Introducing Professor Gabriele Multhoff, European Regional Editor

Lawrence E. Hightower, Editor-in-Chief

Dear Colleagues

It is a pleasure to welcome Gabriele Multhoff as our new European Regional Editor. Dr Multhoff succeeds Professor Olivier Bensaude, our founding European Regional Editor. Dr Bensaude will remain on the Editorial Board, where we will benefit from his years of experience. Our European colleagues comprise the second largest group of subscribers to *Cell Stress & Chaperones*. They have been strong supporters of the journal both as reviewers and authors during the past 9 years and Europe will remain a very important region for the future development of our journal.

Gabriele Multhoff is Professor for Molecular Oncology, Department for Hematology–Internistic Oncology at the University Hospital Regensburg, Germany. She was born in Munich in 1961, and she received her PhD at the University of Munich Institute of Immunology on the characterization of cytotoxic T lymphocytes recognizing self-Major Histocompatibility Complex associated Epstein Barr Virus antigens in 1990. After her PhD, she moved to the University Hospital Grosshadern, where she received a Möllemann Habilitation Stipend to perform her habilitation on a clinically oriented research project in the Department of Hyperthermia. Here, Rolf Issels had successfully treated patients with malignant sarcomas with regional hyperthermia in combination with chemotherapy. From that time onward, she became interested in research on the role of heat shock proteins (Hsp) in eliciting immune responses against cancer (Multhoff and Hightower 1996). The topic of her habilitation was the characterization of therapy-induced (hyperthermia, chemotherapy) modulations of tumor and immunocompetent effector cells. As a senior scientist, she established xenograft tumor mouse models to study the effects of adoptively transferred immunocompetent effector cells. Under the guidance of Pramod Srivastava, she learned a method of isolating Hsp–peptide complexes from tumor and normal tissues. A major goal of her research was the identification of an unusual membrane expression of Hsp70 (Multhoff et al 1995; Hantschel et al 2000) as a tumor-specific

recognition structure for natural killer (NK) cells. Normal tissues were found to be negative for membrane-bound Hsp70 (Gastpar et al 2004). Since early 1990, it has become more and more clear that highly conserved Hsp exhibit an enormous immunostimulatory capacity. Pramod Srivastava, who discovered that Hsp elicit T cell-mediated immune responses against cancer, uses Hsp as carriers for cross-presentation of tumor-derived immunogenic peptides. Alexander Asea found that Hsps also have the capacity to stimulate the innate immune response by initiating the release of proinflammatory cytokines by antigen-presenting cells after contact with Hsp70. Gabriele Multhoff's laboratory identified the immunostimulatory capacity of Hsp70 on NK cells. A 14-mer peptide of the C-terminus of Hsp70 was identified using Pepscan analysis as the minimal immunostimulatory sequence for the stimulation of human NK cells against Hsp70 membrane-positive tumors (Multhoff et al 2001).

In 1999, Gabriele Multhoff moved to Regensburg as a group leader of the research group "NK cells." Together with Claus Botzler, MBA, she founded Multimmune GmbH in the same year. The company focuses on the exploration and exploitation of the immunostimulatory capacity of Hsp on the innate immune system in the treatment of cancer and infectious diseases. In 1998, the company's business plan received several regional awards. In 2002, Gabriele Multhoff became Associate Professor for Molecular Oncology and she is also a consulting immunologist.

The proof of the principle that Hsp70-peptide activates NK cells has been shown in tumor mouse models (Moser et al 2002). In collaboration with Walter Koelch's laboratory at the University of Glasgow, the mechanism of lysis of Hsp70 membrane-positive tumors has been characterized as a granzyme B-mediated apoptosis (Gross et al 2003b) and the interaction of NK cells with Hsp70 membrane-positive tumors was related to the C-type lectin receptor CD94 (Gross et al 2003a). On the basis of these preclinical results, a clinical phase-I trial was performed using ex vivo Hsp70-peptide-activated autologous NK cells in the treatment of cancer patients suffering from colorectal and lung carcinomas at the University Hospital Regensburg (Krause et al 2004).

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Much of Professor Multhoff's pathbreaking work has appeared on the pages of *Cell Stress & Chaperones*. To give readers a further sense of the impact of European authors, I note that they contributed 4 of the 10 most frequently accessed articles on the web version of *Cell Stress & Chaperones* and 2 of the top BioOne articles in 2004. These articles along with the others in the top 12 are discussed in an accompanying article. In addition, 2 of the articles in this issue have European authorship. Following up on a report that the cellular content of Hsp70 increases during CD95-mediated apoptosis, Afshin Samali, Lea Sistonen, and colleagues studied the mechanism of this increase. Surprisingly, they found that an increase in Hsp70 stability and reduced turnover were responsible for the increased accumulation of Hsp70 (Concannon et al 2005). In the second article, Michael Evgen'ev and coworkers used ProteinChip® Array technology to identify variant peptides by trypsin fingerprinting and microsequencing in members of the Hsp70 family in closely related species in the *virilis* group of *Drosophila* (Zatsepina et al 2005). This approach is especially useful for understanding evolutionary variation among proteins having similar functions.

It is a pleasure to publicly thank our outgoing founding European Editor Olivier Bensaude. Olivier's high professional standards and dedication to the journal have had an important role in the submission and publication of high quality manuscripts from our European colleagues. We are confident that Professor Multhoff will extend this tradition of excellence into the second decade of *Cell Stress & Chaperones*. Manuscripts for the European Editor or any other section of *Cell Stress & Chaperones* can now be submitted electronically at our new website <http://cellstress.allentrack.net>.

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