BİLKENT UNIVERSITY

MOLECULAR BIOLOGY AND GENETICS

DEPARTMENTAL SEMINAR

"Rac1-mediated membrane raft localization of PI3K/p110β is required for its activation by GPCRs or PTEN loss"

Assist. Prof. Onur Çizmecioğlu

Dept. of MBG, Bilkent University

The plasma membrane is the major site of phosphoinositide 3-kinase (PI3K) activation and integration of divergent growth factor signals. We aimed to understand how spatial compartmentalization in the plasma membrane might contribute to the functions of the ubiquitous class IA PI3K isoforms, p110α and p110β. We found that p110β localizes to membrane rafts in a Rac1-dependent manner. This localization potentiates Akt activation by G-protein-coupled receptors (GPCRs). Thus genetic targeting of a Rac1 binding-deficient allele of p110α to rafts alleviated the requirement for p110α-Rac1 association for GPCR signaling, cell growth and migration. In contrast, p110β, which does not play a physiological role in GPCR signaling, is found to reside in nonraft regions of the plasma membrane. Raft targeting of p110β allowed its EGFR-mediated activation by GPCRs. Notably, we found that p110β dependent, PTEN null tumor cells critically rely upon raft-associated PI3K activity. Collectively, our findings provide a mechanistic account of how membrane raft localization regulates differential activation of distinct PI3K isoforms and offer insight into why PTEN-deficient cancers depend on p110β.

Date-Time : Wednesday, September 28, 2016 – at 15:40
Place : SBZ-14
Host : Serkan Göktuna