

Human Cervical Cancer

Over 1,200 deaths per year in the U.K. alone

Caused by infection with
Human Papilloma Virus (HPV)

High risks HPV types

Geographical and other considerations

Human cervical cancer

Selective targeting of the HPV virus may permit selective targeting of the cancer cells without adverse side effects upon normal cells.

i.e. raises the possibility of a drug which enters all cells but which only kills the HPV-positive cancer cells.

RNA interference

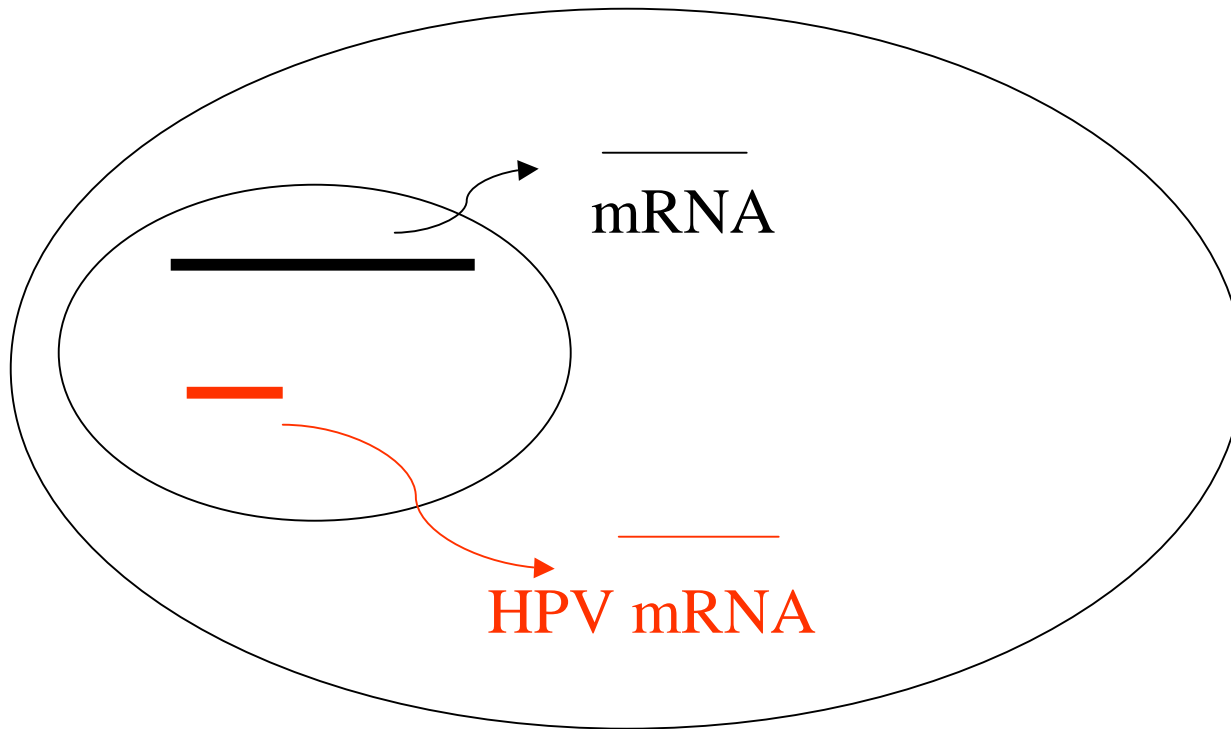
-destroys mRNA expressed from target genes

-self-replicating process

-highly selective

-induced by small ds RNA molecules

Aim: to selectively destroy
viral mRNA



Choice of viral target gene(s)

