THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

CHAO HUANG

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
GRADUATE COLLEGE DEPARTMENT OF PHYSIOLOGY

Tuesday, December 6, 2016, 12:00 p.m.

Room 631, BMSB, OUHSC

HOW CD82 REGULATES CANCER CELL MIGRATION A LIPID DEPENDENT PROCESS

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ABSTRACT: Tetraspanin CD82 regulates cancer cell migration in a lipid dependent manner. CD82 is localized to membrane lipid raft and CD82 interacts with lipid raft species such as gangliosides GM2/GM3, which contributes CD82 inhibition on integrins and growth factor receptors functions. The mechanism how CD82 is associated with lipid raft and why lipid raft association is important for CD82 function remain unknown. We identified several cholesterol binding motifs in CD82 amino sequence which were shown to be revolutionarily conserved. Upon mutagenesis of one of the cholesterol binding motifs, CD82 inhibitory function on cancer cell migration was lost, and CD82 localization to lipid raft was decreased, CD82 physical association with gangliosides GM2/GM3 was also disrupted. Additionally, we observed that CD82 down-regulated several tetraspanin enriched microdomain (TEM) proteins, whose localization to lipid raft were promoted by CD82 WT but not CD82 mutant. However, expression of the cholesterol binding motif deficient mutant increased cell surface level of TEM proteins. Further analysis with endocytosis assay show CD82 stimulated endocytosis of CD82 associated TEM proteins, such as endocytosis of integrins α3 and β1, which is cholesterol binding motif dependent. We also observed that CD82 association with integrin β1 is galectin dependent, and galectin-3 promotes CD82 endocytosis. Therefore, we conclude that CD82 regulates cancer cell migration through down-regulation of TEM proteins by stimulating TEM proteins endocytosis, and CD82 Interacts with TEM proteins through galectins and CD82 interacts with lipid raft through lipid recognition, by promoting TEM proteins localization to lipid raft, CD82 down- regulates TEM proteins cell surface level and inhibits cancer cell migration.