UNIVERSITY of GUELPH

COLLEGE of BIOLOGICAL SCIENCE

DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY

Seminar SPEAKER SERIES

2019 - 2020

SEP **WED 18** **10:30 AM**

Summerlee Science Complex
SSC 2315

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Dynamic cell surface nanoscale organization of EGFR controls receptor signaling in breast cancer cells

The Epidermal Growth Factor Receptor (EGFR) controls cell proliferation, survival and migration. Disruption of EGFR regulation contributes to tumor growth and drug resistance in triple-negative breast cancer (TNBC) and other cancers. Understanding the mechanisms that control EGFR activation and function, and how disruption of this control drives TNBC growth and progression is thus important to develop better treatments for TNBC. Upon binding ligand, EGFR exhibits autophosphorylation, recruitment of intracellular signaling proteins and changes in nanoscale organization at the plasma membrane, which are associated with a reduction in EGFR mobility. We used fluorescence microscopy and automated image analysis methods for single-particle tracking and find that EGFR displays heterogeneous mobility and ligand-binding capabilities at the cell surface, which is correlated to recruitment into several possible distinct nanodomains. We have resolved novel mechanisms by which one such nanodomain formed by the endocytic protein clathrin controls EGFR signaling at the cell surface leading to activation of PI3K-Akt prior to receptor internalization. Various normal and TNBC cell lines exhibited differences in the distribution of EGFR within specific nanodomains, receptor mobility, and sensitivity of EGFR mobility and signaling to tyrosine kinase inhibitors. In summary, we resolved that EGFR ligand binding and signaling are not receptor intrinsic but strongly dependent on nanoscale organization in specific nanodomains. Further, as we find distinct control of EGFR mobility and confinement between various normal and TNBC cell lines, targeting of the plasma membrane nanoscale organization of EGFR may represent a novel approach to treat TNBC and other cancers.

All welcome to attend
Light refreshments will be served

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