Thu., **4 July**, 4:00pm

Jukhyun Bio Auditorium(RM.121)

Korean

MFF REGULATION OF MITOCHONDRIAL INTEGRITY IS A THERAPEUTIC TARGET IN CANCER

Speaker | Jae Ho Seo, Ph.D.

Affiliation | Wistar Institute

Host | Prof. Jihwan Park

광주과학기술원 생명과학부
Gwangju Institute of Science and Technology School of Life Sciences

School of Life Sciences

Seminar Series

No. 2019-17

Thursday, **4 July** 2019, 4:00 pm

Jukhyun Bio Auditorium(RM.121)

Speaker Jae Ho Seo, Ph.D.

Education/Experience

1997-2003	B.S., Dept. of Biological Sciences, Chonnam National University, Gwangju, Korea
2003-2005	M.S., Dept. of Biology, Chonnam National University, Gwangju, Korea
2005-2010	Ph.D., School of Biological Sciences and Technology, Chonnam National University (Advisor: Ho Zoon Chae)
2008-2009	Visiting Research, Lab of Biochemistry/NHLBI/NIH, Bethesda, MD, USA
2010-2011	Postdoc Fellow, BK21 Higher Education Center for Bioregulator Research, Chonnam National University, Korea
2011-2012	Postdoc Fellow, Winship Cancer Institute in Emory University, Atlanta, GA, USA (Mentor : Jing Chen)
2013-2016	Postdoc Fellow, Wistar Institute, Philadelphia, PA, USA (Mentor : Dario C. Altieri)
2017-present	Associate Staff Scientist, Wistar Institute, Philadelphia, PA, USA (Mentor : Dario C. Altieri)

Research Interest

The aim of research is to understand how mitochondria can regulate tumor cell proliferation and metastasis eventually discover druggable targets. Rapidly growing tumors are constantly exposed to unfavorable growth conditions on the tumor microenvironment including nutrient deprivation, hypoxia and augmented level of reactive oxygen species (ROS). This requires a process of adaptation or "plasticity" that improves tumor fitness via genetic and nongenetic changes, buffers stress signals and reprograms metabolism for tailored bioenergetics needs. Therefore, discovery of tumor cells' endeavor to be able to overcome adverse growth condition represents attractive therapeutic targets.

Abstract

The regulators of cell death in cancer are not completely understood and this has hampered the development of new therapies. Here, we show that protein isoforms of Mitochondrial Fission Factor (MFF), a molecule that controls mitochondrial size and shape, i.e. mitochondrial dynamics, are highly expressed in patients with primary and metastatic prostate and lung cancer, compared to normal tissues. Structurally, MFF1 and MFF2 form homo- and heterodimer complexes with the voltage-dependent anion channel-1 (VDAC1) at the mitochondrial outer membrane, inserting into the interior hole of the VDAC1 ring. In turn, this maintains oxidative bioenergetics, opposes mitochondrial cell death and supports tumor growth, in vivo. Structure-based peptidyl mimicry identified an MFF Ser223-Leu243 peptidomimetic that disrupts the MFF-VDAC1 complex in vivo, triggers mitochondrial cell death in tumor but not normal cells, and delivers cytotoxic activity in patient-derived glioblastoma neurospheres, primary tumor organoids and prostate cancer xenograft models. Therefore, the MFF-VDAC1 complex is a novel regulator of mitochondrial cell death and actionable therapeutic target in cancer.