

To: The Dean of Graduate Studies

From: PhD student

Name: Hanan Abu Tayeh

I.D. 036651024

Department: Human biology

Stage: (please circle) 1st Stage/ **2nd Stage**

Annual Progress Report

Submission to the Graduate studies Authority by the departmental secretary only

Part A – designated for PhD Student

My research goals are to test whether expression of a gene called integrin beta 3 in breast cancer cell lines will promote their reversion to a normal like breast tissue thus normalizing their malignant phenotype.

To this end we addressed the following specific objectives:

- 1. Characterize human luminal breast cancer cells overexpressing Intβ3 for their cancer progenitor cell like properties.**
- 2. Determine whether Intβ3 expression will induce malignant normalization of luminal breast cancer cells.**
- 3. Determine whether knock down of Intβ3 in normal human breast cell line will disrupt their polarization.**
- 4. Elucidate the molecular mechanisms by which Intβ3 expression in human luminal breast cancer cells promotes their differentiation to a normal like phenotype.**
- 5. Evaluate whether overexpression of Intβ3 in luminal cancer cells will promote early dissemination of tumor cells *in vitro* and *in vivo*.**

I have successfully carried out Aims 1 and 3 and currently I am finalizing Aim 2 and Aim 4, and have started Aim 5. Our results demonstrate that cancer progenitor like cells expressing Intβ3, in MCF-7 (MCF-7-Intβ3) and T47D (T47D-Intβ3) breast cancer cell lines underwent phenotypic reversion resembling a normal like acini when cultured *in vitro* in the physiological relevant 3 dimensional basement membrane extract (3D BME system), which is a novel model that recapitulates numerous features of breast epithelium *in vivo* (Aim 1 and 3). Importantly, the reversion of MCF-7-Intβ3 cells to a normal like phenotype induced a dormant state when they cultured in the 3D BME model compared to MCF-7-vec cells (Aim 2). Thus, we wish to further study whether overexpression of Intβ3 in MCF-7 cells will promote their malignant normalization also *in vivo*. Furthermore, we demonstrated that the reversion of MCF-7-Intβ3 cells to a normal

like phenotype was mediated by down-regulation of Notch4 expression and downstream signaling and can be partially reversed by inhibiting $\alpha V\beta 3$ activation (Aim 4). Therefore, we seek to further unravel the potential mechanisms that can be applied to redirect cancer luminal progenitor cells to commit and differentiate to a normal-like tissue, thus normalizing their malignant phenotype. This approach may lead to novel therapeutic strategy to treat recurring breast cancer disease. Finally, we already have preliminary results demonstrating that overexpression of Int β 3 in luminal cancer cells can promote early dissemination of tumor cells from the primary site in an *in vitro* and *in vivo* (Aim 5) model systems paradoxically resembling the invasive ductal carcinoma *in vivo*. Thus, the different luminal breast cancer cell lines overexpressing Int β 3, will be further tested for their metastatic potential *in vitro* and *in vivo*.

Estimated date for submitting PhD research proposal/ dissertation to the PhD departmental committee: April 2016

Ph.D. student Name: Hanan Abu Tayeh Signature: _____ חנאן Date: 23.6.14

Please refer to the student progress and to the estimated date for submission of research proposal / dissertation

Hanan has done a remarkable progress in her PhD. Her work was already presented in several meetings and we are currently preparing a manuscript that we intend to send to high tier journal. Her work is groundbreaking and may have a great impact on breast cancer research. Hanan proposed 5 Aims in her PhD studies and successfully completed Aim 1 and 3 and currently finalizing Aim 2 and Aim 4, and started Aim 5.

Hanan will submit on time her PhD dissertation March 2016.

PhD research evaluation

(The evaluations relate to all researches previously supervised by you)

Evaluation	Poor	Average	Good	Very good	Ranked in the top 5%
Novelty					x
Clarity of research and hypothesis					x
Criticism					x
Knowledge of Background material					x
Knowledge of research methods					X
Comments	Hanan is very talented and highly motivated student and is conducting a complex and innovative research with great success.				

Supervisors Name: _____ Dalit Barkan _____ Signature:  _____

Date: 26.6.2014

Chairperson of PhD Committee Name: _____ Signature: _____ Date: _____