THERAPY

Through the barricades

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URLs
ERBB2
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=2064

breast cancer
http://www.cancer.gov/cancertopics/types/breast

The blood–brain barrier serves to protect the brain from blood-borne infections and toxic agents, making the treatment of brain metastasis with systemic agents particularly difficult. For the most part this has been overcome by injecting chemotherapy agents into the cerebrospinal fluid, but this approach is not ideal. With the advent of new targeted therapies, such as the monoclonal antibody trastuzumab (Herceptin) that effectively treats ERBB2-positive breast cancers, a need has arisen to deliver such agents to the brain to help eradicate brain metastasis. Manabu Kinoshita and colleagues have succeeded in getting trastuzumab to cross the blood–brain barrier in mice through the use of focused ultrasound.

Focused ultrasound, used at a high frequency, is able to concentrate acoustic energy on an area of tissue a few millimetres in diameter and is used to kill tumour tissue. The addition of an ultrasound contrast agent that produces bubbles results in transient changes in cell-membrane permeability and is known to disrupt the blood–brain barrier. The authors tested whether high frequency ultrasound could be used to transiently disrupt the blood–brain barrier so that trastuzumab could reach brain tissue in mice. Magnetic resonance imaging was used to guide the beam of focused ultrasound.

Initially Kinoshita and colleagues showed that this technique could disrupt the blood–brain barrier to enable the entrance of the vital dye trypan blue. They then injected trastuzumab systemically into 13 mice; 9 mice were given ultrasound with a contrast agent, the other 4 were not. Significantly more trastuzumab was detected in the brains of mice that were treated with ultrasound compared with those that were given the antibody alone. Importantly, even where there was evidence of significant disruption to the blood–brain barrier the underlying brain tissue was not damaged.

This technique might prove useful for the treatment of brain metastasis with antibody-based targeted agents.

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ORIGINAL RESEARCH PAPER Kinoshita, M., McDannold, N., Jolesz, F. A. & Hynynen, K. Noninvasive localized delivery of Herceptin to the mouse brain by MRI-guided focused ultrasound-induced blood–brain barrier disruption. *Proc. Natl Acad. Sci. USA* **103**, 11719–11723 (2006).
FURTHER READING Kennedy J. E. High-intensity focused ultrasound in the treatment of solid tumours. *Nature Rev. Cancer* 5, 321–327 (2005)