Book review

Microbial Subversion of Immunity: Current Topics

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Anti-immunomodulators – a new approach to the rational design of antiviral agents.

Chapter 4 – Viral Immune Evasion: An Overview by Antonio Alcami

Most current screens for antiviral activity depend on the inhibition of virus coded functions that are essential for virus replication in cell culture. Indeed, the majority of efficacious compounds in clinical use, to date, interact with virus enzymes or virion structural proteins. An alternative approach has been to target cellular functions that are required for efficient virus replication. However, it is becoming increasingly obvious that many virus coded functions are not simply required for efficient virus replication, but are instead concerned with enabling the virus to subvert the innate and/or adaptive immune responses allowing the virus to survive in the host. These functions may not be essential for virus replication in cell culture.

It is obviously much more difficult to design appropriate screens for potential inhibitors of ‘inessential’ proteins. However, interference with such functions can have marked effects on the pathogenesis of infection and can be an effective approach to reduce or prevent clinical signs of disease. Without detailed knowledge of the particular virus proteins involved in these processes and their interaction with the tissues of the host this goal is, however, going to be very difficult to achieve. Notwithstanding, these proteins may provide alternative targets for the development of drugs for use alone or together with conventional antiviral agents. One approach to antiviral chemotherapy has involved compounds that modulate the immune response of the host’s immunomodulating agents. However, an alternative approach is to seek agents that may counter the immunomodulation brought about by viruses themselves – these might be termed ‘anti-immunomodulators’!

A few years ago it was realized that viruses of vertebrates have evolved highly specific mechanisms for evading the immune and inflammatory responses of their vertebrate hosts. At first only one or two particular mechanisms were recognized in respect of a couple of virus families. It has become increasingly obvious that all viruses have evolved not one but numerous mechanisms to enable their survival. Thus, large DNA viruses such as members of the *Herpesviridae* or *Poxviridae* are thought to have more than 100 genes coding for proteins in this category. However, all the viruses that establish infection in the vertebrate host are able to do so only because they have evolved a complex array of strategies to evade the defence mechanisms of the host’s both innate and adaptive immune mechanisms. In order to prevent destruction by viruses, multicellular hosts have evolved a barrage of defence mechanisms. The interplay of these measures and countermeasures give rise to the complex patterns of pathogenesis that characterizes many virus infections. Very often pathology observed in viral infections is not caused directly by viral replication but is a consequence of the immune and inflammatory responses to viral infection that may damage the host. Topical examples being the respiratory pathology produced by SARS and influenza viruses.

Those interested in developing new approaches to antiviral chemotherapy and want a comprehensive introduction to the subject of microbial subversion of the immune response should refer to the chapter by Dr Antonio Alcami: Viral Immune Evasion. This is one of nine comprehensive reviews gathered together in the volume: Microbial Subversion of Immunity edited by Peter Lachmann and Michael Oldstone in the Current Topics series. In particular, Dr Alcami provides the reader with a comprehensive bibliography providing further reading for those who wish to pursue this line of thinking. Hopefully, reading this remarkably lucid chapter will provide inspiration to those seeking a new approach to antiviral chemotherapy from among the many specific examples that Dr Alcami draws attention to in his chapter.

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