

Treating cervical cancer with gene editing.

Nanoparticle delivery in mice clears tumours.

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Australian Government

Australian Research Council

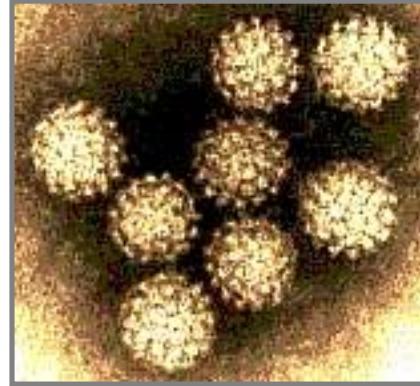
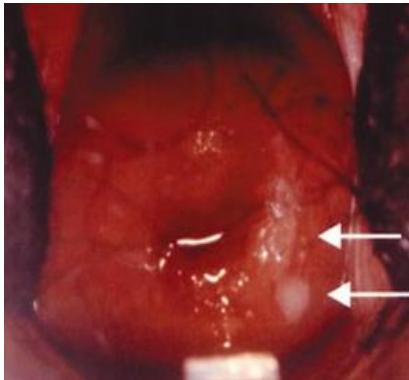


Australian Government

National Health and Medical Research Council

Human papillomavirus

- E6/E7 drive the cancer
- Cancers are “addicted” to these oncogenes
- Their loss will kill cancer cells
- How do we get rid of these virus genes?



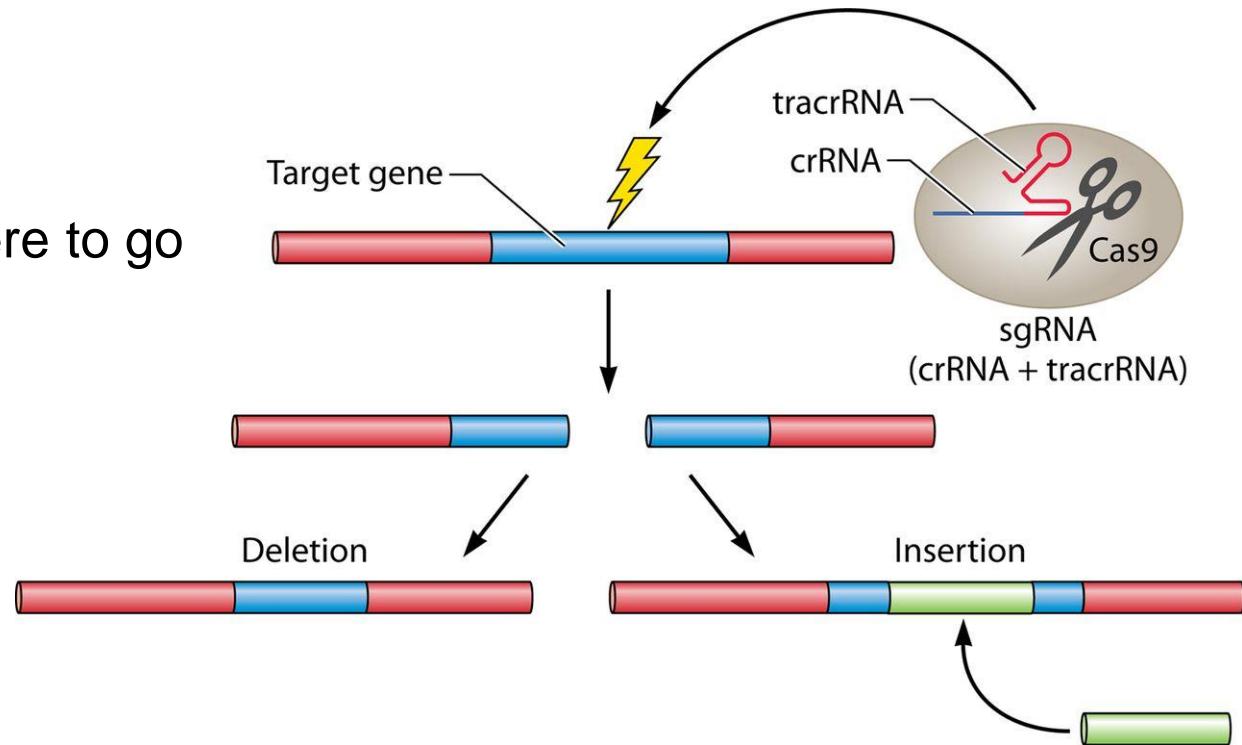
*Gene Editing to directly remove these genes will work.
HPV is an ideal model system for this technology.*

Genome editing (CRISPR-Cas9).

