2020 Award Winner Spotlight Series: Part I

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ISEH Headquarters July 9, 2020

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Deconstructing Blood Cell Research
Building the Hematology Community

This week on *Simply Blood* we are beginning our 2020 Award Winner Spotlight Series. In Part I we are featuring the ISEH 2020 McCulloch & Till Award Winner: **Mark Dawson, MBBS; BMedSci; FRACP; FRCPA; PhD**. Dr. Dawson answers questions about his work, trends in hematology, mentorship, and more. Have additional questions for Dr. Dawson? Don't miss his session at this year's Virtual Scientific Meeting.

1. What key question would you like to answer with your science?

My research has primarily focused on understanding the role of chromatin / epigenetic regulators in the initiation & maintenance of cancers (especially haematological malignancies). We have also been particularly interested in understanding how epigenetic regulators may facilitate acquired resistance to cancer therapies.

Our interest in this area has been shared by many labs across the work and over the last 10-years work from a number of labs, including mine, have contributed substantial insights into all these fundamental processes. In brief, it is now clear that epigenetic regulators, which are collectively the most common mutational targets in cancer, play an integral role in the initiation and maintenance of the malignant process in both solid and haematological cancers. It also becoming increasingly clear that resistance to conventional and targeted therapies are frequently driven by non-genetic processes including transcriptional and phenotypic plasticity which is underpinned by epigenetic regulators. These insights have driven the development of a wide range of epigenetic therapies - many of which have already been tested in clinical

trials. What we have learnt is that whilst these therapies are largely well tolerated, they are not very efficacious, at least as mono-therapies. Ultimately, I would like the science that my lab does to help understand how best to target epigenetic regulators to improve the outcome for patients with cancer. This is an extremely difficult task as epigenetic regulators are ubiquitously expressed and have cell context dependent functions. Therefore, a systemic therapy can have both beneficial and deleterious effects in different cells within the same patient - ultimately manifesting as no overall benefit to the clinical outcome. We believe that by understanding tumour heterogeneity at single cell resolution, studying the influence of the (tumour) microenvironment, leveraging the host capacity of anti-tumour immune surveillance and coupling these efforts to innovations in chemical biology we will continue to contribute to finding a solution to combat cancer.

2. What do you think will be the next big trend in experimental hematology in the next ten years?

It is clear that we have grossly under-appreciated the cellular heterogeneity that underpins normal development and cancer. As we develop more sensitive methods to assess normal and malignant haematopoiesis the challenge ahead lies in being able to develop strategies to reproducibly influence this heterogeneity to drive a desired outcome.

This may take the form of influencing the balance of lymphoid or myeloid cell fate, response to localised or systemic infection. In cancer, it may involve methods to minimise plasticity and adaptive potential. These strategies need to extend beyond a simple compendium of single cell data sets involving genomics, transcriptomics and chromatin landscapes at a single snap-shot in time. We need to be able to follow these trajectories with accurate spatial and temporal dynamics and importantly intervene with reliable and reproducible strategies (chemical or genetic) to change the pre-determined outcome. This is certainly where I want my lab to head over the next decade.

3. What do you most value in a student or a member of your team?

The two traits I most appreciate in any scientist but particularly my students are (i) curiosity and (ii) fearlessness. In my opinion, nothing significant in science can ever be achieved without these two essential traits. Students have always been the mostly likely individuals to have these as they are are at the very start of their academic journey and are filled with possibilities. Importantly, they are also not limited by the trepidations that past experience(s) in science can bring in terms of what is technically possible or what is too difficult a question to answer.

When I was about to start my own lab, I had a memorable one-on-one mentoring meeting at the Wellcome Trust with Venki Ramakrishnan - I asked him what advice he would give me with regards to my students. What he said has always stuck with me. He said "give your

students the most challenging and interesting project as they are not encumbered by experience and will take it on with gusto - but always have a back up easier project in case your desired question really does turn out to be too difficult". He recounted that in all his years studying the structure and function of the ribosome this was the strategy that bore most fruit and he rarely had to rescue a student with a 'new' project. This really resonated with me as in part it reflected my own journey as a PhD student. Fingers crossed - but so far I have never had to rescue any of my students with a new 'easier' project.

4. What advice can you offer aspiring new scientists?

Science should never be a job, it is a privilege and a vocation - if you are looking for a well paid job with security - please do something else. Above all, I feel the most important thing I have learned to sustain me through the highs and lows of science has been how important it is to love what you do. When I was a child, I had to interview my grandfather for a school project and I asked him 'how would you describe your work?" - he said "my work is love made visible" - I remember being very confused by this answer but over the years the meaning of these words, derived from the poet Kahlil Gibran, have rung ever true.

5. What do you enjoy doing, apart from science?

My family are my greatest love and balance in life. I have an incredible wife, who is also a clinician-scientist and who I have shared virtually every step of the academic journey since medical school. Although we run separate labs we work very closely together - so work could have become all encompassing if it were not for our amazing 2 sons. They rightfully consume all of our time outside work and thank god for that as it brings perspective and balance to the highs and lows of work. Getting the same greeting and joy from the kids on a day you have a grant rejected or a big paper accepted provides incredible grounding and makes the journey so much more tolerable.

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