

P024 Ubiquitin-independent *in vitro* degradation of nuclear hormone receptors by 20S and 26S proteasome.
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Nuclear Hormone Receptor (NRs), and its turnover, play a vital role in general gene regulation. Proteasome mediated degradation is the main protein turnover pathway in mammalian cells. Usually proteasome degradation requires previous poly-ubiquitylation of target proteins. We are interested in the determination of degradation pathways of NRs by the ubiquitin-proteasome pathway. *In vitro* studies were performed by obtaining the corresponding NRs by *in vitro* transcription-translation and labelling with ³⁵S Met/Cys and subjected to degradation by purified 20S and 26S proteasome. To our surprise some NRs were efficiently degraded by 20S and 26S proteasome, as compared with I κ B α , a known substrate to be directly degraded by 20S proteasome (Alvarez-Castelao, B. and Castaño, J.G. (2005). FEBS Lett. 579, 4797-4802). For example, Class I NRs; VDR, RAR α and T3R β are efficiently degraded, whereas T3R α is not degraded. This degradation is completely inhibited by addition of proteasome inhibitors MG132, Lactacystin and Epoxomicin. Furthermore we will be presenting the influence on the *in vitro* degradation of NRs in the presence of the corresponding receptor ligands and the influence of homo- or hetero-dimerization of NRs on its degradation rates by the proteasome.