

2019 International RB Conference
Sunday, September 29th – Wednesday, October 2nd

The 2019 International RB Conference announces its annual call for abstracts to be presented at the 5th annual meeting.

Abstract Submission Guidelines:

E-mail abstract as a **MS Word** document to lloydki@musc.edu by **5:00 pm Thursday, August 1st**. Please use the format of the attached sample. Abstracts will be reviewed and scored based on scientific content, including: cancer significance of research, novel research aims and methods. Up to 12 abstracts will be selected for oral presentation at the conference. Authors whose abstracts are selected for oral presentation will be notified. All submitted abstracts will be printed in the conference booklet.

ABSTRACT COVERSHEET

Submitter Name: _____

Predoctoral **Postdoctoral** **Clinical Resident/Fellow**

PI/Sr. Investigator:

Other Collaborators:

Project Title:

Institution:

Department:

Funding Source Name/Number (*e.g.*, NCI R01CA123456):

Abstract Narrative: Summary description of research project in 300 words or less (single-spaced, 12 point Calibri). Sample attached.

(Single-spaced, 300 words or less 12 point Calibri)

SAMPLE: Different roles of Sphingosine kinase isoenzyme in cancer cells and characterization of SphK isoenzyme selective inhibitors

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Department of Pharmaceutical and Biomedical Sciences

Funding Source Name/Number: NIH#

Two Sphingosine kinases (SphKs) isoenzymes, SphK1 and SphK2, play only partially overlapping roles in tumor epithelial cells proliferation and migration although both of them catalyze the formation of sphingosine-1-phosphate. Our genetic approach (siRNA) in multiple cancer cell lines revealed that SphK2 knockdown had more inhibitive effects on cancer cell proliferation and migration than SphK1 knockdown. Both qPCR and a novel florescence-based HPLC method measuring SphK activities confirmed the increased SphK1 induced by SphK2 knockdown could not rescue the cells from apoptosis. Western results showed SphK2 ablation has different effects on several key cell survival

pathways including p21, p53, FAK, VCAM1. Most surprisingly, knocking down SphK2 decreases not only expression but also activation of ERK2 compared to less effects caused by SphK1 ablation. However, as the dominant isoenzyme, SphK1 ablation did increase the total amount of ceramide species. In order to confirm the results from the genetic approach, we developed pharmacological approaches that used SphK isoenzymes selective inhibitors to dissect the functions of SphK isoenzymes. After the structure optimization of the lead compounds identified by high throughput screening, two compounds were identified as SphK inhibitors: 3-(4-Chlorophenyl) adamantane-1-carboxylic acid (pyridin-4-ylmethyl) amide hydrochloride salt - termed ABC294640 and 3-(4-Chlorophenyl) adamantane-1-carboxylic acid [2-(3, 4-dihydroxyphenyl) ethyl] amide – termed ABC294735. The inhibition specificities of these compounds were characterized. ABC294640 is a SphK2 selective inhibitor (K_i 10 μ M), while ABC294735 (K_i^{SphK1} 2.5 μ M, K_i^{SphK2} 3.5 μ M) is a dual inhibitor. Lineweaver-Burk plots using the data from recombinant SphK1/2 active enzymes and kinase assay kit revealed ABC294640 and ABC294735 were SphK competitive inhibitors. A possibly SphK1 selective inhibitor had also been identified, but kinase profiling data revealed it as a pan-inhibitors for several important kinases.