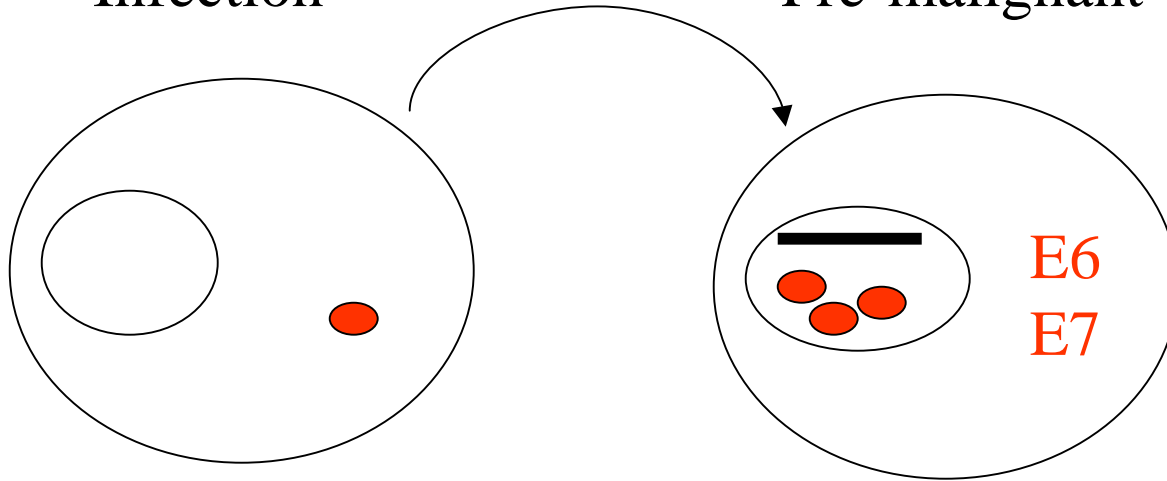
E6

E7

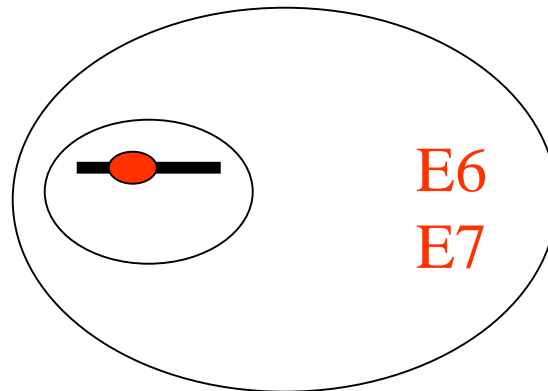
These two viral genes are the driving force of malignancy

Infection

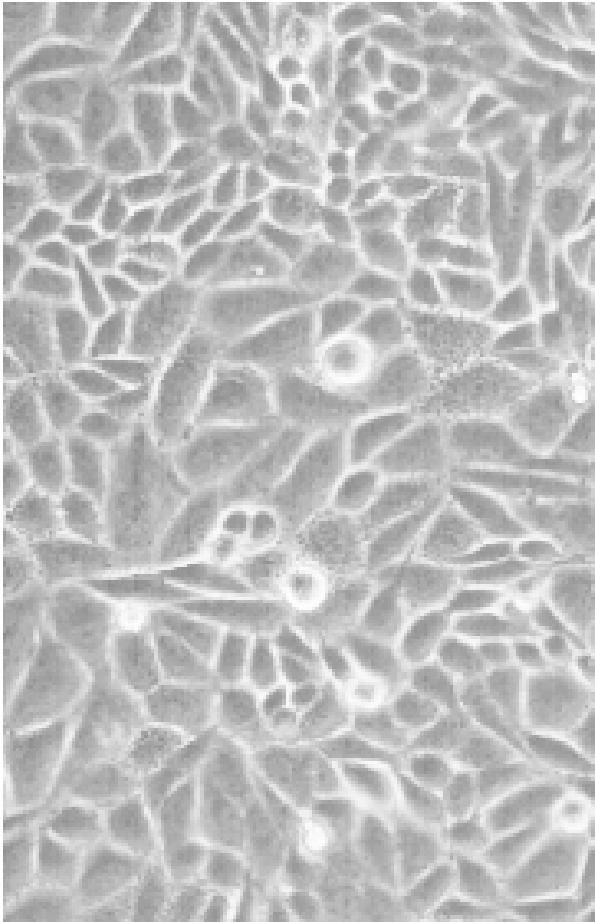
Pre-malignant



Malignant



● = Viral genome

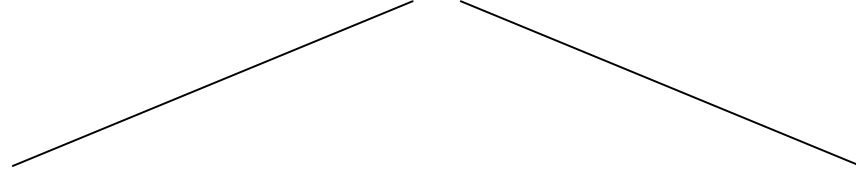


Human
cervical cancer
cells growing
in cell culture
(HPV-16)

