T cells engineered to home in on brain cancer

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Published on : September 5, 2018

Nature **561**, 319-320 (2018)

doi: 10.1038/d41586-018-05883-7

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Outline

- Introduction
- Proposed Approach
- Results
- Some Challenges
- Conclusion
- References

Introduction

- T cells play a major role in immunotherapy but unable to infiltrate the blood-brain barrier.
- Encephalitis enables transendothelial migration of T cells.
- In glioblastoma the endothelial cells produce little or no ICAM-1 and VCAM-1 but overexpress ALCAM.

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Proposed Approach

- A synthetic ligand for ALCAM, i.e. CD6 (HS–CD6) is generated.
- The synthetic ligands are introduced into T cells using a retrovirus construct.
- T cells are also engineered to express an antigen receptor that was designed to bind to human epidermal growth factor receptor 2 (HER2)
- These cells are then introduced into mice in whose brains human glioblastomas had been surgically implanted.

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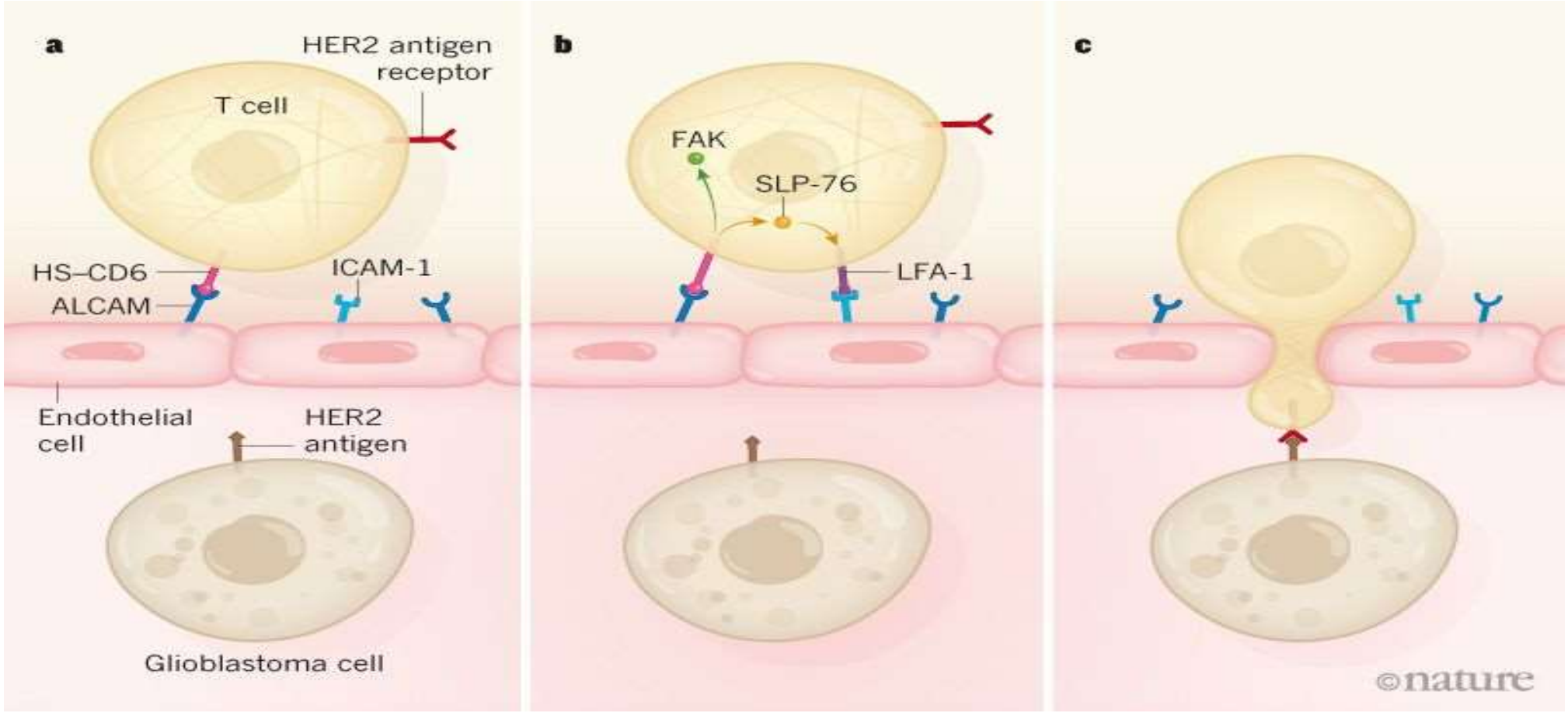
Proposed Approach Contd…



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Results

- The presence of multimeric HS-CD6 on T cells enhanced adhesiveness between these cells and ALCAM-expressing endothelial cells.

- T cells that expressed both HS–CD6 and the HER2-specific antigen receptor infiltrated the glioblastomas.

- T cells harbouring only the antigen receptor (which are typically used for cancer immunotherapy) did not infiltrate the tumour.

Some Challenges

- Translate the discovery from mice to patients.
- The group did not investigate the persistence and activity of the HER2-targeting T cells in the body.
- T cells entering a glioblastoma will encounter a profoundly immunosuppressive microenvironment.
- Successful therapy will allow enough active tumour-specific T cells to enter and persist in the tumour microenvironment.

Conclusion

- A new approach to infiltrate T cells into brain is developed to cure brain cancers.
- Requires further investigations on side effects and clinical trials.

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Thank You!!