Decoding heat shock signalling in the African trypanosome

Cher-Pheng Ooi,[1,2] Corina Benz,[1,3] Caroline Dewar,[1] Marianne Aelmans[1] and Michael D Urbaniak[1,*]

[1] Biomedical and Life Sciences, Faculty of Health and Medicine, Lancaster University, Lancaster, LA1 4YG, UK
[2].Current address: Department of Biology, Biosciences Building, Edge Hill University, Lancashire L39 4QP, UK.
[3] Current address: Institute of Parasitology, Biology Centre, Czech Academy of Sciences, 37005 České Budějovice, Czech Republic.
*corresponding author: m.urbaniak@lancaster.ac.uk

The African trypanosomes *Trypanosoma brucei* and *Trypanosoma congolense* are vector borne parasites of domestic cattle and are a major cause of economic hardship in sub-Saharan Africa, with two sub-species of *T. brucei* also causing fatal infections in humans. Their ability to sense and respond to their host environment is critical for their survival and virulence, and is achieved despite a near complete lack of transcriptional control that results in a reliance on RNA binding proteins. Symptoms of human and animal African trypanosomiasis include periods of fever as high as 41 ^{0}C, eliciting a heat shock response in the parasites that is essential for their survival. Eukaryotic cells respond to heat shock by triggering a general arrest in protein translation through phosphorylation of eIF2alpha and transcriptional up-regulation of heat shock protein (HSP) expression to aid protein folding and degradation. This general response appears to be conserved in trypanosomes, but the mechanisms mediating the response are divergent and post-transcriptional in nature.

To capture the molecular events involved in sensing and responding to heat shock in the mammalian infective form we have conducted an initial SILAC-based quantitative proteomic and phosphoproteomic analysis of *T. brucei* cells treated at 41 ^{0}C for 1h [1]. Our analysis indicates that protein abundance does not rapidly respond (≤1 h) to heat shock, and that the changes observed in phosphorylation site abundance are larger and more widespread. The heat shock responsive phosphorylation sites included RNA binding proteins with putative roles in heat shock response such as P-body / stress granules components and the eukaryotic translation initiation 4F complex, but no phosphorylation of eIF2alpha occurred. Dynamic phosphorylation of zinc finger protein ZC3H11 was observed for the first time, a key regulatory RNA binding protein that stabilises heat shock responsive mRNAs and up-regulates HSP expression [2]. We have demonstrated that heat shock causes a specific and reversible cell cycle arrest, and are exploiting temporal quantitative proteomic and phosphoproteomics to reveal the molecular mechanism of heat shock response and recovery. We are also examining the conservation of heat shock response and recovery in *T. congolense*, the major cause of animal African trypanosomiasis.

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References:

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