

PhD PROJECT SYNOPSIS
School of Life Sciences

Project title: 3D CANCER MIMETICS INCORPORATING FLUID FLOW AND PRESSURE

Cross College/Department Project? NO

If YES, name of other College/Departments: N/A

Name of research group/centre: CANCER RESEARCH GROUP

Background to research and synopsis (200 words max)

Intra-tumour fluid pressure (IFP) prevents the penetration of anti-cancer drugs into tumours limiting their effectiveness. We tissue-engineered 3D tumouroids incorporating type-1 collagen/cancer cells for the dense central tissue (characteristic of tumours) nested in further type-1 collagen to recapitulate the surrounding extracellular matrix (ECM). Tumouroids maintained under fluid flow with increased IFP down-regulated markers of EMT and exhibited decreased sensitivity to the chemotherapeutic drug doxorubicin.

In this study, tumouroids will be prepared with breast and prostate cancer cell lines of different subtypes. The tumouroids will be nested in collagen type-1, laminin, fibronectin, collagen IV in a stepwise manner. Cell growth and invasion will be monitored (EVOS FL 2 Auto, ThermoFisher).

A matrix-index (MI) describing ECM proteins influencing cancer cell growth/invasion under fluid flow/pressure will be described. Transcriptomic analysis, validated using immunohistochemistry, will focus on the Wnt-signalling pathway and levels of ion channels/pressure sensing genes to determine their role in tumouroid response to drugs, including DNA damaging agents and inhibitors of signalling pathways.

The relationship between tumouroid drug responsiveness (dose response curves), matrix composition and increased IFP will be determined. The role of the Wnt signalling pathway and tumouroid response to treatment in different ECMs will be identified.

Supervisory Team:

Supervisor Name	Role (DoS, 2 nd / 3 rd Supervisor)	No. of successful PhD/ MPhil supervisions	Current number of students supervised in academic year 2019/20 (FTE)	Have you been a DoS for a UoW-funded Research Scholar in last 5 years? i.e. since academic year 2013/14?
Dr Miriam Dwek	DoS	9	2	yes
Dr Pinar Uysal Onganer	2 nd	1 PhD co supervision 5 MRes supervisions	2 MSc extended projects	no

Recent publications by supervisors that are relevant to the project:

The interaction of Wnt-11 and signalling cascades in prostate cancer. Koushyar S, Grant GH, Uysal-Onganer P. Tumour Biol. 2016; 37(10):13049-13057.

Prostate-specific PTen deletion in mice activates inflammatory microRNA expression pathways in the epithelium early in hyperplasia development. Dart DA, Uysal-Onganer P, Jiang WG. *Oncogenesis*. 2017; 14;6(12):400.

Efficacy of DOPE/DC-cholesterol liposomes and GCPQ micelles as AZD6244 nanocarriers in a 3D colorectal cancer in vitro model. López-Dávila V, Magdeldin T, Welch H, Dwek MV, Uchegbu I, Loizidou M. *Nanomedicine (Lond)*. 2016; 11(4):331-44.

Cellular glycosylation affects Herceptin binding and sensitivity of breast cancer cells to doxorubicin and growth factors. Peiris D, Spector AF, Lomax-Browne H, Azimi T, Ramesh B, Loizidou M, Welch H, Dwek MV. *Sci Rep*. 2017; 22; 7:43006.

HER2 expression levels of breast cancer cell lines grown in 2D and 3D cell culture and sensitivity to chemotherapeutic drugs. Azimi T, Markiv A, Dwek MV, *Breast Cancer Now Conference Proceedings*. Royal College of Physicians, London. July 2016

Informal enquiries (email address of Director of Studies) and any web links that prospective applicants would be referred to:

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<https://www.westminster.ac.uk/about-us/our-people/directory/dwek-miriam>

<https://www.westminster.ac.uk/about-us/our-people/directory/uysal-onganer-pinar>

<https://www.westminster.ac.uk/cancer-research-group>

To make your application:

<https://digital.ucas.com/courses/details?coursePrimaryId=e7c9d7be-c31f-5d83-792e-ce8450014647&courseOptionId=>