News Release

Title

An immuno-wall microdevice exhibits rapid and sensitive detection of IDH1-R132H mutation specific to grade II and III gliomas

Key Points

- A micro-sized device "immuno-wall microdevice," has been constructed, which can determine whether a sample is positive for the IDH1 mutation using only a small sample.
- This device features a chip with an attached highly-specific antibody, HMab-2, that binds to the protein produced by the gene in which the mutation has occurred.
- This novel approach takes only less than 15 minutes, potentially allowing surgeons to identify the specific type of brain tumor they encounter, and to delineate its margin during real-time surgical procedures, enabling full removal while sparing normal brain tissue.

Summary

Gliomas are tumors occurring in the brain or spinal cord. They are difficult to treat as they lack clear edges, which complicates full surgical removal. This leads to high levels of recurrence and mortality. However, previous findings have identified a particular mutation very common in gliomas but rare in other cancers and in normal tissue.

Dr. Atsushi Natsume, Department of neurosurgery, Nagoya University Graduate School of Medicine (Dean: Masahide Takahashi, M.D., Ph.D.), and colleagues develops a device for quick, accurate identification of a mutation strongly associated with a cancer that affects the central nervous system, potentially enabling accurate removal of the entire tumor during an operation.

Research Background

Gliomas are tumors occurring in the brain or spinal cord. They are difficult to treat as they lack clear edges, which complicates full surgical removal. This leads to high levels of recurrence and mortality. However, previous findings have identified a particular mutation very common in gliomas but rare in other cancers and in normal tissue.

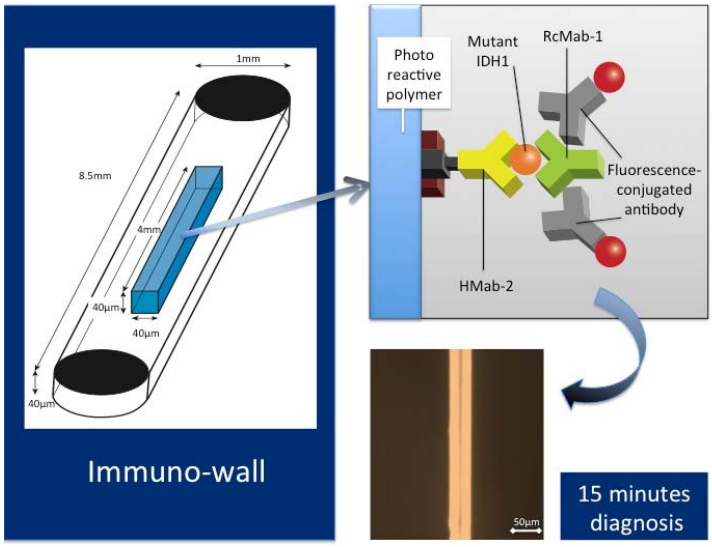
Tumors must be identified with high precision, and if they are malignant, the anticipated speed they will spread is also critical to ascertain. If full excision of the tumor is planned, it is also necessary to determine where tumorous tissue ends and normal tissue begins. This is particularly important for brain tumors, as the removal of any tissue can impair key brain functions. Gliomas are difficult to treat because they expand into surrounding tissue inconsistently, blurring their margins. However, most do have a specific genetic mutation rarely found in other central nervous system cancers.

Research Results

The researchers reported their breakthrough device, which they call an "immuno-wall microdevice," in Science and Technology of Advanced Materials. The device features a chip with an attached highly-specific antibody, HMab-2, produced by Yukinari Kato at Tohoku University that binds to the protein produced by the gene in which the mutation has occurred. When a sample containing the mutated protein is added to the device, the protein binds to the antibody, which is then specifically detected by a source of fluorescence. In contrast, if the sample is from normal tissue without this mutation, or is from a tumor other than a glioma, no fluorescence occurs.

The immuno-wall determines whether a sample is positive for a specific mutation in the isocitrate dehydrogenase 1 gene, which is present in around 70%–80% of grade II and III gliomas. The results for a range of cancerous cell lines and actual tumor samples both positive and negative for this mutation were very promising. The device was proven highly accurate, as confirmed by complete sequencing of the gene in question in each sample.

The small sample size required for the device reduces the invasiveness of sample harvesting. In fact the process takes only 15 minutes, enabling completion during an operation. The immuno-wall could markedly increase success of glioma treatment by rapidly providing data to inform the course of the operation and tissue to remove.



Research Summary and Future Perspective

The data indicate that a sample with just 500 cells or 500 ng of protein is sufficient to give a positive result. The key to success in the immuno-wall assay is that we luckily have HMab-2, the highly-specific antibody to the mutant IDH1. This means the immuno-wall can identify the margins of tumors where only low numbers of cancerous cells are present. Alternatively, sampling could even involve only obtaining blood or cerebrospinal fluid, rather than removing brain tissue, making the procedure even less invasive.

Article

Akane Yamamichi, Toshihiro Kasama, Fumiharu Ohka, Hiromichi Suzuki, Akira Kato, Kazuya Motomura, Masaki Hirano, Melissa Ranjit, Lushun Chalise, Michihiro Kurimoto, Goro Kondo, Kosuke Aoki, Noritada Kaji, Manabu Tokeshi, Toshio Matsubara, Takeshi Senga, Mika K. Kaneko, Hidenori Suzuki, Toshihiko Wakabayashi, Yoshinobu Baba, Yukinari Kato, Atsuhi Natsume. An immuno-wall microdevice exhibits rapid and sensitive detection of IDH1-R132H mutation specific to grade II and III gliomas. *Science and Technology of Advanced Materials,* Oct.4, 2016.

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