

## Prof. Simon C. Robson: “Science curiosity” is the most important element in research, as this thirst for knowledge results in new discoveries, ultimately translating to practice of clinical medicine and serving to help people

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Prof. Simon C. Robson (*Figure 1*) has taught, conducted research and practiced in Hepatology and Transplantation in three countries over three continents for more than three decades. He has served as the Division Chief of Gastroenterology and Hepatology as well as a founding member of the Transplant Institute at the Beth Israel Deaconess Medical Center. He is currently the Charlotte F. & Irving W. Rabb Professor of Medicine at Harvard University. He has a Ph.D. in Immunology, Fellowships of the Royal College of Physicians of London (by examination) and Ireland (honorary) and was recently elected as a Fellow of the American Association for the Study of Liver Diseases. He is recognized internationally as a physician-scientist and clinician. He is also a well-regarded educator and has received several awards for his excellence in research, teaching and clinical practice.

Prof. Robson is a long-standing member of the American Association for the Study of Liver Diseases, Transplantation Society and recently of American Gastroenterological Association. He was Secretary-Treasurer of the South African Immunology Society and the African Association for the Study of Liver Disease where he helped develop hepatitis B mass infant immunization programs in South Africa. He has also served on the AASLD Basic Research Committee and organized Liver Fibrosis Special Interest Group (SIG) programs, amongst others. He has been Chairman of Scientific Committees and organized International Workshops on Purinergic Signaling, including a recent Keystone Symposium in Molecular and Cellular Biology in Vancouver in 2016. His diverse life experiences, global perspective, organizational skills and multiple academic contacts have facilitated access to international thought leaders in many areas.

We met Prof. Robson during the Liver, Microbiome and Academic Skills Workshop held from September 8–9,



**Figure 1** Prof. Simon C. Robson and Isabella.

2017 in Beijing and were honored to have conducted an interview with him about his decisions on becoming a physician, passion in research, and his advice to budding doctors. We greatly appreciate that he found time to share his experiences and perspectives with us.

**HBSN:** *You’ve been a doctor for many years. Why did you initially choose medicine as your profession?*

**Prof. Robson:** My first love really was the sea, as I grew up in the port town of Hartlepool—until my family emigrated to South Africa. So, I first wished to become a marine biologist and to study oceanography, but my father who had worked in the British Merchant Navy had other thoughts. He asked, “*If you are interested in science, and are so fascinated by the recent heart transplants done in Cape Town by Christiaan Barnard, why don’t you look into the practice medicine?*” So, I agreed to start my first year of medical school in Cape Town and took in some extra courses in science and mathematics because I was really interested in the underpinning scientific discoveries of medicine as well as biology.

There, I found I really liked to talk to people and help

patients to heal, as well. So, I ended up training in medicine in South Africa and later in the UK. In the English system, as also applied there in South Africa, you can go straight from high school to medical school – there is no undergraduate program before Medical School. While at the University of Cape Town, I could make the decision to study first Basic Science and then went on to do Medicine.

**HBSN: Why did you choose to become a physician instead of a surgeon?**

**Prof. Robson:** I was always going to be a physician-scientist, as I was always interested in common aspects of blood coagulation and immunity, as well as liver biology and transplantation. I really think (and hope) my life has followed many aspects of the great philosophical traditions of Chinese origin, which emphasize living in harmony with the "Tao". One's choices appear sometimes to be dictated by the conditions of our lives as well as our own talents. There must be importance attached to what is called "wu wei" (effortless action), "naturalness", simplicity, spontaneity, and what I read make up the three treasures: "compassion", "frugality", and "humility". I think many qualities of the physician scientist or the academic surgeon meet these ethical requirements.

Sometimes you have made decision to do one thing and yet you look back a few years later and see you've taken a modified or different path because of better opportunities and altered circumstances. Despite these caveats, focus is important and one must have a passion to do what you chose to do. Life is too short and transient to work at something which you don't enjoy doing. Originally, I was looking to do transplantation work and to that end I trained as a physician and still see patients with liver transplants. Transplant biology is where a lot of my research has been directed. So, it seems that my interests and career have largely coincided and developed together, which is a happy circumstance.