What you need.

Guide RNA – tells where to go on genome

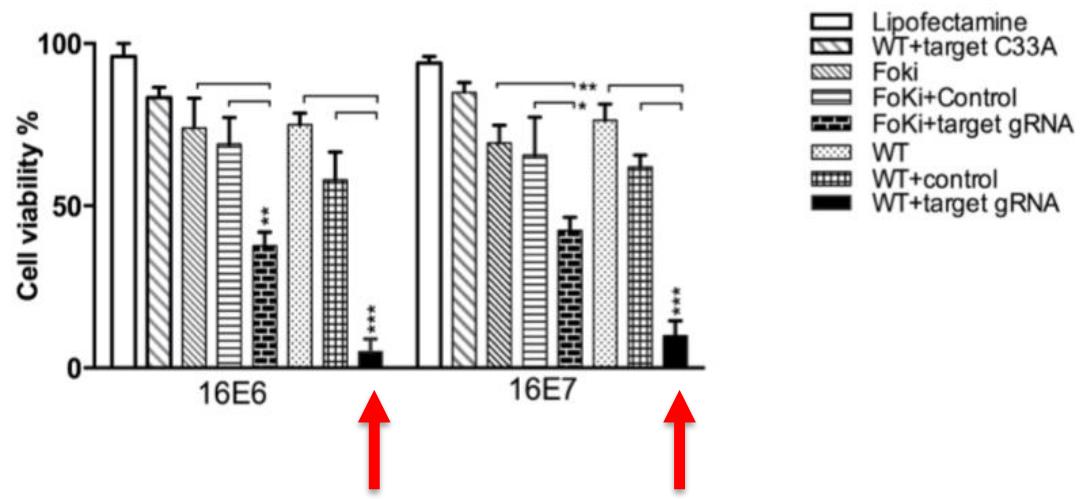
Cas9 – cuts genome



Yoshizumi Ishino et al. J. Bacteriol. 2018;
doi:10.1128/JB.00580-17

Gene Editing in cells.

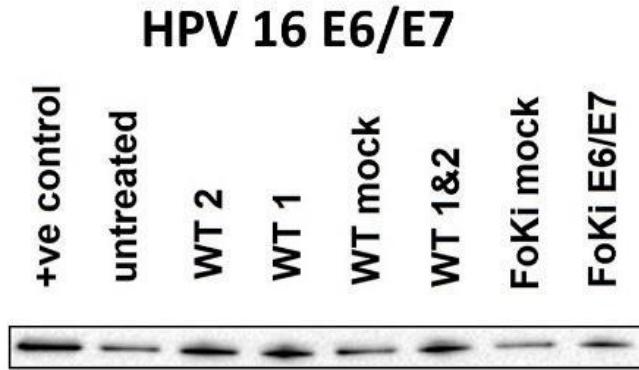
Removing Oncogene kills cells



A

Protein levels are reduced

Rb

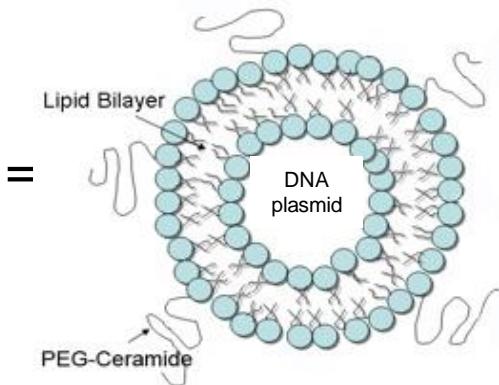


Red arrow pointing to the FoKi E6/E7 band.

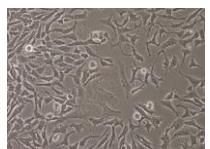
Testing E7 CRISPR/Cas in animal models.