E6 mRNA

1

477



Dimer Loop

E6

5'-GAGGUAUAUGACUUUGCUUTT

-0.1

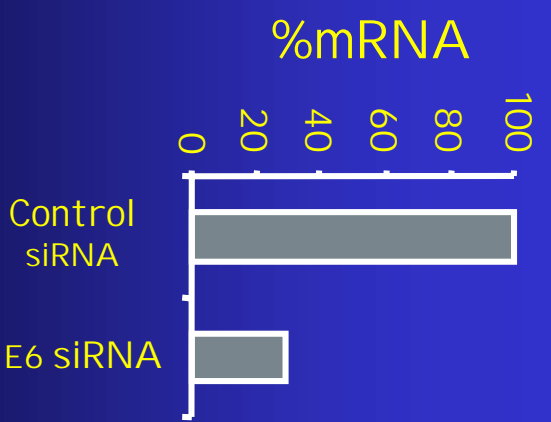
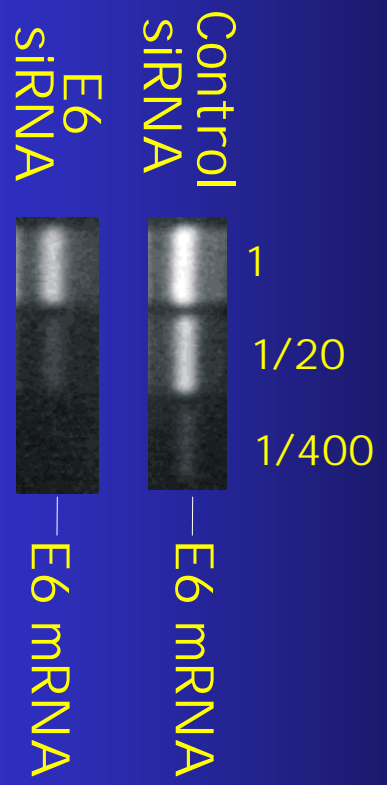
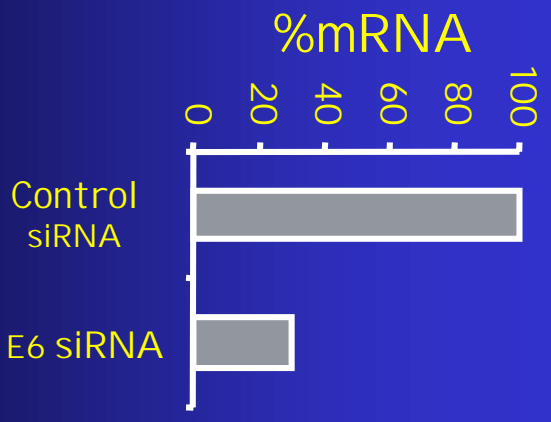
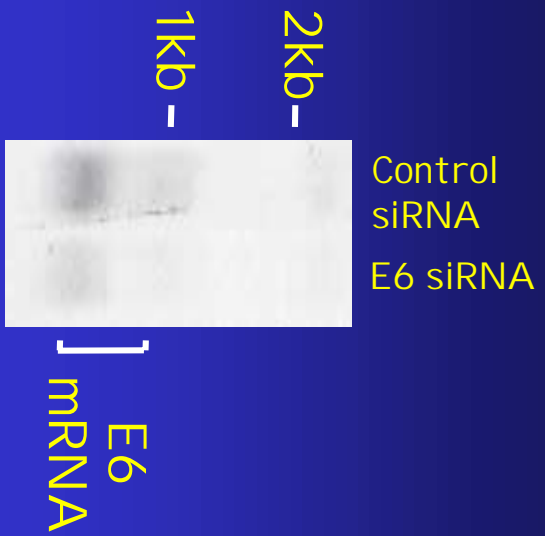
0

