Hsp60 in embryonic and adult submandibular salivary gland: quantitative distribution patterns in normal tissue and comparison with benign and malignant tumors

Charbel Basset1, Francesco Cappello1,2, Giovanni Tomasello1, Francesca Rappa1, Ada Maria Florena3, Abdo Jurjus4, Alberto J. L. Macario2,5, and Angelo Leone1

1Department of Biomedicine, Neuroscience and Advanced Diagnostic, Section of Histology and Embryology, University of Palermo, Italy
2Euro-Mediterranean Institute of Science and Technology (EMEST), Palermo, Italy
3Department of Medical and Surgical Sciences, University of Messina, Messina, Italy
4Promotion della Salute, Materneo-Inferme, di Medicina Interna e Specialistica di Eccellenza “G. D’Alelessandro”
5American University of Beirut, Department of Anatomy, Cell Biology & Physiology, Faculty of Medicine, Lebanon

Department of Microbiology and Immunology, University of Maryland at Baltimore-Institute of Marine and Environmental Technology (IMET), Baltimore, MD, USA.

Abstract

Introduction: Heat Shock Protein 60 (Hsp60) is a member of the chaperone system that assists protein folding inside mitochondria and plays other roles beyond these arginules. It is implicated in the carcinogenic processes in various types of cancer. In human salivary glands, Hsp60 has not yet been measured or mapped in detail and its role in gland development and functioning is virtually unknown. Consequently, its potential as biomarker for gland diseases, including malignancies cannot be assessed. The S-100 protein, a known marker for schwannomas, has been found also in myoepithelial cell carcinomas of the salivary glands. Here, we present our initial findings on the anatomic-histological distribution of Hsp60 in human submandibular salivary gland (SMG) at various stages of development and its changes during tumorigenesis, in parallel with changes of S-100 in salivary gland tumors.

Methods: Adult human submandibular gland (normal and tumoral) and embryonic head tissue samples were processed by standard methods for routine histological analysis. Additionally, these sections underwent immunohistochemical staining using antibodies against Hsp60 and S-100. Specimens from patients were obtained from the archives of the Human Pathology Section, Department of Health Science, University of Palermo, Italy. All procedures were in accordance with the Helsinki Declaration. We determined the percentages of cells immunopositive for Hsp60 or S-100 and made comparative evaluations applying the one way ANOVA.

Results: Hsp60 was present in the acini and ducts of embryonic salivary glands but had a different distribution pattern in adult glands: it occurred only in the ducts and in a few acini. In contrast, Hsp60 was not detected in Pleomorphic Adenoma (PA) or Warthin’s tumor (WT), whereas its levels were high in Adenoid Cystic Adenocarcinoma (ACC). S-100 was present in the nuclei and/or in the cytoplasm in PA and ACC and its levels in the nuclei of ACC was lower than in the PA ones.

Conclusions: Since the chaperonin is abundant in acini and ducts of embryonic salivary glands, it can be hypothesized that it actually participates in the developmental process leading to the formation of a wholly functional adult, mature organ. Hsp60 and S-100 immunoposivities were high in the malignant tumor implying their involvement in neoplasm formation and progression. These results foreshadow the diagnostic and prognostic potential of Hsp60 and S-100 when measured side by side as biomarkers useful for distinguishing between benign and malignant tumors.

Keywords: Submandibular salivary gland (SMG); Heat shock protein (Hsp); Hsp60; salivary glands; molecular chaperone; embryo vs. adult patterns; Pleomorphic Adenoma (PA); Warthin’s tumor (WT); Adenoid Cystic (Adenocarcinoma (ACC)); S-100 protein (S-100).

1. Hsp60 is present in the acini and ducts of human embryonic SMG

2. Hsp60 is present in the ducts of adult human SMG like in the embryonic counterparts but, in contrast to the latter, it is scarce in the acini

3. Hsp60 was undetectable in the nucleus or the cytoplasm of WT cells

4. S-100 but not Hsp60 is present in the nuclei and cytoplasm of PA cells

5. Hsp60 and S-100 are both present in the nuclei and cytoplasm of ACC cells

6. The quantitative distribution pattern of Hsp60 in the benign tumors WT and PA is different from that of the malignant SMG carcinoma ACC

- High levels of Hsp60 were detected in acini and ducts of the submaxillary gland (SMG) of 13-week old embryos, suggesting that the chaperonin is implicated in the anatomic and physiological development of this gland.

- In adult SMG the distribution pattern of Hsp60 was different from that observed in embryos. The predominant localization of Hsp60 in salivary ducts rather than in acini of adult healthy SMG suggests a shift in its role with age. In the adult SMG, the chaperonin may be involved in the mechanism of saliva secretion.

- The distinctive quantitative and distribution patterns of Hsp60 and S-100 that characterize normal SMG, WT, PA, and ACC, are noteworthy, and point to their potential in differential diagnosis and in the histopathological monitoring of patients.