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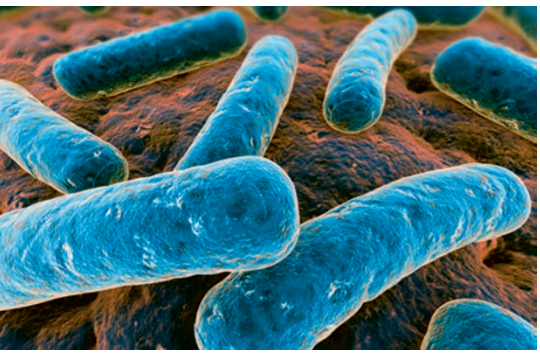
IMMUNOTHERAPY

The treatment bug—fighting cancer with bacterial infection

The hypoxic conditions within tumours are implicated in resistance to therapy, but might provide the ideal environment for the growth of anaerobic bacteria capable of killing cancer cells. In a new study, spores of an attenuated form of the obligate anaerobe *Clostridium novyi* (*C. novyi*-NT) were used to treat cancer in dogs; the experience in the first patient treated with this therapy in an ongoing phase I clinical trial was also reported.

Dogs were used because, similarly to humans, they often develop spontaneous, genetically heterogeneous tumours.



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"We were initially unable to get reproducible or robust responses when the spores were delivered intravenously," explains Saurabh Saha, who led the study. "However, when we switched to directly injecting the spores into tumours, the results were impressive, leading to partial and complete responses." 16 dogs received up to four weekly doses of 1×10^8 spores; 14 dogs were evaluable at day 21, revealing three complete and three partial responses, and five instances of stable disease. "We witnessed a remarkably precise border between what was once tumour cells and the normal tissues," says Saha. "The bacteria acted as a type of cancer biosurgery, leaving a nice margin between tumour and normal cells."

The researchers subsequently treated a metastatic lesion in a woman with leiomyosarcoma that had progressed after multiple lines of therapy. A single dose of only 10,000 *C. novyi*-NT spores was used and induced extensive tumour necrosis. At the end of the study period, the patient had a good performance status and no sign of infection. However, considerable, but manageable, adverse effects consistent with infection, including fever, pain, and tumour inflammation and abscesses, were observed in this patient and the dogs soon after injection of the spores. An indirect fracture that occurred after treatment due to the bone being destabilized was also seen in the patient.

Nevertheless, these symptoms suggest a robust innate immune response that could potentially drive adaptive antitumour immunity. "We believe that *C. novyi*-NT may act as a potent immune modulator," states Saha. He concludes, "as most patients with cancer die of metastatic disease ... our next steps will be to explore the combination of *C. novyi*-NT and immune checkpoint inhibitors to see if the adaptive immune system can be primed further to destroy non-injected lesions."

David Killock

Original article Roberts, N. J. *et al*. Intratumoral injection of *Clostridium novyi*-NT spores induces antitumor responses. *Sci. Transl. Med.* **6**, 249ra111