**Project :** Systems-based integration and analysis of a deeply phenotyped GBM cohort correlating

to ‘extreme’ and ‘poor’ responding patients

**As part of the Horizon 2020 MSC ETN PhD Program GLIO-TRAIN:**

<http://www.systemsmedicineireland.ie/2017/european-training-network-15-new-phd-student-positions-application-closing-date-friday-10th-nov-2017/>

<http://www.systemsmedicineireland.ie/wp-content/uploads/2017/09/GLIOTRAIN_PhD-Student-Positions.pdf>

<https://www.euraxess.ie/jobs/246941>

**Location:** Royal College of Surgeons in Ireland

**Principle Investigator:** Prof Jochen Prehn (kprehn@rcsi.ie)

Collaborators: Dr Alexander Kel (geneXplain, Germany), Dr Ahmed Idbaih (ICM Institute for Brain and

Spinal Cord, France), Prof Diether Lambrechts (VIB Leuven, Belgium).

**Project Summary:** The project will molecularly phenotype and functionally interrogate patient

cohorts correlating to ‘extreme’ and ‘poor’ GBM responders. The strategy will employ the process of

‘natural pre-selection’ to identify key differences in the underlying biology facilitating identification

of new functional master drivers. Natural pre-selection been successful in describing metabolic

aberrations leading to diabetes and obesity, but has thus far not been employed in GBM. To identify

novel GBM resistance mechanisms, the PhD student 9, hosted at RCSI will focus on deep

phenotyping a cohort of gender balanced n=100 GBM patients grouped according to favourable or

unfavourable clinical outcome despite similar (histo)pathological features. The PhD student will be

seconded to UPMC for 3 months to identify and prepare a collection of n=100 GBM samples for

subsequent analysis. On return to RCSI, (s)he will commence molecular subtyping of this cohort of

‘poor’ and ‘extreme’ responders to include WES, RNA seq, metabolomic profiling (NMR

spectroscopy) and reverse phase protein array -based protein and phosphoprotein analysis (>150

validated antibodies). The PhD student will employ deterministic models developed by RCSI to

quantitatively identify key biological differences between ‘poor’ and ‘extreme’ responders, and to

relate these differences to GBM subtypes. Subsequently during a 5 month secondment to SME

beneficiary GEX, PhD student 9 will link transcriptomic profiles to master transcription regulators

and upstream, targetable signalling pathways, Back at RCSI, (s)he will integrate outputs from

molecular profiling, deterministic systems modelling and GEX platform analysis to define specific,

targetable master drivers of ‘poor’ and ‘extreme’ responders and their interaction with key signalling

pathways and GBM subtypes.

**Specific Requirements:**

  MSc or BSc in Bioinformatics / Human Genetics / (Bio)Engineering or a related discipline with preference given to those candidates with experience in Tumour Biology/Oncology.

  Experience with Analysis of Genomics Data / Next Generation Sequencing (RNA Seq, Shallow Sequencing etc) or Proteomics data.

  Programming skills and/or Statistical Analysis Methods are of advantage

**References:**

Raoof R, Jimenez-Mateos EM, Bauer S, Tackenberg B, Rosenow F, Lang J, Onugoren MD, Hamer H, Huchtemann T, Körtvélyessy P, Connolly NMC, Pfeiffer S, Prehn JHM, Farrell MA, O'Brien DF, Henshall DC, Mooney C. Cerebrospinal fluid microRNAs are potential biomarkers of temporal lobe epilepsy and status epilepticus. Sci Rep. 2017 Jun 12;7(1):3328

Tivnan A, Heilinger T, Ramsey JM, O'Connor G, Pokorny JL, Sarkaria JN, Stringer BW, Day BW, Boyd AW, Kim EL, Lode HN, Cryan SA, Prehn JH. Anti-GD2-ch14.18/CHO coated nanoparticles mediate glioblastoma (GBM)-specific delivery of the aromatase inhibitor, Letrozole, reducing proliferation, migration and chemoresistance in patient-derived GBM tumor cells. Oncotarget. 2017 Mar 7;8(10):16605-16620.

Haunsberger SJ, Connolly NM, Prehn JH. miRNAmeConverter: an R/Bioconductor package for translating mature miRNA names to different miRBase versions. Bioinformatics. 2017 Feb 15;33(4):592-593.

Kinsella S, Prehn JH. In the Middle of a Chain Interaction. Mol Cell. 2016 Oct 20;64(2):217-218.

Salvucci M, Würstle ML, Morgan C, Curry S, Cremona M, Lindner AU, Bacon O, Resler AJ, Murphy ÁC, O'Byrne R, Flanagan L, Dasgupta S, Rice N, Pilati C, Zink E, Schöller LM, Toomey S, Lawler M, Johnston PG, Wilson R, Camilleri-Broët S, Salto-Tellez M, McNamara DA, Kay EW, Laurent-Puig P, Van Schaeybroeck S, Hennessy BT, Longley DB, Rehm M, Prehn JH. A Stepwise Integrated Approach to Personalized Risk Predictions in Stage III Colorectal Cancer. Clin Cancer Res. 2017 Mar 1;23(5):1200-1212.