

## DEFECTIVE INTERFERENCE

Defective Interference has the potential to offer a wide-spectrum immunity against a range of influenza strains. Although the principle has been known about for over 50 years, it is only recently that its potential has been fully investigated. Researchers in the School of Life Sciences at Warwick have pioneered this work. The idea is relatively simple; a defective interfering (DI) influenza virus is missing part of its genome and therefore cannot replicate properly (and therefore cause infection). However, when a normal influenza virus invades, the defective virus hijacks the normal virus's replication machinery and produces many more copies of itself. In this way the normal virus is rapidly out competed and disease is prevented.

This project provides the opportunity to model and analyse some of the data being generated. There is now a relatively good understanding of the cell-level processes, but as yet few models have been used to translate these ideas to the whole-body scale.

As such the project will consist of a mixture of data analysis, model development and parameter inference; so a wide mix of skills would be an advantage -- although there is the scope for the project to be pushed in multiple directions.

The ideal end-point of the project would be a simple working model of Defective Interference, which operates on populations of cells (initially within culture medium, but extendable to within host) and that is consistent with the experimental data.

In principle this process has the potential to offer a universal flu vaccine -- where one injection protects against multiple strains. However, a more holistic understanding of the protection is required before this is achievable.

There is potentially scope to extend this work further in a range of directions, from a more detailed understanding of the within-cell competition, to the dynamics within a host, to the potential for this as a population-level treatment. In addition, there are several novel elements that have been elucidated by recent experiments including: the incorporation of the competition that has been demonstrated in which the DI genome displaces the wild type segment, and the effect on the synthesis of RNA from specific genome segments

## REFERENCES

- Noble, S., McLain, L. & Dimmock, N. J. (2004). Interfering vaccine: a novel antiviral that converts a potentially virulent infection into one that is subclinical and immunizing. *Vaccine* **22**, 3018-3025. (<http://wrap.warwick.ac.uk/8087/>)
- Marriott, A. C. and Dimmock, N. J. (2010). Defective interfering viruses and their potential as antiviral agents. *Reviews in Medical Virology* **20**, 51-62.
- Easton A. J., Scott, P. D., Edworthy, N. L., Meng, B., Marriott, A. C. and Dimmock, N. J. (2011). A novel broad-spectrum treatment for respiratory virus infections: influenza-based defective interfering virus provides protection against pneumovirus infection *in vivo*. *Vaccine*, **29**, 2777-2784.
- Scott, P. D., Meng, B., Marriott, A. C., Easton A. J. and Dimmock, N. J. (2011). Defective Interfering Virus Protects Elderly Mice from Influenza. *Virology Journal* **8**, 212.
- Scott, P. D., Meng, B., Easton, A. J., Marriott, A. C. and Dimmock, N. J. (2011). Defective interfering influenza A virus protects *in vivo* against disease caused by a heterologous influenza B virus. *Journal of General Virology* **92**, 2122-2132.
- Scott, P. D., Meng, B., Marriott, A. C., Easton, A. J. and Dimmock, N. J. (2011). Defective interfering influenza virus confers only short-lived protection against influenza virus disease: evidence for a role for adaptive immunity in DI virus-mediated protection *in vivo*. *Vaccine* **29**, 6584-6591.