Science Progress (2010), 93(4), 393–402
doi: 10.3184/003685010X12871628232041

The overlooked link between non-virus microbes and cancer

MILTON WAINWRIGHT

ABSTRACT

For more than a hundred years every generation of microbiologists has isolated so called "cancer germs" from animal and human tumours and some cancer researchers have claimed that these organisms cause cancer and also that in some cases, vaccines could be developed from them to treat this dreaded disease. Despite this longstanding evidence linking microbes and cancer, today's cancer experts believe that, except in the case of a limited number of virus-cancers, microbes do not play an important causative role in cancer. Here, the evidence linking non-virus microorganisms with cancer is discussed and a plea is made that more research interest and funding be directed towards the cancer germ hypothesis.

Keywords: *non-virus microbes, cancer, causes of cancer*

Milton Wainwright is a lecturer and researcher in the Department of Molecular Biology and Biotechnology, University of Sheffield. He is Honorary Professor at the University of Cardiff, where he is also Honorary Fellow of the Centre for Astrobiology. He has wide interests in microbiology including recent ongoing research on the isolation of bacteria and fungi from the stratosphere, work which relates to his interest in panspermia, *i.e.* the theory that life on Earth originally came from space and continues to do so. He also actively researches the history of the germ theory and the development of antibiotics, notably penicillin. He has written three books, *Miracle Cure the Story of Antibiotics*, *An Introduction to Fungal Biotechnology* and *An Introduction to Environmental Biotechnology*. He may be contacted at m.wainwright@sheffield.ac.uk

Introduction

What if the cause of cancer had been known and ignored for more than a century? What if all the suffering and deaths over this period resulting from the ''big C'' could have been prevented, or at least reduced by the acceptance of a simple theory? What if the medical research establishment and its funding agencies continue to ignore this theory and are content to pursue, at great effort and expense, incorrect or at best peripheral ideas about what causes cancer?

In this article, I wish to provide an polemic in favour of this theory, namely that non-virus microorganisms (NVM) are the principal, and largely overlooked, causes of cancer. I will begin my argument with a historical quote which remains highly relevant, even today:

> "*Still from recent researches on the origin and development of human parasites, it is by no means an impossible supposition, that cancer may be formed in the body, from germs or corpuscles of a very different form and appearance, originally existing externally, but undergoing transformation after being imbibed by the system*."

This quote by Dr Joseph Bell, a physician at Glasgow's Royal Infirmary, made in 1857, appears to be the first ever reference to the possibility that cancer can be caused by an external, infective agent. As we shall see, some 150 years later, evidence continues to be presented showing that microorganisms play a role in all types of human cancers; the so-called ''cancer-germ'' theory.

The view that bacteria, fungi and other NVM are involved in cancer has a long history[1] and lone scientists (including James Young in the 1920s, Figure 1) from every generation since the above quote was given, to the present day, have linked these common organisms with cancer, some even claiming that they developed vaccines which achieved cancer cures[2]. The simple fact that the cancer germ hypothesis is not widely held today and that its application has not resulted in the demise of cancer suggest that either the idea is a non-starter, or that cancer researchers continue to ignore the truth, namely that cancer in humans is largely a microbial disease. At first sight, the first viewpoint must be correct, but if this is the case why has the link persisted for more than a hundred years and why, even today, are research papers appearing which support a link between microorganisms and cancers? In my experience, few cancer experts know of this extensive research linking cancer and non-virus microorganisms, yet most are vocal when it comes to

Figure 1 *James Young, one of the many scientists who have isolated pleomorphic bacteria and linked them with cancer. Young worked on the "cancer germ" during the early 1920s.*

dismissing the possibility out of hand. This, of course, is a very worrying situation and those people, taxpayers and donors to cancer charities, in particular, who are directly, or indirectly, suffering from the scourge of cancer, must wonder why research monies are not being directed to work on the ''cancer germ hypothesis.''

