When heresies collide – extreme bacterial pleomorphism and the cancer germ

Cancer remains an enigma despite over 150 years of intense scientific research. While considerable research effort has been devoted to demonstrating that viruses cause cancer, the potential role of non-virus micro-organisms in cancer aetiology has largely been ignored. This was not always the case, however, since there is a considerable historical literature which suggests a direct link between cancer and non-virus micro-organisms, particularly bacteria, fungi and protozoa (12).

Scientific impasses, such as the cancer problem, are often solved only when a radically new approach is considered. Alternatively, new insights can be gained when previously dismissed evidence is reassessed in the light of modern research.

My intention here is to provide such an insight into the cancer problem by bringing together two heresies in microbiology that appear to offer such a radical new approach. Although based largely upon historical literature, this approach is reinforced by more recent studies.

The heresies in question maintain that even common bacteria routinely exhibit extreme pleomorphism and are the cause of cancer. Let us consider each of the heresies in turn and see what happens when they collide.

**Heresy number one – highly pleomorphic bacteria and the bacterial life cycle**

Nearly all modern bacteriologists are monomorphists. We believe that, with only a few exceptions, bacteria are simple organisms which undergo binary fission and exhibit little in the way of morphological variation. It may therefore come as a surprise to many microbiologists to learn that as late as the end of the 1930s a school of bacteriologists, the pleomorphists, believed that most bacteria show extreme variations in morphology and undergo complex life cycles. I have discussed this history of extreme bacterial pleomorphism elsewhere (13). Suffice to say here that common bacteria were said to undergo all manner of morphological changes, producing filamentous (fungoid) forms, ascospore-like structures and most importantly a so-called symplass, or amorphous stage, which often lay unseen when infecting human cells. The pleomorphists also reported the existence of L-forms, conjugation tubes and filterable bacteria, all of which were initially dismissed as fantasies. In addition, they believed that most bacteria routinely undergo sequential morphological changes which come together to form a life cycle.

Opponents of pleomorphism argued that the whole edifice was built on contamination and that, aided by vivid imaginations, the pleomorphists arranged the various contaminants into a supposed bacterial life cycle. It should be stressed, however, that the pleomorphists were not cranks, but bona fide microbiologists who published in the standard literature and appeared to take every effort to avoid the obvious criticism that their observations resulted from contamination.

While the many historical reports of extreme bacterial pleomorphism have been conveniently forgotten, a small number of recent reports of the phenomenon have appeared, particularly in relation to species of Azotobacter and Mycoplasma (2, 5).

**Heresy number two – the cancer germ**

A considerable amount of historical literature suggests that bacteria, and other non-virus micro-organisms, can be isolated from cancers, and that these organisms play a direct role in the formation of most types of cancer. Some of these studies also purport to show that cancers can be caused by the injection of so-called 'cancer germs' into experimental animals (12). This work has been largely ignored and few cancer experts or microbiologists appear to be aware of it. The most common reaction to this work is dismissive on the basis that it must have long-since been proved to be wrong. However, as is the case with extreme pleomorphism, no experimental evidence was ever produced that completely discredited the cancer germ hypothesis.

The historical view that bacteria are involved in the formation of cancers has been strengthened by recent findings indicating a link between stomach cancers and the bacterium *Helicobacter pylori* (9). In addition, there is a developing literature which suggests that other bacteria are involved in cancer aetiology, largely by inducing inflammation, or by producing carcinogens *in situ* in the cell (8, 10).

**GUIDELINES**

Communications should be in the form of letters and should be brief and to the point. A single small Table or Figure may be included, as may a limited number of references (cited in the text by numbers, and listed in alphabetical order at the end of the letter). A short title (fewer than 50 characters) should be provided.

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Microbiology Comment

The two heresies collide

These two heresies enter into collision because many of the historical reports on the cancer germ mention the involvement of highly pleomorphic bacteria that undergo complex life cycles (13). The frequency with which apparently highly pleomorphic bacteria have been isolated from cancers is consistently high. In many cases, the life cycles of these supposed cancer germ were said to involve a hidden or filterable phase (12, 13). Recent studies which suggest a role for highly pleomorphic bacteria in cancer aetiology have been published by, amongst others, Wuerthle-Caspe Livingston and Alexander Jackson (12, 15).

The fact that it is received wisdom that highly pleomorphic bacteria do not exist consistently high. In many cases, the life cycle of these supposed cancer germ were said to involve a hidden or filterable phase (12, 13). Recent studies which suggest a role for highly pleomorphic bacteria in cancer aetiology have been published by, amongst others, Wuerthle-Caspe Livingston and Alexander Jackson (12, 15).

Although there is considerable evidence linking highly pleomorphic bacteria with cancer, it should be noted that the concept of extreme pleomorphism could be dismissed without compromising the view that bacteria in general cause cancer (11, 12). It is also worth noting that extremely pleomorphic bacteria have recently been associated with a wide range of infections, including rheumatic fever and Crohn’s disease (4).

Hopefully, bacteriologists will now be encouraged to re-examine the question of whether or not bacteria exhibit extreme bacterial pleomorphism and, together with cancer experts, re-assess the role of both pleomorphic and non-pleomorphic bacteria in cancer aetiology. For the sake of balance, the reader is also referred to papers by Winogradsky (14) and an anonymous article (1), which, respectively, are critiques of pleomorphism and the existence of specific cancer-causing bacteria.

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Presence of the ribulose monophosphate pathway in Bacillus subtilis

A recent publication of genomic data suggests the existence of the ribulose monophosphate (RuMP) pathway in various non-methylo trophic bacteria, including Bacillus subtilis (2). For B. subtilis, I recently could validate this finding by using the transketolase (TKT; EC 2.2.1.1)-defective B. subtilis strain ATCC 21951.

When the tkt-mutant B. subtilis strain ATCC 21951 is grown on d-glucose as the sole source of carbon and energy, d-glucose is partly converted via the oxidative pentose phosphate cycle into d-ribose 5-phosphate and d-xylulose 5-phosphate (Fig. 1). Due to TKT-inactivity, the ketogroup of d-xylulose 5-phosphate is not transferred to d-ribose 5-phosphate, a reaction step that generates d-erythrose 4-phosphate and d-fructose 6-phosphate. B. subtilis ATCC 21951 instead converts d-xylulose 5-phosphate (via d-ribulose 5-phosphate) into d-ribose 5-phosphate, which accumulates at the TKT-conversion point. To overcome feed-back inhibition effects exerted by this intermediate, the strain dephosphorylates d-ribose 5-phosphate and secretes it as d-ribose into the medium (1) (Fig. 1).

**Fig. 1.** Glucose catabolism in the presence of formic acid by the d-ribose-producing and TKT-defective B. subtilis strain ATCC 21951. The numbers depict the major enzymes that are involved, namely: 1, formate dehydrogenase; 2, formate dehydrogenase; 3, hexulose-phosphate synthase; 4, hexulose-6-phosphate isomerase; 5, TKT (EC 2.2.1.1); 6, lactate dehydrogenase (EC 1.1.1.27); 7, actinoyl reductase (EC 1.1.1.4). The double bar at the TKT-conversion point symbolizes TKT-negativity. PPC, pentose phosphate cycle.