

P033 Remodeling of the ubiquitin proteasome system in response to Interferons

Ulrike Seifert*, Lukasz Bialy*, Dawadschargal Bech-Otschir, Frederic Ebstein, Melanie Rieger, Ulrike Kuckelkorn, Peter-M. Kloetzel, and Elke Krüger
***contributed equally**

*Charité Universitätsmedizin, Institut für Biochemie,
Monbijoustraße 2, 10117 Berlin*

Peptide generation by the ubiquitin-proteasome-system (UPS) is rate limiting in MHC class I restricted antigen presentation. The current knowledge of MHC class I antigen presentation follows the hypothesis that many antigenic peptides are derived from newly translated polypeptides or short-lived proteins. Here we report the analysis of interferon (IFN)-induced early effects on the UPS in target cells resulting in an unforeseen picture on how IFNs consecutively regulate the UPS at different levels. IFNs induce the transient accumulation of ubiquitin-conjugates, the accelerated formation of immunoproteasomes and the rapid and increased production of **newly translated polypeptides**. **These observations** are due to two events: 1. the IFN induced up-regulation of the ubiquitin modification machinery combined with enhanced ubiquitylation activity, and 2. a transiently decreased proteasomal activity in cells as long as immunoproteasome formation occurs. 26S immunoproteasome formation results in the accelerated elimination of accumulated high molecular weight ubiquitin-conjugates *in vitro* and *in vivo*. This increases the generation of MHC class I epitopes at both the quantitative and qualitative levels thereby actively improving the immune responsiveness of target cells. Together our data indicate that besides their role in antigen presentation immunoproteasomes may serve also other physiological functions.