FORM E – PROJECT SYNOPSIS, School of Life Sciences

Project title: The Effect of cellular disorganisation on breast cancer behaviour

Cross School Project? **Yes/No, but joint project within the School**

If so, name of other School/s:

The proposal falls into the following priority area(s), Please underline: East Medicine, Ageing Research, informing policy and practice, **New technologies for Biosciences**

Background to research and synopsis

Background: Analysis of molecular mechanisms required for the correct organisation of the Golgi apparatus by microtubules is absolutely necessary for understanding cell behaviour and may offer potential as a target aimed at preventing cancer metastasis.
Microtubules and microtubule motors play important roles in the organisation and behaviour of intracellular membranes, such as the endoplasmic reticulum (ER) and the Golgi apparatus. In normal cells the Golgi apparatus is located near the centrosome. Under disease conditions or when cells are treated with a drug that depolymerises microtubules the Golgi apparatus fragments and disperses through the cytoplasm. This process and proteins involved in microtubule motors are not well understood. Furthermore, Golgi apparatus function and in particular the effect on post-translational modification of proteins for example, by glycosylation, is not well characterised to date.

Synopsis: The aim of this project is to investigate the effect of microtubules depolymerisation on the structure of the Golgi apparatus and on membrane protein glycosylation. Our hypothesis is that microtubule depolymerisation and the Golgi apparatus fragmentation has a detrimental effect on protein glycosylation. Our knowledge of protein engineering and previous experience with fluorescence fusion proteins will allow construction of fluorescent probes for microtubular proteins and the study of Golgi apparatus dynamics in living cells using high resolution molecular imaging. At the same time changes in membrane protein glycosylation can be analysed using recombinant fluorescently labelled glycoprobes before and after exposure to cytotoxic drugs. The student will gain experience of molecular cell biology and live cell imaging techniques, take part in the School Research Training Programme and be part of a collaborative research project involving links with research groups in other institutions. **The Outcome:** These studies will provide new insights into the role of microtubule depolymerisation and Golgi apparatus in cancer cell metastasis and may identify therapeutic possibilities for regulating Golgi function in malignancy. This project is directly relevant to the research area “New Technologies for Biosciences”.

Supervisory Team and Research Environment

Supervisor Name	Role (DoS, 2nd Supervisor, 3rd Supervisor)	No. of successful PhD/ MPhil supervisions	Current student load for 2012/13 (FTE)	School (for cross School projects)
Dr Anatoliy Markiv	DoS	0	0	
Dr Miriam Dwek	2nd Supervisor	6	1 (2nd supervisor)	
Dr John Murphy	3rd Supervisor	7	1 (DoS)	

Please list recent publications by supervisors relevant to the project:
Markiv, A., Peiris, D., Curley, G.P., Odell, M., Dwek, M.V., 2011, Identification, cloning and characterisation of two N-acetylgalactosamine binding lectins from the albumen gland of *Helix pomatia. Journal of Biological Chemistry*, 286, 20260-20266.

Markiv, A., Anani, B., Durvasula, R.V. and Kang, A.S., 2011, Module based antibody engineering: a novel synthetic REDantibody. *Journal of Immunological Methods*, 364, 40-9.
Informal enquiries (email address of Director of Studies) and any web links that prospective applicants would be referred to: **A.Markiv@westminster.ac.uk**