

## Introduction for N. A. Mitchison

J. Klein<sup>1</sup>

Ladies and Gentlemen,

When I started in immunology, Professor Mitchison was already a legend. Not because he was that much older than I, but because he had made important discoveries early in his scientific career and because even at that time, more than 25 years ago, there were many interesting stories circulating about him. I shall skip the stories and concentrate on Professor Mitchison's scientific contributions.

When you are asked to introduce a famous person and you have to ask yourself what he has actually done, sometimes you may have difficult a time answering this question. Not so when you are asked to introduce Av Mitchison! If anything, you find you have just the opposite problem of choosing a few representative contributions from amongst the many he has made. I have chosen four, which I would now like to mention.

The first contribution he made in 1954, while working solo (at that time you could still work alone and publish papers without 15 other people coauthoring them). He asked a simple question: What is responsible for the rejection of a transplanted tumor? And to answer it he did a simple experiment. He took lymphocytes and serum separately from a mouse that had just rejected a tumor graft, and transferred each into another mouse, which he then

grafted with the same tumor. He observed that the mouse that received the cells rejected the tumor, whereas the mouse that received the serum did not. He concluded that tissue grafts are rejected by lymphocytes and not by antibodies, and this conclusion you now find in every immunology textbook, not as an isolated fact, but as a discovery that brought about the era of cellular immunology.

The second discovery I would like to mention you might not even have heard of. It, too, was made in 1954, and it, too, was very simple. Av noticed that when you want to induce an immune response against bacteria, you have to put the bacteria on a cell. As far as I know this was the first experimental demonstration of the requirement for antigen presentation by cells, and it marked the beginning of a path that led – by way of Lawrence and Kindred to Zinkernagel and Doherty – to the discovery of Mhc restriction. Again, it was not an isolated fact that Av discovered, but the beginning of an era.

The third discovery was made by Av, I believe, in 1964. It was the finding that if you injected small amounts of bovine serum albumin into mice and you did it often over a long time, the mice, instead of being immunized, built up a tolerance to this antigen. This experiment represented the discovery of low-zone tolerance, another milestone in cellular immunology.

Finally, the fourth discovery has to do with haptens and carriers. As you know, haptens are small molecules, and when you place them on the large carrier molecules you can make antibodies against them.

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What Av did was to immunize one set of mice with a hapten and another set with a carrier, and then mix lymphocytes from the two sets of animals and inoculate immunized recipients with the mixture. He observed that these recipients then produced hapten-specific antibodies as if they were immunized by the hapten-carrier complex itself. This finding showed that there were two kinds of cells, one recognizing the hapten and the other the carrier. From here it was only a small step to the discovery of T and B lymphocytes and of T-B collaboration.

I have selected these four examples because each of them marks the beginning of something momentous; each opens a new pathway in immunology. These were not discoveries that were in the air – that anybody could have made but which Av made because he was quicker or luckier. They were unexpected, highly original discoveries that inspired a whole generation of immunologists. They did not follow the beaten track; they opened up new tracks.

However, making original discoveries is not the only way in which Av has made his presence felt in immunology. The other way is through his intellectual influence on

his fellow immunologists. This effect is difficult to express in any objective terms and for this reason I can only tell you how Av has influenced me.

I rarely, if ever, read any of the many proceedings of meetings that are published, simply because I do not find them inspiring. I do, however, make one exception – I read the contributions by Av Mitchison. I read these because I know that they are not mere conglomerations of data either already published or in print in one immunology journal or another. I know that they will contain an intelligent assessment of the topic they deal with, and that they will make me think about it in a different way from the way I might have thought earlier.

Also, when I discuss ideas with people and they tell me “I think you are wrong,” without being able to tell me why, I do not lose much sleep over it. However, if Av tells me “I think you are wrong,” I get nervous. I know of no better compliment I can pay to a person’s intellect.

And with these words, ladies and gentlemen, I present to you one of the most original and most inspiring of contemporary immunologists, Professor Avrion Mitchison.