pCAS9
E7 sgRNA

+ Lipids/PEG



Developed by
Sherry Wu



Day 0

8

12

16

S.C. inj-tumour cells
and wait till 20mm³

I.V. inj

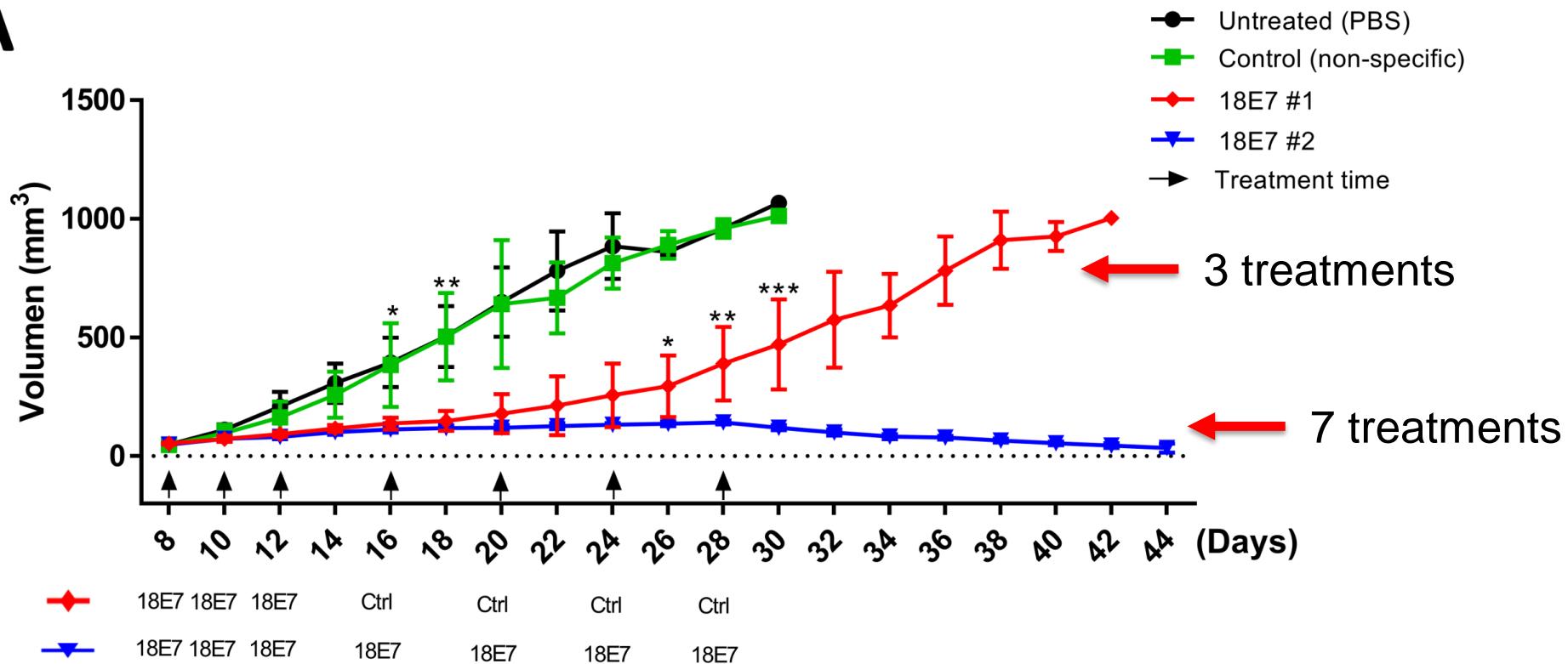
I.V. inj

I.V. inj

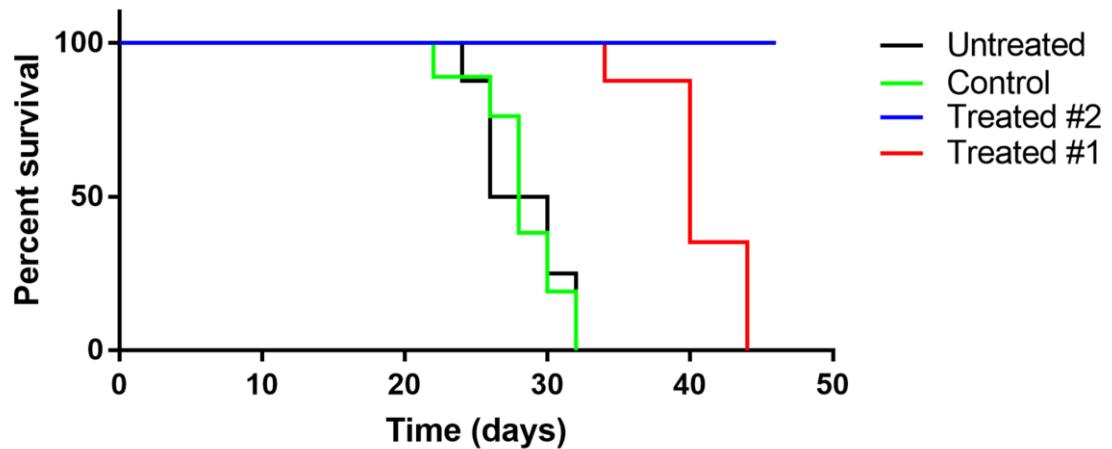


Cervical Cancer cells (HeLa) in mice.

