

Report to the European Society of Cardiology (ESC) for the First Contact Initiative Grant to visit Prof Deepak Srivastava in Gladstone Institute of Cardiovascular Research (November 2nd-16th 2013).

I have recently been appointed to the position of non-clinical lecturer in the Centre of Experimental Medicine (CEM) at Queen's University Belfast (QUB). This is a vibrant research centre of excellence which will soon be enhanced by moving to an almost-completed £32M Research building (~4,742m²) partly funded by a Wellcome Trust-Wolfson Capital Award. In this new academic post I am establishing my own independent programme in the area of direct reprogramming and vascular stem cell biology in the context of vascular disease. Over the last 8 years, I have developed significant expertise and experience in stem cells, reprogramming, cell signalling and endothelial cell biology in the Cardiovascular Division of the BHF Centre of Excellence at King's College London. The impact of my research has been recognised by several prestigious awards, including the PAPANIKOLAOU Prize from the Hellenic Medical Society (October 2012, for significant contribution to medical research) and the prize for outstanding performance and scientific research awarded by the Cardiovascular Division, BHF Centre of Excellence, King's College London (December 2012).

I have recently spent 3 months in the core ES and iPS cell facility at Boston Children's Hospital, Harvard Medical School, working with Prof. George Daley who is world-leader in stem cell research. Through this collaboration I have benefited from the group's experience in cell reprogramming and generation of human iPS and Partial-iPS (PiPS) cells. This will be of enormous benefit as I develop my programme and also fits with the strategic priorities or area is of key strategic importance for the CEM as we seek to translate such basic research into benefits for patients.

I was awarded a First Contact Initiative Grant from the European Society of Cardiology (ESC) to visit and establish collaboration with the laboratory of Professor Deepak Srivastava in Gladstone Institute of Cardiovascular Research in University of California, San Francisco (UCSF). Professor Srivastava's group is internationally recognised for their studies in cell reprogramming. This ESC grant has provided me with an unparalleled opportunity to expand my own area of research and establish collaborations with leading laboratories in the world.

During my visit to the Gladstone Institute I had the opportunity to interact with and learn from Professor Deepak Srivastava's group which focuses on the fundamental events involved in cell fate determination and differentiation and organogenesis. They also study transcriptional and post-transcriptional steps, including those involving microRNAs. I benefited from their impressive reprogramming strategies to directly reprogram fibroblasts into cardiomyocyte-like

cells for regenerative purposes and learnt a number of *in vitro* and *in vivo* reprogramming models. I also gained skills in new methods for efficiently reprogramming induced pluripotent stem cells from blood cells using novel approaches. I had also the privilege to meet and discuss with Dr Kathy Ivey, the Director of the Gladstone Stem Cell Core. We talked about reprogramming and differentiation models and discussed possible limitations and challenges of cell reprogramming, especially in terms of efficiency, and stability. Dr Kathy Ivey has offered me expert suggestions and advice based on these novel techniques including provision of detailed protocols for continuous support of my research.

As I am very interested to established *in vivo* reprogramming models to study the potential of the direct reprogrammed endothelial cells which I have recently generated, this visit has totally fulfilled my expectations and enriched my understanding of *in vivo* reprogramming, the limitations, the challenges and the advantages. As stated, the Gladstone institute in UCSF is a centre which provides cutting-edge facilities and new technologies in a collaborative and very supportive environment. I was delighted to have the chance to visit it and establish collaborators with outstanding group leaders.

Also during my visit I met Professor Bruce R. Conklin, and I was impressed of the technology and the tools which his group generates genome-engineered human induced pluripotent stem cell lines to study human disease. This has led to an established collaboration with Professor Conklin, which will enhance my knowledge in genome engineering of reprogramming cells and benefit to address the question of my research using these high standard technologies.

I have also had the honour to meet and discuss with Professor Yamanaka's group in Gladstone Institutes in UCSF. I have learned and discussed about new approaches of induced pluripotent stem cell generation, about switch of cell fate and how to improve the efficiency of cell reprogramming. Importantly, I had the chance to discuss about novel strategies to perform RNA-binding assays. I was very excited to learn about these techniques since one of the main focuses of my research is to elucidate the signalling pathways of RNA-binding proteins which play fundamental roles during direct reprogramming towards vascular cell lineages.

I was also delighted to meet and discuss with Dr Katherine Pollard and Dr Alisha Holloway in the Bioinformatics Core at the Gladstone Institutes. The Bioinformatics Core in Gladstone Institutes has strong expertise on experimental design and data analysis of complex data sets with a specialization on analysis of large-scale data sets acquired from cutting-edge sequencing and gene expression technologies, especially RNA-seq, and ChIP-seq. I have

established collaborations with Dr Alisha Holloway, the Director of the Core Bioinformatics at the Gladstone who will contribute in my research projects by applying her extensive knowledge in bioinformatics and biostatistics for the design, and data interpretation of the RNA-binding protein immunoprecipitation coupled with high-throughput sequencing in order to identify target RNAs.

Importantly, during my visit in Professor Deepak Srivastava's laboratory in Gladstone Institute I have also actively participating in lab meetings, project-related discussions, talks, conferences and I have been invited to give a talk on my research.

In a personal level I was delighted to communicate with Professors Srivastava and Conklin who have agreed to act as international mentors for me and provide advice in these early stages of my academic leadership. They shared fundamental principles of the establishment of a successful and productive research team and provided me with full support and guidance.

In this stage I would like to express my sincerely gratitude to European Society of Cardiology for giving this great opportunity to expand my knowledge and acquired excellent training from leading laboratories in the world.

I would also like to sincerely thank Professor Deepak Srivastava and his groups for being a great host institution during my visit in Gladstone Institute of Cardiovascular Disease in UCSF who have significantly contributed to my progress in both personal and scientific levels.

Last but not least I would like to thank and express my gratefulness to the CEM in QUB and Professor Alan Stitt, the director of our Centre for all their support to acquire the best training options for me to develop my career.

Sincerely Yours,

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