**HBSN: Can you tell us about your latest research? Have there been any breakthroughs?**

**Prof. Robson:** Yes, there is now major interest in the area of purinergic signaling, specifically in cancer. The major metabolite on which all life depends is ATP, which serves as the energy currency of normal and malignant cells. This biochemical factor and other nucleotides can be released at high levels from immune or malignant cells, particularly in

the latter case in the setting of damage from radiotherapy or chemotherapy. Extracellular ATP provokes inflammation by "purinergic signals" and plays a significant role in promoting anti-tumor responses. My colleagues and I have shown that tumors subvert immunity by being proficient at converting ATP into the product adenosine. This is done through the expression of an ectonucleotidases on cancer cells, and the associated regulatory immune cells and the vasculature. This derivative adenosine interferes markedly with immune responses to the cancer by serving as a "checkpoint inhibitor" and also promotes the blood supply by "angiogenesis".

Colleagues and we have been working in the characterization of these innovative molecular pathways, over the past 10 or 20 years. I have had inputs in basic research of a novel immune cell signaling network, which involves the conversion of these extracellular nucleotides. We have studied how CD39, regulates how cells respond to extracellular ATP, and the derivative nucleosides such as adenosine. We discovered this role of CD39, the prototype of a family of ecto-enzymes that regulate these pathways: in both T regulatory cells as well as on the vasculature. This approach is to basically target "checkpoint inhibitors" such as CD39. So if you wish to harness inflammation to reject cancers, where there is too much CD39 activity on lymphocytes or tumor vasculature, you inhibit the ectonucleotidases. Hence, we are looking at ways of blocking CD39 by antibodies and hence boosting purine-mediated inflammation in cancer of liver, pancreas and colon, as well as melanoma.

Our research has another main track, which is to control immune responses in conditions and diseases where there is a lot of inflammation from a deficiency or relative lack of CD39 bioactivity, for example, as in transplant rejection and also in IBD e.g., Crohn's Disease.

In short, we can manipulate the same signaling pathways centered on CD39. This can be to suppress inflammation as in a transplanted organ by boosting CD39 activity versus our newly developed abilities to boost immune responses by blocking CD39 activity, to enhance inflammation within cancer, and ultimately reject these tumors.

**HBSN: In your opinion, what is the most important quality one should have when researching and studying medicine?**

**Prof. Robson:** I think it would be "scientific curiosity"—

wanting to discover something that nobody else knows about, and to do something entirely new that may have a major impact, not only in science, but also in clinical medicine. And I think if you discover and work on such fundamental pathways, you'll be able to work continuously in the field with great focus and passion.

With respect to the ectonucleotidases and purinergic pathways we've discovered, others and we have found that they are not just operational in humans, but across the whole animal kingdom, and sometimes even in plants and bacteria. That's really curious that we have this very conserved pathway, which targets the fundamental biochemical factor of life, ATP. CD39 seems to be very important in human disease, in immune responses, and is probably also very important in evolution. You can propose roles of these ecto-enzymes in adjusting how the host organisms interact with the microbiome, bacteria, and parasites.

**HBSN: Do you ever get tired of doing research?**

**Prof. Robson:** No, I'm never tired of research and discovery. I also love to work with the most wonderful colleagues, I have, including the very wonderful people back in Boston (viz. Yan Wu who is here with me on this trip) and here in Beijing including Dr. Haitao Zhao and Dr. Yilei Mao. However, I have to admit for full disclosure that I occasionally become a little tired of all the linked bureaucratic administration. Over the last ten years, federal funding in the United States has been quite significantly limited. So one can write a wonderfully interesting grant proposal, which most likely would have been funded a decade ago, and now is sent back.

Still, there are a lot of other avenues to get the research funding done, not just from the Federal government in USA, but also from philanthropists, pharmacological and biotech companies. I mean, if you're doing something, it has to be useful clinically, and that's another way of getting the funding done.

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**HBSN: Could you please give us some words of encouragement to young medical students?**

**Prof. Robson:** I think if you work hard, are ethical and organized and exclude all ambiguity in your future directions, you are going to be very successful. You have to trust in yourself, have confidence in yourself and your chosen focus, and then you can look back on what has transpired. As I said above, you flow along the river of your life, and can only see where it takes you in retrospect. What is around the next river bend is mostly unknown—but one should be alert for water falls or white-water rapids!

Often you have an idea that there will be a future for you in a certain field and sometimes your discoveries and the currents of science will lead you in a different direction. For me, when I went from South Africa to the USA, I wanted to study thrombosis in transplanted organs, and because platelets are controlled by these purines/ADP, that's how I went into this area of inflammation. That is how we discovered all of these pathways. I think curiosity, confidence, diligence, patience and just doggedness in moving forward will help. If one is fortunate, one will end up with these really great discoveries and making a major impact. One has to be confident, passionate and seize every opportunity to make an impact.

Good luck, the next decades promise to be the most interesting time in medicine and science in all of history!

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None.

**Footnote**

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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