

Newsletter

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NEWS

Federica Sallusto and Greta Guarda.

L-selectin-negative CCR7⁻ effector and memory CD8⁺ T cells enter reactive lymph nodes and kill dendritic cells *Nature Immunology* June 2007. Armed 'killer' cells can re-enter lymph nodes to destroy dendritic cells – a specialized type of immune cell – according to a report published this week online in *Nature Immunology*. Such killing by antigen-specific T cells reduces further priming of naive immune cells of similar specificity, thereby preventing excessive immune cell activation.



Nature Immunology, June 2007

The results overturn prevailing notions that lymph nodes provide restrictive environments that prevent entry of activated T cells. Sallusto and colleagues show 'resting' lymph nodes continue to bar entry to previously activated immune 'killer' cells called effector memory CD8⁺ T cells. Upon inflammatory signals that occur during infection, however, lymph nodes are activated and transiently express a chemical signal called CXCL9 and recruits memory T cells directly from the bloodstream. These memory cells express a receptor called CXCR3 that recognizes CXCL9.

In addition to checking further immune activation, the CXCL9 entry pathway provides a means to combat pathogens, including viruses such as HIV that replicate in lymph

node tissues. The study should also be instructive to those working toward more effective vaccine development and improving efficacy. The work was carried out by Greta Guarda who defended her PhD Thesis, "GENERATION AND FUNCTION OF MOUSE CENTRAL MEMORY AND EFFECTOR MEMORY T CELLS" under the supervision of Federica Sallusto of the IRB and Prof. Hans Acha-Orbea of the University of Lausanne Biochemistry Department the following week.



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Gates Foundation Grand Challenge meeting held in Lugano.

From June 4 to 6 the participants of the Gates Grand Challenge 4 met in Lugano for a Scientific Progress Meeting. IRB researcher Markus Manz and his team are part of the distinguished international team dedicated to meeting Gates Foundation Grand Challenge Number 4 to: "Devise Reliable Testing Systems for New Vaccines".

The 65 Participants at the meeting were able to exchange ideas and experiences in an intensive three-day session in Lugano. The next meeting will be held in Cape Town, South Africa. The purpose of the meeting is to update the collaborators on progress made and to identify potential problems to be solved. **Background of the Grand Challenges:** In January 2003, Bill Gates announced the establishment of a medical research initiative focused on finding solutions to critical problems in global health. Since then, scientists and public health experts around the world have worked together to define the Grand Challenges in Global Health and

develop proposals to solve them. **Why Grand Challenges?** The Grand Challenges in Global Health initiative aims to engage creative minds from across scientific disciplines -- including those who have not traditionally taken part in global health research -- to work on critical problems that usually receive little attention.

The 14 Grand Challenges in Global Health serve seven long-term goals to improve health in the developing world:

- **Goal 1** - Improve Childhood Vaccines.
- **Goal 2** - Create New Vaccines.
- **Goal 3** - Control Insects that Transmit Agents of Disease.
- **Goal 4** - Improve Nutrition to Promote Health.
- **Goal 5** - Improve Drug Treatment of Infectious Diseases.
- **Goal 6** - Cure Latent and Chronic Infection.
- **Goal 7** - Measure Health Status Accurately and Economically in Developing Countries.

The initiative's partners are the Bill & Melinda Gates Foundation, the Canadian Institutes of Health Research, the Foundation for the National Institutes of Health, and the Wellcome Trust.

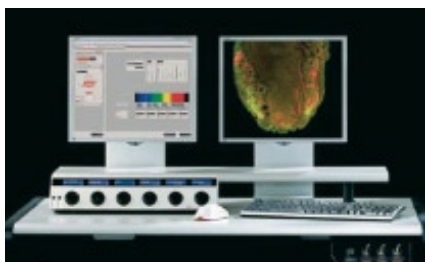


IRB Fund raising goal reached for new-microscope!

The Swiss National Fund agreed recently to fund half of the cost of the purchase of a highly sophisticated microscope. The generosity of a local foundation has agreed to cover the other half of the 850'000.- cost of the instrument. This latest step in improving the infrastructure of the IRB underlines the strategic importance of improving the instruments available to IRB scientists enabling their ambitious programs. Under its R'EQUIP Programme (Research Equipment), the Swiss National Science Foundation (SNSF) supports the purchase, development and moderniza-

tion (upgrading) of research equipment, which is essential for the launch of new research facilities.

