Spring 2017 Organic Seminar Series

Department of Chemistry and Chemical Biology

Dr. Zoltán Székely

Ernest Mario School of Pharmacy
Rutgers Cancer Institute of New Jersey

Friday, April 21, 2017
3:30pm, WL 260
Host: Lawrence Williams

"Targeting Activated Matriptase by Antibody-drug Conjugates for the Treatment of Lung, Breast and Prostate Cancers"

The outcomes of the treatments for patients with advanced solid tumors that include triple negative breast cancer (TNBC), non-small cell lung cancer (NSCLC), and castration-resistant prostate cancer (CRPC) remain very poor due to lack of effective therapies. We have identified a membrane bound protease, "activated" matriptase, as an attractive target antigen for highly selective antibody delivery of cytotoxins as activated matriptase expression is restricted to epithelial tumors and some B-cell lymphomas. Preliminary *in vivo* studies have shown that this enzyme plays regulatory roles in both initial cancer development as well as in tumor progression such as invasion and metastasis. We generated a novel ADC by linking M69, a mouse antibody specific to activated matriptase, to monomethyl auristatin E (MMAE) *via* a PEGylated, releasable Val-Cit-PABA linker as a proof-of-principle prototype utilizing copper-free click chemistry. Both in cell lines and in human xenograft models of TNBC, NSCLC and CRPC, the conjugate was found to exhibit potent anticancer activity without toxicity. Encouraged by these results, we are also exploring the use of this ADC against gastric and pancreatic cancer, and in combination with chemotherapy and immunotherapy.

If you would like to schedule a meeting with Dr. Zoltán Székely , please contact Robin Pacitti at 848-445-1554 or rp902@chem.rutgers.edu

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