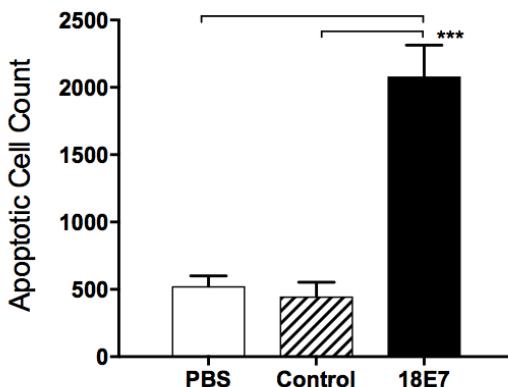
A



HeLa (HPV18) xenografts.

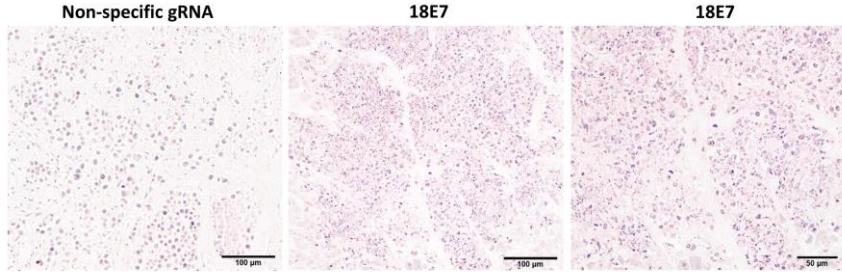


72 post
single treatment

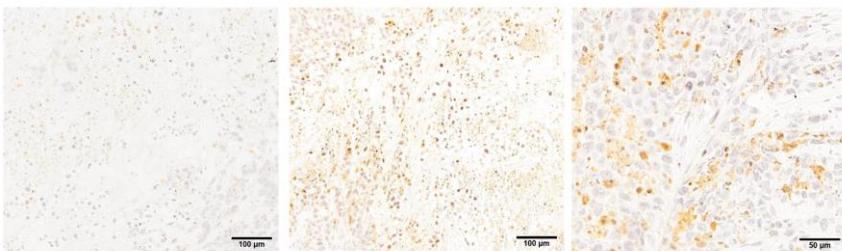


HeLa (HPV18) xenografts.

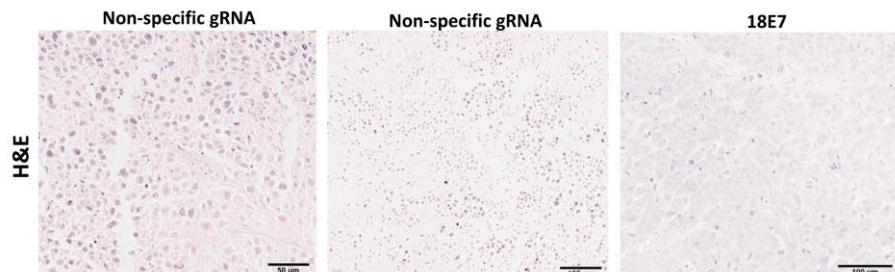
H&E



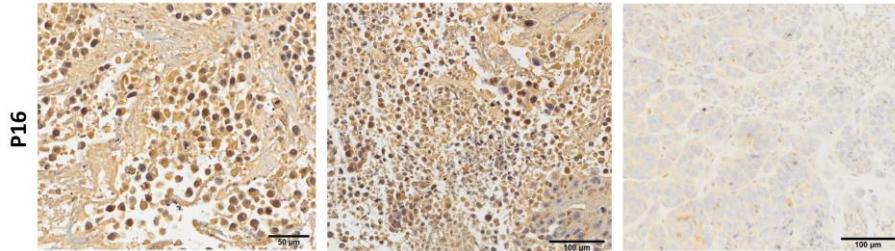
Cleaved Caspase-3



H&E



P16



Apoptotic death

HPV tumour cells gone (no p16)

Conclusion

- Gene editing of E6/E7 works well
- Death by apoptosis
- In vivo delivery results in significant tumour loss and 100% survival.
- You need to give sufficient treatments to avoid escape.
- C/Cas is a viable solution for treatment if you know your target and target is critical to survival