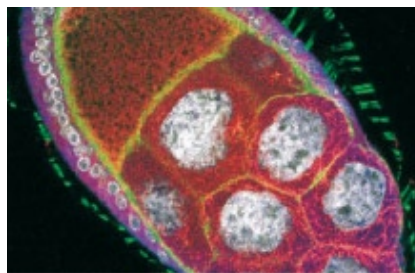
In many research areas success is dependent on the availability of top quality equipment. In recent years, investment in such research equipment at Swiss higher education institutions has declined to a relatively low level. The SNSF has set itself the objective with its R'EQUIP Programme of forestalling this trend before any deficits become evident in the national research infrastructure.



Confocal microscope

Advanced imaging technology has become essential for timely, competitive biomedical research and the lack of such equipment in Ticino has blocked development of numerous projects. The successful application to the SNF for funding demonstrates how 6 independent research projects of relevance to Immunology, Hematology, AIDS, and Alzheimer's disease, each from a different SNF-funded Groups, will be advanced by access to the new microscope equipment. These projects are but the "tip of the iceberg", when one considers the enormous potential utilization of state-of-the-art microscopy by investigators from IRB and collaborating institutions. **Basic concept:** the principle of confocal imaging was patented by Marvin Minsky in 1957. In a conventional (i.e., wide-field) fluorescence microscope, the entire specimen is flooded with light from a light source. In contrast, a confocal microscope uses point illumination and a pinhole in an optically conjugate plane in front of the detector to eliminate out-of-focus information. Only the light within the focal plane can be detected, so the image quality is much better than that of wide-field images. As only one point is illuminated at a time in confocal microscopy, 2D or 3D imaging requires scanning over a regular raster (i.e. a rectangular

pattern of parallel scanning lines) in the specimen.



The thickness of the focal plane is defined mostly by the square of the numerical aperture of the objective lens, and also by the optical properties of the specimen and the ambient index of refraction.

Bird Flu antibodies shown to protect and cure.

Avian influenza survivors' antibodies effective at neutralizing H5N1 strain.

Adults who have recovered from the potentially deadly H5N1 strain of avian influenza may hold the key to future treatments for the virus, according to an international team of researchers. In a study published today in the open access journal PLoS Medicine, the researchers have shown how specific antibodies taken from avian flu survivors in Vietnam can be reproduced in the laboratory and prove effective at neutralizing the virus in vitro and in mice.

The H5N1 influenza virus has caused disease and death in millions of poultry across the globe and has occasionally been transmitted to humans. By mid-May 2007, according to the World Health Organization, there had been 306 known cases in humans, 185 of them fatal.

Research led by Antonio Lanzavecchia in collaboration with the Hospital for Tropical Diseases in Ho Chi Minh City, Vietnam, and the National Institute of Allergy and Infectious Diseases in Bethesda, US, have shown that monoclonal antibodies generated from blood of human survivors of the H5N1 virus are effective at both preventing infection in mice and at neutralising the virus in those already infected.

The research had been fast-tracked for funding by the UK's Wellcome Trust and is also supported by grants from the National Institutes of Health in the US and the Swiss National Science Foundation.

The researchers found that the antibodies provided significant immunity to mice that were subsequently infected with the Vietnam strain of H5N1. This reduced the amount of virus found in the lungs and almost completely prevented the virus reaching the brain or spleen. In those people in Vietnam who died from the H5N1 strain, the virus was found to

have spread from the lungs; this was not the case in those who survived. "We have shown that this technique can work to prevent and neutralise infection by the H5N1 'bird flu' virus in mice," says Dr Cameron Simmons, a Wellcome Trust researcher at the Oxford University Clinical Research Unit, Vietnam. "We are optimistic that these antibodies, if delivered at the right time and in the right amount, could also provide a clinical benefit to humans with H5N1 infections."

"In particular, we found that it was possible to administer the treatment up to 72 hours after infection. This is particularly important as people who have become infected with the virus do not tend to report to their local healthcare facilities until several days after the onset of illness."

"We can't say for certain that a pandemic influenza virus will resemble the H5N1 strain that we have been studying or that the monoclonal antibodies generated using our technique will be able to tackle such a virus", says Professor Lanzavecchia. "Nevertheless, we are encouraged by the broad neutralizing activity of these antibodies in the lab and the moderate doses required."

Using administered antibodies has a historical precedent. During the 1918 Spanish H1N1 influenza pandemic, there were multiple reports of physicians administering blood taken from survivors to patients infected with the disease. A recent review suggested that this treatment was associated with a halving in mortality. However, directly administering blood carries a risk of infection with other blood diseases, such as Hepatitis C and HIV.

These studies provide proof of concept that fully human mAbs with neutralizing activity can be rapidly generated from the peripheral blood of convalescent patients and that these mAbs are effective for the prevention and treatment of H5N1 infection in a mouse model. A panel of neutralizing, cross-reactive mAbs might be useful for prophylaxis or adjunctive treatment of human cases of H5N1 influenza.



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