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Deciphering the enemy's ID

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Immunologists at LMU have come up with a new technique that can be used both to fight tumors and to treat autoimmune diseases. A new grant from the Federal Ministry for Education and Research will enable the method to be developed further.

The primary task of the immune system is to defend its host against infectious agents and tumors. So-called T cells play a crucial role in this process, because they carry surface receptors that recognize and bind to foreign ("non-self") antigens. However, the precise nature of most of these antigens is unknown. Cytotoxic T cells are particularly important because they may recognize pathogen-derived protein fragments (peptides) on infected cells, and eliminate the invaders by killing the cells that harbor them. Moreover, they may extinct tumors by recognizing tumor-specific antigens. However, they can sometimes be misled into attacking and destroying healthy tissues. The result is an autoimmune disease, such as multiple sclerosis or psoriasis.

A team led by Privatdozent Dr. Klaus Dornmair of the Institute for Clinical Neuroimmunology in collaboration with Prof. Jörg Prinz at the Dermatological Clinic recently reported a novel technique which, for the first time, permits rapid identification of the antigens recognized by individual cytotoxic T cells.

The researchers will now be able to refine their method with the aid of a generous grant from the VIP Program (VIP stands for "Validation of the Innovation Potential of Scientific Research") administered by the Federal Ministry of Education and Research (BMBF). Over the next

three years, the Ministry will provide several million euros to fund the development of the technology to a stage at which it is sufficiently mature for commercial exploitation. In this endeavor, the team will also have the support of VDI/VDE-IT, a technology and innovation consultancy, which will be responsible for project management. In light of its great promise, a patent application for the technology has already been filed.

Improved diagnostics, new therapies

"Our technique makes it possible to analyze millions of antigens within the space of few hours. This may not only simplify and improve diagnostic procedures, it may also allow the design of targeted, long-term therapies," says Privatdozent Dr. Klaus Dornmair, who is leading the project. "Indeed, it may provide the basis for a whole series of innovations, since cytotoxic T cells play a major role in many disorders." The technology has a wide range of potential applications, and can be used in the context of viral diseases and malignancies, as well as in the diagnosis and treatment of autoimmune diseases. The LMU researchers therefore expect that demand for the technology will be brisk, and will offer it as a contract research service.

The technique itself uses two types of genetically engineered cells to identify both the antigen-specific receptor of interest and the antigen it recognizes. T cells are first isolated from patients, and the genetic directions for the synthesis of their antigen receptors are introduced into a T-cell line that grows well in culture. This line also carries a gene that codes for an indicator protein, attached to the Green Fluorescent Protein (GFP). These cells are then mixed with cells that have been programmed to express millions of different peptides on their surfaces. When a T-cell receptor recognizes a cognate peptide displayed by one of these cells, the indicator gene is activated, and the T cell can be identified by its green fluorescence, and recovered together with the adjacent cell that activated

it. This allows the reactive receptor to be characterized, while the antigen it naturally recognizes can be identified on the basis of the amino-acid sequences of the peptides to which it binds.

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