ISCT TALKING WITH GIANTS

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International Society ISCT Cell & Gene Therapy®

5 Questions with Dr. Malcolm Brenner

As one of cell and gene therapy's premier clinical scientists, Dr. Malcolm Brenner's renowned work and passion has taken him from the collegiate grounds of Cambridge, England to the humid bayous of Houston, Texas. Born and raised in London, Dr. Brenner received both his medical degree and his PhD at the distinguished University of Cambridge. In 1990 he crossed the Atlantic to work at St. Jude Children's Research Hospital in Memphis, Tennessee as the director of the Cell and Gene Therapy Program where he conducted the first human gene therapy studies on bone marrow stem cells – a truly pioneering achievement. Since that time, Dr. Brenner has held a number of positions including President of ISCT from 1999 to 2000 and President of the American Society of Gene Therapy from 2002 to 2003. From Memphis, Dr. Brenner moved 600 miles south west, finding his current home as a full-time faculty member at the Center for Cell and Gene Therapy at Baylor College of Medicine, Texas Children's Hospital and Houston Methodist Hospital. Over the years, Dr. Brenner has been recognized as a pioneer in cell and gene therapy with a number of accolades that include the American Society for Gene and Cell Therapy Outstanding Achievement Award, Human Gene Therapy's Pioneer Award, the American Society of Hematology Mentor Award, the European Society of Gene and Cell Therapy Outstanding Achievement Award, and most notably being elected as a member of the American Association of Physicians and of the National Academy of Medicine.

Dr. Brenner sat down with ISCT to talk about what cell and gene therapy was like in the 70s, where the field will be in five years and why mentorship is so important to up-and-coming professionals in the cell and gene therapy field.

1 How is the cell and gene therapy field different now compared to when you started? How has it evolved?

I started a long time ago, in the 70s, which was really the beginning of cell therapies. In the 70s, bone marrow transplantation came along and it was realized that this procedure could actually cure people who had otherwise untreatable diseases. It was during this time that people began to understand how bone marrow transplant really cured people which was mainly due to the immune effects of the transplant rather than the high-dose chemotherapy and rescue effect as originally postulated. Then, a little bit later, people started showing how lymphocytes surrounding tumor cells could be extracted and would have anti-tumor activity. So it was a period when we finally got to grips with what cellular components could do for cancer. But most importantly, people started to wonder about what else cells could do for regenerative medicine and that vision has brought us to where we are today.

Now, we're going through a period where we're making use of defined cellular components for the patient, a much more complex process.

2 Where do you see the cell and gene therapy field in 5 years? Where do you see it headed?

At the moment, most of the focus clinically is on cell therapy for cancer treatment – I think that is going to be very important. But I think these therapies are going to spread beyond cancer. For example, the information we have learned about manipulating immunity for the treatment of cancer will become very important for autoimmunity and inflammatory disorders which cause a huge number of common, currently incurable, diseases.

3 Why are you so passionate about working in the cell and gene therapy field?

I was always interested in using the immune system as a way of targeting and curing diseases. Other treatments have been developed to improve symptoms and to ameliorate rather than cure and are not very specific. I always thought that cell therapy really was about targeting and curing diseases not just treating the symptoms – that's really important. What attracted me to cell therapy and gene therapy was that it was possible for someone who is both a physician and a scientist to be able to help with both the research and clinical sides of the equation. In cell and gene therapy, you can improve the treatment of the patient whose disease you are researching.

4 What are the biggest challenges facing the development of new cell and gene therapies? Reimbursement challenges? Regulatory challenges?

I would probably say it's cost and complexity. The costs of developing these therapies are going to remain very high, unless we change the business model. They are also very complex to manufacture at scale. They're not small molecules...they're not even proteins. You can't readily say that one cell preparation is going to be identical in function to another cell preparation, even if you made them in the exact same way for the same purpose.

The other challenge that you alluded to is regulatory. If we want to continue to make progress with these complex therapeutics, we're going to have to constantly modify them and improve them. If we have to go back to the beginning pilot phase of clinical development every time we make an improvement to an established cell therapy, that's really going to destroy innovation.

5 For young people just starting out in this field now, what would be the one piece of advice you would give them based on your wealth of experience?

I have been recognized in the past for mentoring young professionals in the field – and I was very happy about that. When I trained in the UK, we didn't really have a concept of what mentorship was. In retrospect, I experienced both good and bad mentorship. (Laughs) There's no question that if you want to succeed now – with all of the scientific, financial and regulatory challenges – you need to have good mentorship or else it's going to be very difficult. So, the one piece of advice I would give is to choose your mentors carefully and wisely – and make sure you have more than one of them. Mentors are there to not just show you how to do things, but also the importance of perseverance and human decency in this field.