Development of *in vitro* methodologies to study the behaviour of targeted drug delivery systems to triple negative breast cancer

Sepideh Khazeni[1], Pegah Varamini[1]

[1]School of Pharmacy, Faculty of Medicine and Health, The University of Sydney, Camperdown, NSW, Australia

Abstract

Statement of the Problem: Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype. Due to the lack of sex-hormone receptors and HER2 overexpression, tumor does not respond to the available targeted drugs. Hence, it is crucial to investigate the design of effective targeted drug delivery system (DDS) for the treatment of TNBC. In this study, we have developed different methods to test the behavior of different DDS based on the Luteinizing Hormone Releasing Hormone receptor (LHRH-R) targeting.

Methodology & Theoretical Orientation: We studied the overexpression of LHRH-R by immunohistochemistry analysis using advanced Confocal Laser Scanning Microscopy (CLSM) on three different TNBC cells and normal breast cell-line. Uptake of different DDSs conjugated with LHRH-R ligand has been investigated by using CLSM and IncuCyte® in these cell-lines. By using small interfering RNA (siRNA) against LHRH-R sequences, we knocked down the LHRH-R in TNBC cell line with 85% knockdown efficiency and compare the uptake of LHRHD-DDS in silenced LHRH-R to wildtype cells by CLSM.

Findings: We observed the overexpression of LHRH-R in TNBC cells but not the control. We detected the uptake of LHRH-based DDS from TNBC cells by CLSM and IncuCyte®. Silencing LHRH-R with siRNA has decreased the uptake of LHRD-DDS in silenced LHRH-R cells.

Conclusion & Significance: In conclusion, we have shown LHRH-based DDSs were selectively uptaken through LHRH-R overexpressed TNBC cells. These findings indicate that LHRH-R ligands are promising carriers to use for future targeted drug design for the treatment of TNBCs. Furthermore, our developed methodologies allowed us to effectively investigate the in vitro behavior of this targeted DDS as a part of the preclinical studies.

Recent Publications

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2. CHANG, C., VARAMINI, P., GIDDAM, A. K., MANSFELD, F. M., D'OCCHIO, M. J. & TOTH, I. 2015. Investigation of Structure–Activity Relationships of Synthetic Anti-Gonadotropin Releasing Hormone Vaccine Candidates. ChemMedChem, 10, 901-910.
3. GHANGHORIA, R., TEKADE, R. K., MISHRA, A. K., CHUTTANI, K. & JAIN, N. K. 2016. Luteinizing hormone-releasing hormone peptide tethered nanoparticulate system for enhanced antitumoral efficacy of paclitaxel. Nanomedicine (Lond), 11, 797-816.
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Presenting author details

Full name: Sepideh Khazeni

Contact number: +61-293517239

Linked In account: Sepideh Khazeni

Category: Oral presentation