# Hope and hype

**INTERFERON: The Science and Selling of a Miracle Drug**

**By Toine Pieters**

Routledge, Taylor & Francis Group, 2005
264 pp., hardcover
ISBN 0415342465

**Reviewed by Erik De Clercq**

When interferon was first discovered, it was initially hailed as the new penicillin, and was expected by many, including my tutor, Pieter De Somer, who pioneered the mass production of penicillin to save the lives of millions of people with viral infections. But the interferon story did not pan out this way. Expectations that the new drug would be the panacea for all kinds of viral infections and cancer have not been fulfilled.

*Interferon: The Science and Selling Of a Miracle Drug* by Toine Pieters takes us on a journey through the early history of interferon research and development. It covers the period from 1957 to 1982, from its discovery to the media-fueled hype and expectation of its success in the 1970s and 1980s. It would be a magic bullet to cure all viral infections and cancer. The book is flavored with many interesting and illuminating anecdotes reflecting milestones along the interferon saga.

In the early days of interferon research, it was perceived as troublesome and high risk—its potency and identity could only be determined by cumbersome and inaccurate bioassays—and companies were reluctant to throw themselves into the interferon morass. Pieters meticulously describes how around 1960 the interest of three British companies was spurred by the postwar penicillin-cephalosporin experience and the perception that interferon, like penicillin for bacterial infections, could be the panoply for the treatment of viral infections.

The purification of chick embryo interferon by Maurice Hilleman's group at Merck in 1963 was a landmark in the interferon saga, as it shifted the emphasis on interferon research from Britain to the US. In Hilleman, interferon had found a champion. In 1963, the drug was regarded as a chemically undefined biological substance that was part of a poorly understood natural mechanism of resistance to viral infections. Skepticism was highlighted with the statement in a 1964 article in the *British Medical Journal* that the use of interferon for controlling viral infections in humans and other animals was likely to be limited. And by the end of 1964, it was not at all clear that interferon really existed. Hilleman made a quantum leap by showing that interferon could be induced in large amounts by double-stranded RNA. Unfortunately, Alick Isaacs, the original discoverer of interferon, was not able to witness this breakthrough. He died on 26 January 1967 in London at the age of 45.

From the late 1960s, experiments carried out in Ion Gresser's lab started to invoke the possibility that mouse interferon, induced by Friend leukemia virus and Rauscher leukemia virus, might inhibit mouse leukemia: this was years before the first demonstration of the causal link between human adult T-cell leukemia (ATL) and a human T-cell leukemia virus (HTLV) by Robert Gallo and his colleagues. For interferon to become an antitumor drug for humans, ATL should have become the first test case. I am still wondering why it did not. Attempts with human leukocyte interferon to demonstrate an antitumor activity against some of the most recalcitrant tumors such as osteosarcoma, as carried out by Hans Strander in collaboration with Kari Cantell were brave, but the outcome was not convincing. The question of impurities as the cause of the effects seen, whether antitumor or toxic side effects, kept fueling skepticism.

The greatest breakthrough in interferon research came in 1979 with the cloning and expression of leukocyte interferon (α-interferon), soon thereafter followed by the cloning and expression of fibroblast interferon (β-interferon) in 1980. The cloning of interferon was for the nonbelievers the final and convincing proof that interferon really existed.

But by this time, the media-generated expectations for interferon were vastly overblown. If not active against one particular disease, another would be found sensitive; if not ATL, it would be hairy cell leukemia. That interferon is a 'molecule for all seasons' has been continuously demonstrated. If a new disease arises, especially viral, interferon is called upon to help, as most recently shown for SARS, for which α-interferon may be considered the drug of choice should it re-emerge. But although success has not translated to humans as universally as once hoped, interferon has found some use in the clinic. For hepatitis C it is now an established treatment, although we are waiting for more effective, less toxic and cheaper compounds. Interferon is thus likely to remain a medical commodity, active as an immunomodulator against hepatitis B virus and as an antiviral against hepatitis C virus.

Overall, *Interferon: The Science and Selling Of a Miracle Drug* is pleasant reading, but in places somewhat redundant. The title is also rather misleading. The author has avoided truly scientific discussions, such as the mechanism of interferon action and induction, and the mechanisms underlying its antiviral, antitumor and immunomodulatory action. Important scientific issues such as the significance of interferon inducers (for example, poly(I).poly(C)), and the cloning of α-, β- and γ-interferon have been addressed cursorily at best. Nor does Pieters tackle one of the major questions in interferon research—why α-interferon is used in hepatitis C and β-interferon in multiple sclerosis, and not the other way around. Perhaps, however, the author is planning a second book, telling the story of interferon for the second 25 years, beyond 1982. If so, we would want to hear more about how interferon became implemented for the treatment of hepatitis C, multiple sclerosis and other diseases, and how it further evolved as an anticancer drug. The book also stops before any 'selling' of the drug, and, from all the information presented interferon did not turn out to be a 'miracle.' The miracle was that interferon was proven to exist, and for those who witnessed the first 25 years of its existence, this could indeed be considered a miracle.

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