Microglial cells in CNS immune reactions and their response to anti-inflammatory agents

William F. HICKEY and David J. GRABER

Department of Pathology and Department of Pharmacology & Toxicology, Geisel School of Medicine at Dartmouth, USA

Many neurological diseases develop by unknown mechanisms. A common feature in many of these is the appearance of so-called “neuroinflammatory changes”. This refers to the widespread activation of microglial cells in the areas where the nervous system is being damaged. It is unclear whether such changes are part of the pathogenesis, or merely a reaction to damage that has occurred. Animal models of such diseases provide evidence that microglial activation may be a key step in the disorder’s development. If this is true, then it might be possible to delay or halt the disease with therapeutic agents specifically targeting the microglial cells. A major impediment in this quest is identifying compounds effectively targeting microglia in CNS tissue. Whole animal testing of each compound would be impossibly expensive and time consuming. In view of this our lab has developed a strategy that can select promising compounds by testing for cellular effects in vitro, then applying a sensitive CNS tissue slice method to detect agents that have anti-inflammatory effects at the tissue level. By using RT-PCR to select agents that inhibit the production of inflammatory mediators such as TNF and IL-1, we can demonstrate the effects of known anti-inflammatory agents and also detect novel compounds with similar effects. The presentation will discuss the method and show how it can be used to test agents for their ability to inhibit neuroinflammatory changes.