What then is the current evidence suggesting a link between non-virus microbes and human cancers? A simple means of becoming introduced to the cancer-microbe link is to search Google for a specific cancer, say breast or colon cancer and then link this with words like bacteria, fungi, mycoplasma, *Staphylococcus*, and *Helicobacter*; such a search will reveal reference to high quality published research on the cancer-microbe link. A search involving the latter term is likely to be particularly fruitful since medical science has accepted that *Helicobacter* is linked with stomach cancer. One might have imagined that this link would have had cancer researchers *en masse* decamping to research on the possible link between cancer and other common bacteria, but this surprisingly has not yet happened. It is as if *Helicobacter* is regarded as some kind of unusual organism, whose ability to cause cancer is a

passing detail of little significance and that this bacterium is somehow divorced from the rest of the microbial world. Let us be clear about this, there is nothing particularly special about *H. pylori*, if this bacterium can induce cancer then so must most other common bacteria.

It could be argued that ignorance of the link between NVM and cancer is due to a lack of published research and reviews on the subject, but this is not the case[3–6]. My own experience of distributing my own reviews to some 50 cancer experts around the world, without eliciting any kind of response whatsoever, suggests that there is little interest in this hypothesis amongst cancer researchers. Perhaps, it could be argued, the link is ignored because no theoretical mechanisms have been suggested explaining how non–virus microbes might induce cancer, but this is certainly not the case[7].

Arguments against the cancer germ hypothesis

How then can the lack of interest amongst the cancer research and funding community in the cancer germ hypothesis be explained? Here are some of the arguments which are often made against the link between NVM and cancer:

(1) There is an overwhelming tendency for cancer experts to emphasise the role of genes in carcinogenesis, a response which may be largely cultural. The gene only theory of cancer is attractive because it involves the use of sophisticated technology whose application appears to offer the certainty of a means of eventually curing or preventing cancer; the direct role of genes in cancer is therefore over-emphasised and exaggerated by those scientists whose research funding and career advancement depend on the link. Of course, genes impact on all aspects of biology and it is certain that if microbes are involved in the aetiology of cancer there will be a genetic link, direct or otherwise.

(2) When the possibility that microbes might be involved in carcinogenesis is suggested, the knee jerk reaction of most scientists is to invoke a role for viruses and ignore bacteria, fungi and other microorganism. While there is no doubt that viruses can induce cancers, the evidence linking them to a causal role in the major human cancers (the exception being cervical cancer) is absent.

    Again this overemphasis on viruses and cancer appears to be culturally based. Cancer is seen as an insuperable problem of almost mythical dimension, therefore its cause must involve some

mysterious element, namely an extremely small unseen parasite, whose existence is outside our day-to-day awareness. What is forgotten is that bacteria can exist in very small forms which can become intracellular, or even intranuculear, and the fact that many can become pleomorphic (that is take on many shapes) shows that they are not morphologically simple organisms (*H. pylori* by the way is pleomorphic).

(3) Surely if microbes cause cancer, it is often argued, then cancer must be infectious and those who care for cancer patients are at risk of becoming infected with cancer. This viewpoint is based on a very simple view of infection and, of course, is not used to deny the possibility that viruses can cause in cancer. It is possible that the bacteria and other NVM which cause cancer persist for long periods in the body without inducing carcinogenesis (this explains why cancers are often associated with old age). These latent cancer-causing microbes then become activated by internal genetic factors and by external environmental ones like smoking. Put simply we all carry simple microbes which given the correct conditions induce the formation of cancer; in most people, however, these bacteria remain dormant.

(4) Where is **the** cancer germ?

Both proponents and critics of the cancer germ hypothesis have tended to suppose that there must be a single "cancer germ" which is responsible for causing cancer in humans. However, the literature shows that a wide variety of commonplace microorganisms, present for a period of time and subject to a variety of genetic and environmental conditions might be expected to induce cancer. Pleomorphism is a characteristic common to most of the bacteria that have been isolated from bacteria[8,9]; beyond this, however, there appears to be no genus or species which can be singled out as **the** cancer germ. Even common bacteria such as members of the genus *Staphylococcus* have been implicated as cancer-causing agents[8].

To most people, it would beggar belief that the cause of the long-standing scourge of cancer could be placed at the door of such a mundane germ; in taking this view we may, however, be condemning ourselves to missing the obvious[10].

