.

Determining the biochemical and biophysical mechanisms underlying the selective efficacy of ceramide in cancer models

We, and others, have documented multiple ceramide binding partners responsible for the pro-apoptotic actions of ceramide. In particular, we have published that ceramide localized within lipid microdomains binds to and activates protein kinase C zeta, which subsequently phosphorylates AKT 1 and 3 at inhibitory sites, inducing cell death. In addition, we have published that ceramide dephosphorylates STAT3, which transcriptionally reduces expression of prosurvival gene products and glycolytic cascade enzymes, which are upregulated in cancers.

The design of calcium phosphosilicate nanoparticles as immune-regulating theranostics

Nanoscale delivery and imaging agents are often limited by toxicology due to agglomeration, charge or lack of biocompatibility. With my colleague, Dr. James Adair, we have engineered non-cationic, nontoxic, non-agglomerating calcium phosphosilicate nanoparticles that encapsulate near infra-red fluoroprobes, whose enhanced quantum efficiencies can be translated into enhanced imaging and therapeutic modalities. In particular, indocyanine green-encapsulated calcium phosphosilicate nanoparticles have been shown to limit tumor tolerance after photo-excitation in multiple in vivo cancer models.

RECENT PUBLICATIONS

- Sphingosine Kinase 1 Cooperates with Autophagy to Maintain Endocytic Membrane Trafficking.Young MM, Takahashi Y, Fox TE, Yun JK, Kester M, Wang HG.Cell Rep. 2016 Nov 1;17(6):1532-1545. doi: 10.1016/j.celrep.2016.10.019.PMID:27806293
- Targeting cancer cells in the tumor microenvironment: opportunities and challenges in combinatorial nanomedicine.Linton SS, Sherwood SG, Drews KC, Kester M.Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2016 Mar-Apr;8(2):208-22. doi: 10.1002/wnan.1358. Review.PMID:26153136
- Preclinical development of a C6-ceramide NanoLiposome, a novel sphingolipid therapeutic. Kester M, Bassler J, Fox TE, Carter CJ, Davidson JA, Parette MR. Biol Chem. 2015 Jun;396(6-7):737-47. doi: 10.1515/hsz-2015-0129. Review.PMID:25838296

RECENT GRANTS

- 5P01 CA171983-02 NIH/NCI Targeted Sphingolipid Metabolism for Treatment of AML
- 5R01 CA167535-02 NIH/NCI "Novel Nanoparticle Therapy for Pancreatic Cancer"
- MF14S-013-LS CIT/CRCF A pH-resistant nanoparticle platform for oral delivery of insulin.

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