

P004 Regulation of SUMOylation by reversible oxidation of SUMO conjugating enzymes

Guillaume Bossis (1,2); Marc Piechaczyk (1);

Frauke Melchior (2)

IGMM, CNRS UMR 5535, 1919 Route de Mende, 34293 Montpellier, France

Biochemistry I, University Goettingen, Humboldtallee 23, 37073 Goettingen, Germany

Sumoylation has emerged as a central regulatory mechanism of protein function. However, little is known about its own regulation. It has been reported that it is increased following exposure to various stresses including strong oxidative stress. Conversely, we report that ROS (Reactive Oxygen Species), at low concentrations, result in the disappearance of most SUMO conjugates. Nevertheless, desumoylation is not achieved at the same speed for each target. In particular, it is very rapid for some transcription factors such as AP-1 proteins c-Fos and c-Jun, whose sumoylation represses transcriptional activity. This ROS-induced desumoylation is due to direct and reversible inhibition of SUMO conjugating enzymes through the formation of a disulfide bond between E1 and E2 catalytic cysteines. The same phenomenon is also observed in a physiological scenario of endogenous ROS production, the respiratory burst in macrophages. Thus, our findings add SUMO conjugating enzymes to the small list of specific direct effectors of H_2O_2 and implicate ROS as key regulators of the sumoylation-desumoylation equilibrium. Our current work aims at understanding the role of ROS induced desumoylation in cell response to both exogenous oxidative stress and endogenous ROS production.