(5) If bacteria cause cancer why did the incidence of the disease not decline with the introduction of antibacterial antibiotics, like penicillin? This criticism presupposes that antibiotics, like penicillin, (a) kill all bacteria or that, (b) susceptible bacteria cannot be in some way protected by their location from antibiotics, or (c) that the course prescribed kills all individual bacteria. It is

Figure 2 *A pleomorphic microbe isolated from a rat tumour by Wainwright and Al Talhi[9]. Although the isolate looks like a fungus, under the electron microscope it is clearly seen to be a bacterium (identified as* Bacillus licheniformis*) which was linked by the above authors to one of the historical "cancer germs".*

instructive to note that the incidence of stomach ulcers (and thereby stomach cancers) did not decrease with the introduction of antibiotics simply because a cocktail of antibiotics (plus bismuth) is generally needed to kill *H. pylori*. It will be intriguing to see if epidemiology shows that the cohort of patients who have received antibacterial treatment for ulcers show a reduction in the incidence of all types of cancer.

Anticancer agents often have antimicrobial effects

When Warren and Marshall discovered the link between *H. pylori* and stomach cancers they noted that bismuth and other antimicrobial agents had long been used to treat ulcers, although the link between antimicrobial activity and the bacterial cause of tumours was never recognised. In a similar way, the fact that a number of antimicrobial agents, including bismuth, mercury and lead (as well as antibiotics) have been found to have antitumor properties, might indicate a microbial involvement in cancer[4]. Hodgkin's disease, for example, can be regressed by long term treatment with the antibiotics, ciprofloxacin and clarithromycin. The obvious problem when discussing such correlations, are: do they result from the inhibition of cancer-associated microorganisms, or do they result from the diverse physiological action of such compounds? Evidence has also recently been presented to show that vitamin D is both

antimicrobial and anticancerous – it is directly antimicrobial, but also induces a variety of antimicrobial proteins, including human cathelicidin; it is noteworthy that the antimicrobial protein hCAP I 8ILL-37 is highly expressed in breast cancer. The antibacterial, tropical fruit mangosteen (*Garcinia mangostana*) has also been shown to be effective against breast cancer, *in vitro* and in animal models. Aspirin is similarly antibacterial and prevents the development of stomach cancers as can the consumption of fresh vegetables and red wine, both of which are rich in salicylic acid. The inference then is that since aspirin, an antibacterial agent prevents cancer, then bacteria may be the cause of cancer. Of course, aspirin may inhibit cancers by a mechanism totally divorced from any antibacterial effect. Doubtless however, the same argument was used in the past to discredit the link between the antibacterial and anti-ulcer properties of bismuth and the suggestion that bacteria cause stomach ulcers. While the link between cancer, aspirin and bacteria obviously does not prove that bacteria cause cancer, it should be suggestive enough for this association to be taken seriously.

Cancer clusters and infection

Considerable evidence is accumulating showing that cancers such as childhood leukaemia and brain tumours are associated with population mixing, as well as other indicators of microbial infection. Although current emphasis is directed towards the potential role of viruses in causing such cancers, the possibility that bacteria may play a role is increasingly being suggested[10]. Hopefully, the emphasis will not be exclusively placed on the potential role of viruses in such cancers. In fact, it may well be that epidemiological evidence will eventually force experts to consider the role of NVM as causal agents of cancer.

Conclusions

The possibility that bacteria and other non-virus microorganisms (NVM) can cause cancer has been suggested for more than a century; every generation of microbiologist has isolated so-called ‘‘cancer germs’’ and suggested that they play a direct role in the aetiology of cancer. The link between cancer and NVM continues to be demonstrated with the aid of modem research technologies, including molecular microbiology[5,7,10,11]. Despite this, the role of bacteria and fungi in cancer aetiology continues to be overlooked;

the obvious exception to this statement being the suggested role for *H. pylori* in gastric cancer. It could be argued that such neglect is due to the lack of convincing evidence which demonstrates such a link, or that, despite the available evidence, cultural factors work against the view that this link exists. One might have expected that the recognition that *Helicobacter* species play a role in carcinogenesis would have led to massive investment in the study of the role of other bacteria, and NVM in general, in cancer aetiology. Surprisingly, this has not yet happened and the fact that *Helicobacter* species can cause cancer has not led the cancer–research establishment to the view that other, and perhaps most, bacteria are potential cancer-causing agents. In reality, *H. pylori*, although it possesses a number of unique features relevant to its existence in the acidic environment of the stomach, is essentially an unremarkable species of bacteria and so, there is no reason why its ability to induce cancer should not be shared by other bacteria and NVM.

