



PRESS RELEASE | PARIS | 14 OCTOBER 2008

A new mechanism of resistance to dengue virus

It is becoming increasingly common to see individuals infected by the dengue virus who develop an ultimately fatal hemorrhagic syndrome, particularly in children during epidemics. However, in most cases, dengue remains a generally benign or even asymptomatic viral infection. One explanation for this phenomenon has just been put forward by researchers from CNRS¹, Institut Pasteur², Inserm³ and the University of Berkeley (California, USA) in a recent publication in the journal *PLoS NTD*. The demonstration of a new mechanism of resistance to dengue virus could form the basis for new strategies to prevent this disease.

Among the cells in the immune system, dermal dendritic cells are described as the initial cell targets of dengue virus at the site of inoculation by its vector, the mosquito. An interaction between the viral glycoprotein envelope and the CD209/DC-SIGN surface molecule of dermal dendritic cells may be the principal event that triggers infection of these cells and then disseminates the dengue virus throughout the infected individual.

The scientists observed that human dermal macrophages⁴ expressing CD209/DC-SIGN were able to capture the dengue virus inoculated by the mosquito without the virus being able to multiply. This unexpected inhibition of viral replication, despite the virus being present in the macrophage, has recently been demonstrated by a group of researchers from CNRS, Institut Pasteur, Inserm and the University of Berkeley who were collaborating on this project on dengue. Their report constitutes the first description of a new resistance mechanism that represents an important innate defence system against dengue virus infection in humans.

*Each year, dengue affects more than 100 million people out of the two billion who live in regions infested by the vector mosquito *Aedes aegypti*. This disease constitutes a growing public health problem linked to the extension of infested zones and the increase in the number of severe cases in regions with high endemicity. It has become the principal emerging vector-borne viral disease in tropical and subtropical regions of South-East Asia and Latin America, including French overseas departments and territories such as the French West Indies and Guiana, and French Polynesia. In mainland France, dengue has been a notifiable disease since 2006.*

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2 Unité Interaction Moléculaires Flavivirus-Hôtes (Institut Pasteur), Unité de recherche de virologie structurale (Institut Pasteur/CNRS),

3 Inserm U872

4 Immune response cells involved in controlling infection by pathogenic agents



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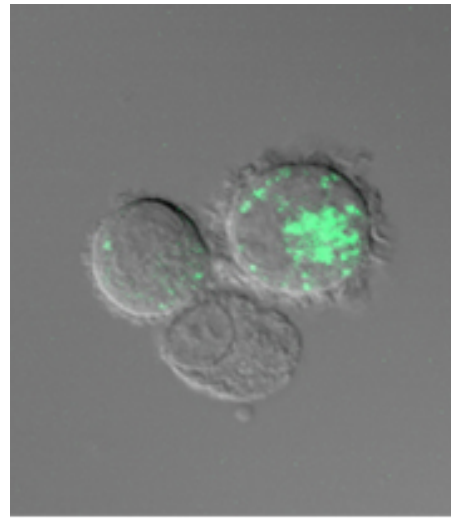
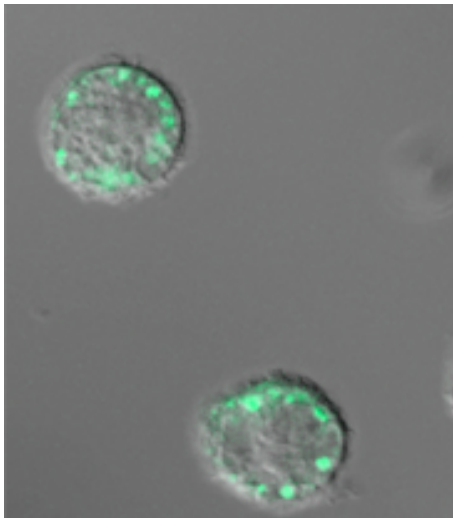
Institut Pasteur



Instituts
thématiques

Inserm

Institut national
de la santé et de la recherche médicale



Internalization of a dengue virus protein (green fluorescence differing as a function of cell type: macrophage vs. dendritic cells)

Macrophages: *The protein is restricted to the cell periphery (thus protecting it from infection)*

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Dendritic cells: *the protein accumulates inside the cell (thus favoring its infection by the virus)*

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Bibliography

Dermal-type macrophages expressing CD209/DC-SIGN show inherent resistance to dengue virus growth, W-H. Kwan, E. Navarro-Sanchez, H. Dumortier, M. Decossas, H. Vachon, F. Barreto dos Santos, H. W. Fridman, F. A. Rey, E. Harris, P. Despres, C. G. Mueller, *PLoS neglected tropical diseases*, online.

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