IJAE
Vol. 116, n. 1 (Supplement): 38, 2011
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

A multipronged approach to unveil the emerging role of Hsp60 in chronic obstructive pulmonary disease

Francesco Cappello[1,2], Antonino Di Stefano[3^], Gaetano Caramori[4], Claudia Campanella[1,2], Chiara Vicari[3], Isabella Gemmi[3], Andrea Zanini[3], Antonio Spanevello[3], Armando Capelli[3], Giampiero La Rocca[1,2], Rita Anzalone[1], Fabio Bucchieri[1,2], Silvestro Ennio D'Anna[3], Fabio L.M. Ricciardolo[5], Paola Brun[6], Bruno Balbi[3], Mauro Carone[3], Everly Conway de Macario[7], Alberto J.L. Macario[2,7], Giovanni Zummo[1]

[1] Dipartimento BIONEC, Sezione di Anatomia Umana, Università di Palermo, Italy. [2] IEMEST, Palermo, Italy. [3] Fondazione S. Maugeri, IRCCS, Italy. [4] Dipartimento di Medicina Clinica e Sperimentale, Università di Ferrara, Italy. [5] Dipartimento di Scienze Cliniche e Biologiche, Università di Torino, Italy. [6] Dipartimento di Istologia, Microbiologia e Biotecnologie Mediche, Università di Padova, Italy. [7] Department of Microbiology and Immunology, School of Medicine, University of Maryland at Baltimore, Baltimore (MD), USA

Inflammation is a major component of chronic obstructive pulmonary disease (COPD) and its cause and mechanisms are still incompletely understood. For example, the role of heat shock proteins (Hsps), many of which are molecular chaperones, has not been explored in detail in COPD, despite the fact that these molecules are known to participate in inflammation in other diseases. It has been shown that extracellular Hsps can signal certain types of T cells, macrophages, dendritic cells, and neutrophils and, thereby, elicit inflammation and immunity. However, these phenomena have not been investigated in COPD despite: a) the increasing awareness of Hsp participation in inflammation and immunity; and b) the fact that this disease is waiting for new knowledge to benefit from effective treatment and continues to be one of the commonest and most serious illnesses in the Western countries. We developed a strategy to study Hsps in COPD involving a multipronged approach, using *in vivo* and *in vitro* methods, which would, at least in part, compensate for the limitations inherent to the analysis of human diseases. We determined the levels of six Hsps in bronchial mucosa biopsies, as well as several inflammatory markers, from patients at various stages compared to smoker and non-smoker controls by immunohistochemistry, and found significant increase of Hsp60, Hsp10, and Hsp40 in COPD but no changes for Hsp27, Hsp70 and Hsp90. We also found that the increase in Hsp60 positively correlated with number of neutrophils, and it localized in them. Hsp60 has been implicated in human inflammatory pathology; hence it was pertinent to investigate whether the chaperonin originated only in the neutrophils or also in other cells. *In vitro* experiments showed that in bronchial epithelial cells submitted to oxidative stress, a characteristic of COPD mucosa, Hsp60 was overexpressed and was released into the extracellular medium. Other measurements indicated that NFkB-p65 was involved in the *hsp60*-gene upregulation whereas HSF-1 apparently was not. All the data we obtained using a battery of complementary *in vivo* and *in vitro* methods coincided to indicate that Hsp60 plays an active role in inflammation in COPD. Hence, one can infer that the chaperonin does contribute to the etiology and/or pathogenesis of COPD and that it is pertinent to investigate this aspect of Hsp60 biology-COPD pathology with renewed intensity. The results could have a significant impact on the developing of strategies for diagnosis, determining prognosis, and treatment that should be centered on Hsp60.

Keywords: Airways, Bronchial mucosa, Heat shock proteins, Chaperones, Inflammation, Neutrophils