

## “ Heat shock proteins in the microbiota-nutrition-immunoregulation interphase. ”



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**Time : 15:00 – 16:30**

**Venue : Lecture room No. 2**

**(Graduate School of Agricultural Science)**



Heat shock proteins (HSP) are immuno-dominant stress proteins, present in both prokaryotes and eukaryotes. By their evolutionary conservation microbial HSP contain T cell epitopes that are shared between microbes and their mammalian hosts. These T cell epitopes are targets of immuno-regulatory T cells (Treg) which have the capacity to suppress inflammation (van Eden et al. 2005). Previously, we have shown the ability of mycobacterial HSP70-derived peptide B29 to induce HSP-specific regulatory T cells (Tregs) in Balb/c mice (van Herwijnen et al. 2012). These peptide-specific Tregs were found to suppress experimental arthritis by cross-recognition of their mammalian HSP70 homologs, mB29a and mB29b, both abundantly present in the MHC class II ligandome of stressed mouse and human antigen presenting cells in inflamed tissues. In the context of human MHC molecules we found a highly promiscuous HLA class II binding pattern of our mouse defined peptide. With the help of HLA-DR4/B29 tetramers more than threefold expansions of self-cross-reactive Tregs were seen in the CD4+CD25+Foxp3+ T cell populations after *in vitro stimulation with B29. On the basis of this, a tolerance inducing therapy for chronic inflammatory diseases is now being developed. Furthermore, the current observations may explain the supposed role of microbiota and possibly also infectious diseases in the creation of resistance against allergies and autoimmune diseases in humans (a possibility known as ‘hygiene hypothesis’). As an alternative approach we have produced a screening method to select compounds that have the capacity to co-induce HSP molecules in vivo* (Wieten et al. 2010). The more abundant presence of HSP after co-induction *in vivo*, can lead to a better performance of Tregs. The discovery of such co-inducing compounds in plants, indicates that it will be possible to develop a nutritional strategy for the prevention or therapy of chronic inflammatory conditions.

### Literature:

- van Eden W, van der Zee R, Prakken B. Heat-shock proteins induce T-cell regulation of chronic inflammation. *Nat Rev Immunol.* 2005 Apr;5(4):318-30. Review
- Van Herwijnen, M. J., Wieten, L., van der Zee, R., van Kooten, P. J., Wagenaar-Hilbers, J. P., Hoek, A., et al. (2012). Regulatory T cells that recognize a ubiquitous stress-inducible self-antigen are long-lived suppressors of autoimmune arthritis. *PNAS USA*, 109, 14134-14139
- Wieten L, van der Zee R, Spiering R, Wagenaar-Hilbers J, van Kooten P, Broere F, van Eden W. A novel heat-shock protein coinducer boosts stress protein Hsp70 to activate T cell regulation of inflammation in autoimmune arthritis. *Arthritis Rheum.* 2010 Apr;62(4):1026-35.

( These lectures are included in Class 2(2) of International Food & Agricultural Immunology Lecture, 2015 and are also highly recommended for Master course students)