siRNA

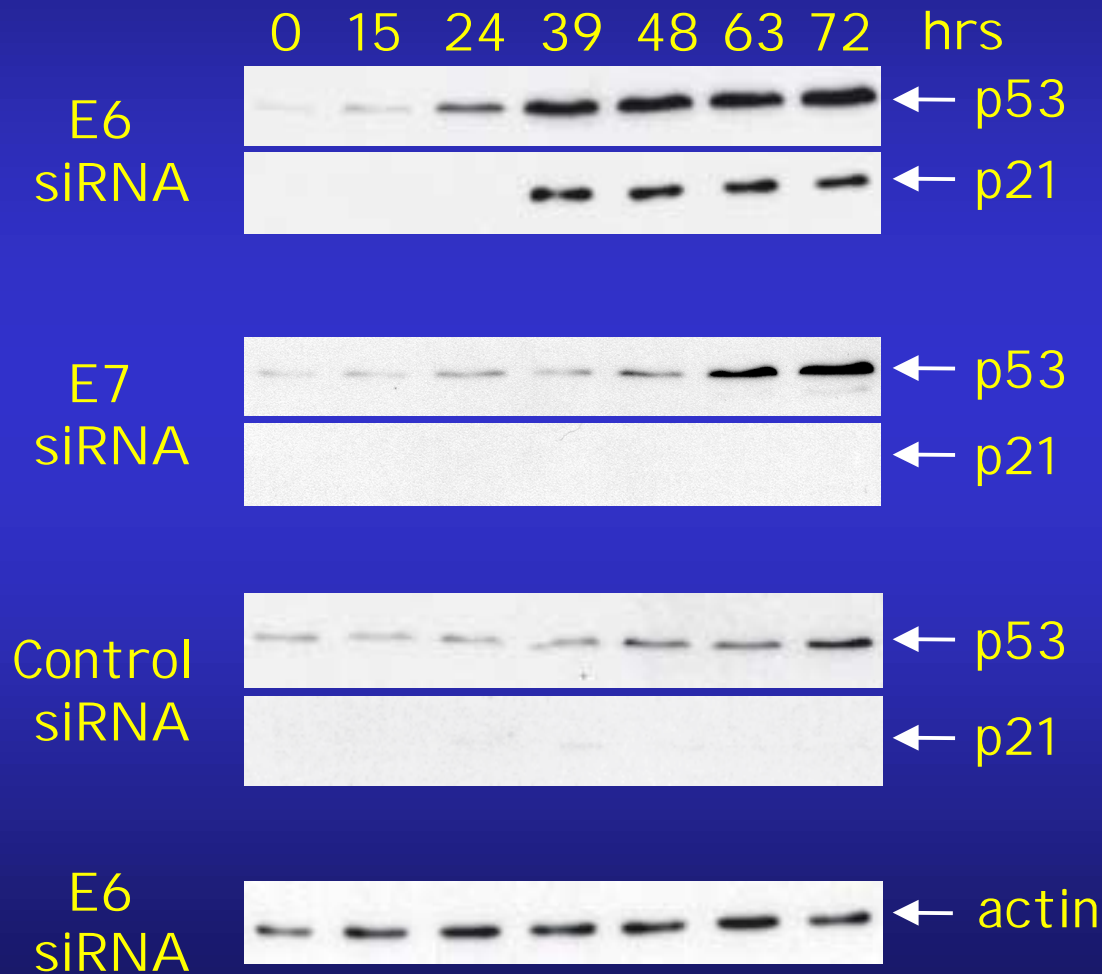
TTCUCCAUAUACUGAAACGAA-5'

