

Changing signals:

exploring repair mechanisms for
brain inflammation

Pietro Ghezzi inaugural lecture

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Cytokines are proteins that signal the presence of infection to the various cells of the immune system. It was first biochemistry, then genetic engineering, applied to immunology that led to the discovery of these signals. More research into these molecules led to the unexpected finding that many cytokines can be harmful, and responsible for several inflammatory diseases.

Understanding the cytokine network has become more and more complex, by the discovery of new cytokines and further knowledge of the new activities of known cytokines. At the same time, some cytokines and their inhibitors have become approved drugs. It is now clear that these mechanisms and signals are not only important in infection and immunity, but also play a role in the response to injury and promote repair.

Professor Ghezzi will give an overview of the discovery of these signals, how they regulate each other and how can switch from defending from infections to causing diseases or inducing repair. In particular, the talk will focus on how the discovery of the protective and repairing abilities of some cytokines is leading to therapeutic strategies targeting brain inflammation, an avenue to the cure of diseases such as stroke and multiple sclerosis.

About Pietro Ghezzi

Professor Ghezzi is the R.M. Phillips Chair in Experimental Medicine. He has a PhD in Pharmacology obtained at the Mario Negri Institute in Milan, Italy where he worked since 1980 and where, from 1991, he has been the head of the Neuroimmunology laboratory. He has worked several times in the 80s and 90s in the laboratory of Charles Dinarello at the New England Medical Center in Boston and from 1998 to 2000 has been Research Associate in the laboratory of Len Herzenberg at the Department of Genetics of Stanford University.

Questions and answers

What inspired you to work in biomedical research?

Almost by chance, when I was a student I met a friend who worked at the Mario Negri Institute in Milan, a private no-profit research institute independent from universities and industry. As soon as I started working in the lab I realized that I was made for that work.

And how did you end up studying inflammatory mediators?

Well, I was working on liver drug metabolism. At that time it was found that infection and inflammation affect drug metabolism and I decided to investigate how the immune system can act on the liver. By chance, this happened at the same time when the first immune mediators, that we call cytokines, were being discovered. Although I was working on a niche topic (an effect on the liver) this put me in touch with the top scientists in the field.

But, why neuroinflammation?

Also by chance, I started collaborating with people in the Institute who were studying neurotransmitters and were fascinated by the idea that the brain could be modulated by the immune system. To them, I was the 'local world expert' in the field of immunity and inflammation! Then I developed an independent interest in neuroinflammation.

What are the research lines you plan to set up at BSMS?

Well, one is the one we mentioned above. That is, to study the effect of cytokines in brain diseases like stroke. In the 1980s, when I started working in the field, the focus was in the role of inflammatory cytokines in aggravating diseases. Now I, like most scientists in the field, am more interested in the cytokines that intervene in this network to stop inflammation and promote repair.

I also continue working on oxidative stress. However, this field has evolved a lot. In the past we were very naive and thought that free radicals would contribute to a long list of diseases and that antioxidant would cure many, if not all, of these diseases. Although, unfortunately, this picture is still administered to a gullible public by advertising and popular magazines. We now know the biology is more complicated than that. Our research suggests that these kinds of oxidation reaction are not always toxic, but have regulatory roles. This work is, I must say, more set within basic biochemistry than the work on neuroinflammation.

What impact do you think your research will have in curing or relieving diseases?

Well, the diseases I am focusing on are stroke and multiple sclerosis. One molecule we are studying may be a promising therapy for these diseases, but we will have to find ways to prevent its undesired effects and have the molecule act only in the desired direction.

Why did you choose this position at BSMS?

As I mentioned before, the institute I was working in Milan was not at the university. However, having worked in an academic environment before, in Boston and Stanford, I feel that academia is much more stimulating. I wanted a career in an academic setting and there were basically no opportunities like this in Italy, for an outsider like me coming from a non-academic institution. Here is more like the US; universities are incredibly flexible.

What does BSMS offer to researchers like you?

As a new medical school, it is still growing in a time when many places I know are shrinking. Having to set up things may be viewed as a negative point, but I find it rewarding; it makes me feel useful. Plus, BSMS is not only BSMS, and working here I can interact with scientists in the campuses of University of Sussex and of Brighton.