Arch Toxicol (2013) 87:1–2
DOI 10.1007/s00204-012-0985-1

EDITORIAL

Role of heat shock proteins in stress response and carcinogenesis

C. Cadenas · R. Marchan · H. M. Bolt

Published online: 27 November 2012

In this issue, a truly international collaboration among colleagues, Stuart Calderwood from the USA, Daniel Ciocca from Argentina, and Andre Arrigofrom France, has produced a comprehensive review on the relevance and mechanisms of action of the heat shock proteins—a group of proteins critical for the folding and unfolding of other proteins (Ciocca et al. 2012b). The discovery, dating back to 1962, was made after the curious observation that heat induced a specific pattern of "puffing" in Drosophila chromosomes (Ritossa 1962; Ritossa and O'Loughlin 1996; Schlesinger 1990). These "puffs" were the consequence of increased expression of heat shock proteins. Today, it is well known that different types of stress conditions, including inflammation, infection, hypoxia, starvation, and—particularly relevant for our community—exposure of chemicals can also increase the expression of these proteins (Choi et al. 2011; Chattopadhyay et al. 2011; Romero et al. 2010; Zainul, 2011; Stewart 2011).

Of particular emphasis in the review (Ciocca et al. 2012a, this issue) is the role of heat shock proteins in carcinogenesis and tumor development. When normal cells are transformed, they undergo several major changes, including altered metabolism (Stewart et al. 2012; Cadenas et al. 2012), redox status (Cadenas et al. 2010), cytoskeleton rearrangement (Martin et al. 2012), and reduced apoptosis susceptibility (Petry et al. 2010). However, an especially relevant step in cancer is the upregulation of heat shock proteins. In the review, the authors highlight mechanisms by which these heat shock proteins contribute to carcinogenesis, including:

- the stabilization of growth factor receptor, signaling proteins (e.g., Akt and PI3K) and oncogenes (Bcr/Abl, Raf-1 and mutated P53)
- anti-apoptotic activities (e.g., by inhibition of ASK1 or by stabilizing mitochondria
- the promotion of angiogenesis
- the potential activation of energy metabolism
- protein trafficking and DNA damage control

We highly recommend the contribution of Ciocca and colleagues to anyone with an interest in stress response and carcinogenesis.

C. Cadenas (✉) · R. Marchan · H. M. Bolt
Leibniz InstitutfürArbeitsforschungan der TU Dortmund,
Leibniz Research Centre for Working Environment and Human Factors (IfADo), Ardeystrasse 67, 44139 Dortmund, Germany
e-mail: cadenas@ifado.de

References

Cadenas C, Franckenstein D, Schmidt M, Gehrmann M, Hermes M, Geppert B, Schormann W, Maccoux LJ, Schug M, Schumann A, Wilhelm C, Freis E, Ickstadt K, Rahnenführer J, Baumbach JI, Sickmann A, Hengstler JG (2010) Role of thioredoxinreductase 1 and thioredoxin interacting protein in prognosis of breast cancer. Breast Cancer Res 12(3):R44

Cadenas C, Vosbeck S, Hein EM, Hellwig B, Langer A, Hayen H, Franckenstein D, Büttner B, Hammad S, Marchan R, Hermes M, Selinski S, Rahnenführer J, Peksel B, Török Z, Vígh L, Hengstler JG (2012) Glycerophospholipid profile in oncogene-induced senescence. Biochim Biophys Acta 1821(9):1256–1268

Chattopadhyay A, Podder S, Agarwal S, Bhattacharya S (2011) Fluoride-induced histopathology and synthesis of stress protein in liver and kidney of mice. Arch Toxicol 85(4):327–335

Choi MR, Jung KH, Park JH, Das ND, Chung MK, Choi IG, Lee BC, Park KS, Chai YG (2011) Ethanol-induced small heat shock protein genes in the differentiation of mouse embryonic neural stem cells. Arch Toxicol 85(4):293–304

Ciocca DR, Arrigo AP, Calderwood SK (2012a) Heat shock proteins and heat shock factor 1 in carcinogenesis and tumor development: an update. Arch Toxicol. doi:10.1007/s00204-012-0918-z

Ciocca DR, Cayado-Gutiérrez N, Maccioni M, Cuello-Carrión FD (2012b) Heat shock proteins (HSPs) based anti-cancer vaccines. CurrMol Med. [Epub ahead of print]

Martin M, Müller K, Cadenas C, Hermes M, Zink M, Hengstler JG, Käs JA (2012) ERBB2 overexpression triggers transient high mechanoactivity of breast tumor cells. Cytoskeleton (Hoboken) 69(5):267–277

Petry IB, Fieber E, Schmidt M, Gehrmann M, Gebhard S, Hermes M, Schormann W, Selinski S, Freis E, Schwender H, Brulport M, Ickstadt K, Rahnenführer J, Maccoux L, West J, Kölbl H, Schuler M, Hengstler JG (2010) ERBB2 induces an antiapoptotic expression pattern of Bcl-2 family members in node-negative breast cancer. Clin Cancer Res 16(2):451–460

Ritossa F (1962) A new puffing pattern induced by temperature shock and DNP in Drosophila. Experientia 18:571–573

Ritossa M, O'Loughlin J (1996) Monoamniotic twin pregnancy and cord entanglement: a clinical dilemma. Aust N Z J Obstet Gynaecol 36(3):309–312

Romero C, Benedí J, Villar A, Martín-Aragón S (2010) Involvement of Hsp70, a stress protein, in the resistance of long-term culture of PC12 cells against sodium nitroprusside (SNP)-induced cell death. Arch Toxicol 84(9):699–708

Schlesinger MJ (1990) Heat shock proteins. J Biol Chem 265(21): 12111–12114

Stewart JD (2011) Metal toxicity. EXCLI J 10:133–134

Stewart JD, Marchan R, Lesjak MS, Lambert J, Hergenroeder R, Ellis JK, Lau CH, Keun HC, Schmitz G, Schiller J, Eibisch M, Hedberg C, Waldmann H, Lausch E, Tanner B, Sehouli J, Sagemueller J, Staude H, Steiner E, Hengstler JG (2012) Choline-releasing glycerophosphodiesterase EDI3 drives tumor cell migration and metastasis. Proc Natl Acad Sci U S A 109 (21):8155–8160

Zainul Z (2011) Dark nights behind the white clouds—risks of tobacco smoking on human health besides the oral health and malignancy. EXCLI J 10:69–84