-0.4

0



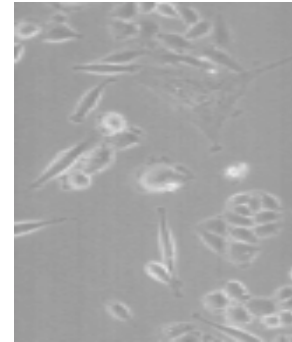
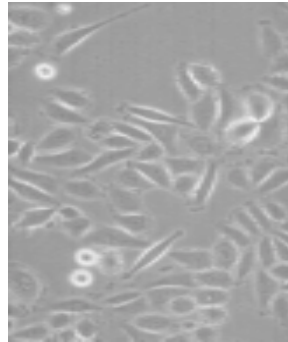
E6 siRNA induce activation of p53



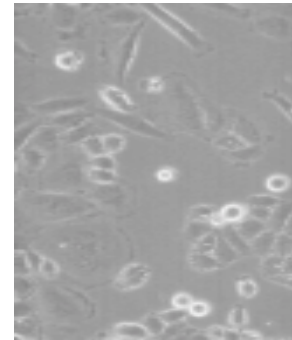
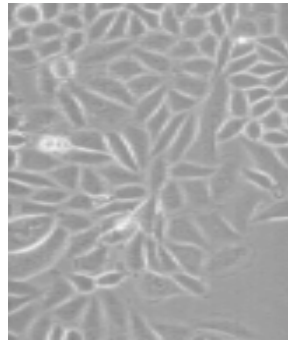
Control
siRNA

E6
siRNA

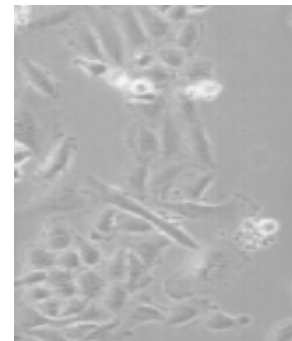
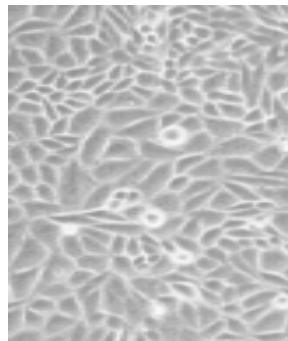
48hrs