The following cancer germ hypothesis can be developed from the above literature:

(1) It seems that most microorganisms, including bacteria, fungi, protozoa and viruses can, under the appropriate circumstances, induce cancer. It appears however, unlikely that there is a single cancer germ, or single cancer-causing group, although some organisms are likely to be better adapted to the role of cancer-causing agents.
(2) It appears that some NVM can lie dormant for long periods within the cell or nucleus from where they induce oncogenesis; such an intracellular existence may be favoured by the ability of bacteria to exist as ultra-small, or cell-wall deficient forms.
(3) Non virus microorganisms appear to be able to promote carcinogenesis by a variety of mechanisms; the involvement of inflammation and toxins being the most frequently cited means by which such oncogenesis might be invoked.
(4) It has frequently been claimed that bacterial vaccines can be effective in curing cancer, or at least alleviating some of the symptoms in near terminal cancers. Such studies, of course must have been less than convincing otherwise such vaccines would be currently in use. Supporters of the cancer germ hypothesis have argued however, that since such vaccines were, almost invariably, used in the later stages of cancer, their true effectiveness in preventing the development of cancers has never been determined. It could of course be the case that that once oncogenesis has been

triggered by NVM, the process is not longer susceptible to vaccines prepared from the causal organism.

(5) The complexity of the interaction between cancer and NVM probably means that it will remain difficult to prove, beyond all doubt, that such organisms cause carcinogenesis. An example of such complex interactions is provided by the fact that *H. pylori*-induced inflammation in mice causes the migration of stem cells, originally present in the bone marrow, to the stomach, where they subsequently develop into gastric tumours. Similarly, the fact that a diverse range of common microorganisms are potentially involved in carcinogenesis will make it difficult to treat cancers by attacking a single organism or taxonomic group. It may however, be possible to inhibit some carcinogenic function that is common to most NVM, such as their ability to act as intracellular persitors, or produce cell wall or pleomorphic forms, toxins or inflammation-inducers. In short, it may prove more fruitful to attack specific cancer-inducing processes shared by many NVM than to try and eliminate individual, so-called, cancer germs.

There are signs that the potential role of NVM in cancer is being taken more seriously, a fact reflected in the recent appearance, of major reviews on the subject; and the consideration of novel approaches such as the possible role of nanobacteria in carcinogenesis. It remains probable however, that until a massive research effort is directed towards determining the role of non-virus microbes in carcinogenesis, we will face another hundred or so years when the solution to the enigma of cancer may be staring us in the face, only to remain overlooked.

References

1. Wainwright, M. (1998) When heresies collide-extreme bacterial pleomorphism and the cancer germ. *Microbiology, UK*, **144**, 595–596.
2. Wainwright, M. (1998) James Young and the cancer germ. *J. Med. Biogr.*, **6**, 203–205.
3. Kuper, H., Adami, H.O. and Trchopoulos, D. (2000) Infections as a major preventable cause of human cancer. *J. Intern. Med.*, **248**, 171–183.
4. Wainwright, M. (2006) The potential role of non-virus microorganisms in cancer. *Curr. Trends Microbiol.*, **2**, 47–59.
5. Vogelmann, R. and Amieva, M.R. (2007) The role of bacterial pathogens in cancer. *Curr. Opin. Microbiol.*, **10**, 76–81.
6. Wainwright, M. (2002) Do fungi play a role in the aetiology of cancer? *Rev. Med. Microbiol.*, **13**, 37–42.
7. Lax, A.J. (2002) How bacteria could cause cancer-one step at a time. *Trends Microbiol.*, **10**, 293–299.

8. Wainwright, M. (2000) Highly pleomorphic staphylococci as a cause of cancer. *Med. Hypotheses*, **54**, 91–94.
9. Wainwright, M. and Al Talhi, A. (2003). Is this the historical cancer germ? *Med. Hypotheses*, **60**, 290–292.
10. Stein, R.A. and Katz, D.E. (2010) Infections causing human cancer. *JAMA*, **299**, 87–838.
11. Hooper, S.J., Crean, S.J., Lewis, M.A.O., Spratt, W.G. and Wilson, M.J. (2006) Viable bacteria present within oral squamous cell carcinoma tissue. *J. Clin. Microbiol*., **44**, 1719–1725.