Obituary

Professor Dr. Jürg Tschopp

The cytokine research community was stunned this week by news of the sudden loss of Professor Jürg Tschopp who passed away on March 22. Dr. Jürg Tschopp, a professor of Department of Biochemistry at University of Lausanne, Switzerland, is a leading scientist in the field of signaling mechanisms activated by the TNF receptor family and pattern recognition receptors. For close on 15 years, Jürg’s laboratory has continued to make pivotal contributions to this area of research. To his many colleagues and friends the abrupt cessation of the fruits of this highly valued body of work is, just as his own demise, incomprehensible.

Jürg’s initiation into research on the TNFR family began with his studies of the regulation of Fas-induced death, following his studies of the mechanisms of cell killing by complement proteins and by components of the granules of cytotoxic T lymphocytes. From that point on, his laboratory kept coming up with discoveries of novel ligands and receptors of the TNF family (DR3/TRAMP, APRIL, BAFF and TRAIL) and the signaling proteins that they activate (cFLIP and vFLIP, CARDIAK/RIP2, RIP4), as well as new information on the functions of these signaling molecules and their mechanisms of action. The latter findings related to a variety of activities of the different proteins, including the function of cFLIP not only as an inhibitor of cell death but also as a mediator of signaling for non-apoptotic functions. They also included the discovery—predating by nearly a decade the current explosion in the field—that the kinase function of RIP1 is required for induction of necrotic cell death by TNF and Fas. Especially notable was Jürg’s contribution to the expansion of knowledge of the signaling complexes in which caspases are activated through associations of the death-fold motifs: the discovery of one of these motifs (the PYR domain); the finding that caspase-8 activation can occur not only via signaling complexes associated with cell-surface receptors but also in cytoplasmic signaling complexes derived from them (the induction of ‘complex I’ and ‘complex II’ by TNF); the signaling complex comprised of PIDD and RAIDD (the ‘PIDDosome’) that activates caspase-2 and NF-κB; and the activation of caspase-1 and the other ‘inflammatory’ caspases by cytoplasmic complexes containing members of a group of death-fold-containing NLRs, the NALPs (the ‘inflammasomes’).

Jürg’s most recent studies were focused on the participation of molecules that the TNF family can activate and of molecules related to them in cellular responses to
pathogen components and to danger signals. Those studies have also yielded a number of important findings: discovery of CARDIF (MAVS/VISA/IPS-1) and the role of TRADD in controlling the response of the CARDIF-containing RIG-I signaling complex to cytoplasmic viral ribonucleic acids; discovery of the role of RIP1 in the response of Toll-like receptor 3 to viral ribonucleic acid; and numerous findings in connection with the regulation of inflammasome function. These latter findings included identification of agents capable of activating the inflammasomes (such as uric acid, asbestos, silica and decreased cytoplasmic potassium concentration); suppression of inflammasome function by type I interferon as well as by T cells (in part through the function of TNFRs such as CD40); and elucidation of the role of mitochondrial damage and reactive oxygen species in inflammasome activation, which Jürg found to be mediated in part through interaction of the thioredoxin-interacting protein (TXNIP) with the inflammasome.

Some leading scientists in our field excel in applying new techniques to discover new molecules. Others distinguish themselves through deepening our understanding of how these molecules act. Jürg was one of the few that demonstrated both kinds of creative activity.

As well as the invaluable input from his own laboratory, Jürg made enormous contributions to the research of his peers through stimulating and friendly interactions. The 10th International TNF Conference that he organized in Lausanne in 2004 will be remembered by all who participated as an intellectual feast.

In the community of scientists who seek to elucidate the mechanisms of cellular responses to cytokines and pathogens, the voice of Jürg Tschopp, in its intensity and originality, stands out among the chorus. It will be sorely missed. At the 13th international TNF congress, we shall dedicate the session about Inflammation to the memory of Dr. Jürg Tschopp.