72hrs



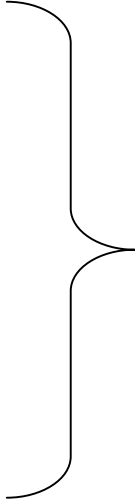
96hrs



Human papilloma virus

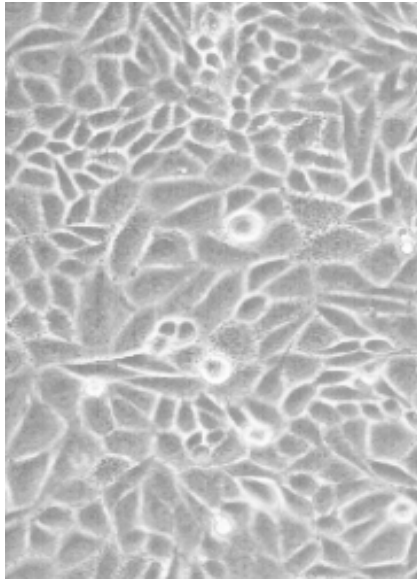
E6

E7

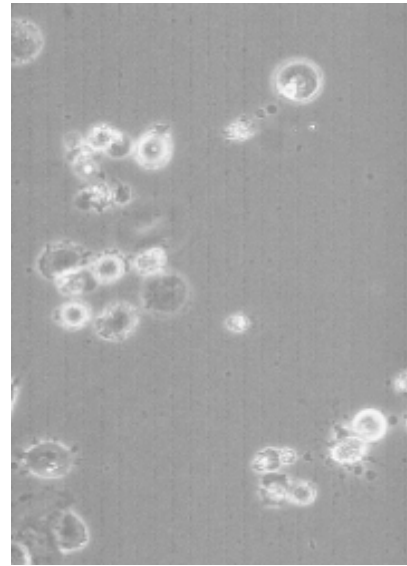


E6 and E7
co-operate
to transform
cell growth

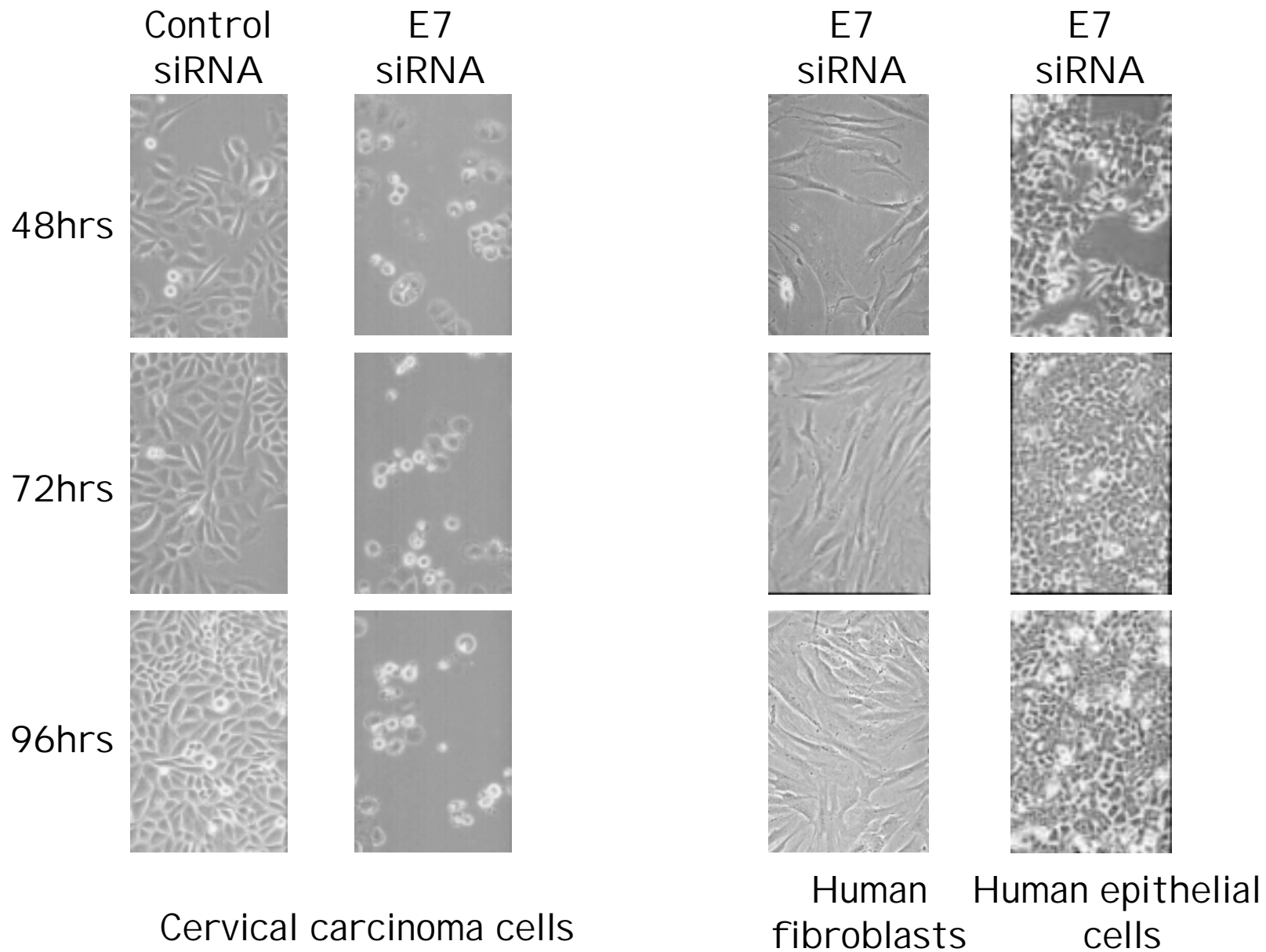
E7 siRNA causes apoptosis of cervical cancer cells



Control siRNA



E7 siRNA



Implications for anti-cancer therapy

- highly specific
- siRNA easily synthesised
- requires no modification to improve efficacy
- different HPV types

RNA therapy for human cervical cancer ?

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