

- [2] Clement P, Scully R. Mullerian adenosarcoma of the uterus: a clinicopathologic analysis of 100 cases with a review of the literature. *Hum Pathol* 1990;21:363–81.
- [3] Chang K, Crabtree G, Lim-Tan S, Kempson R, Hendrickson M. Primary uterine endometrial stromal neoplasms. *Am J Surg Pathol* 1990;14:415–39.
- [4] Amant F, Moerman P, Cadron I, Neven P, Berteloot P, Vergote I. The diagnostic problem of endometrial stromal sarcoma: report on six cases. *Gynecol Oncol* 2003;90:37–43.
- [5] Michener C, Simon N. Ovarian conservation in a woman of reproductive age with Müllerian adenosarcoma. *Gynecol Oncol* 2001;83:424–7.

### **HSP60 and HSP10 as diagnostic and prognostic tools in the management of exocervical carcinoma**

To the Editor:

For two decades, many studies have focused on the role of heat shock proteins (HSPs), a family of molecules involved in many cellular functions, such as protein folding, in genitourinary carcinogenesis including the uterine cervix. In this journal, for example, Park et al. [1] suggested that HSP70 is frequently found to be positive on immunohistochemical analysis in uterine cervical cancer, especially in the early stages, and that it could be useful in management of the disease.

We recently investigated the diagnostic and prognostic roles of HSP60 and HSP10, two strictly related mitochondrial chaperons, in a number of carcinogenic models. In particular, in two recent articles [2,3], we showed that these proteins, on immunohistochemical and biomolecular analyses, may aid in the diagnosis of exocervical lesions, in both invasive and preinvasive stages. Indeed, the lesions showed an intracytoplasmic accumulation of these molecules, and positivity increased from normal to dysplastic to neoplastic tissues. Moreover, low-grade squamous intraepithelial lesion (L-SIL) and high-grade squamous intraepithelial lesion (H-SIL) showed a different pattern of localization, since in the former both proteins localized only in the cells of basal and para-basal layers of exocervical epithelium, while the latter showed an diffuse positivity in all layers. We know that dysplasia arises when germinal cells of the basal layer of the epithelium, following exogenous or endogenous stimuli, lose their ability to divide and differentiate into mature cells and accumulate in thicker epithelium. Moreover, the biological distinction between L-SIL and H-SIL is that the latter completely lacks mature elements and in the former differentiation is slower. We found the immunohistochem-

ical features between L-SIL and H-SIL to be distinct, in agreement with pathogenetic knowledge on how dysplasia arises and the finding that HSP accumulation is possibly related to the altered differentiation of basal cells.

In summary, we postulate a role for HSPs in carcinogenesis of the uterine exocervix, as well as in other areas [4,5]. The exact nature of this role is far from being understood. We are working to detect the presence of gene mutations in HSP60 and HSP10. Since the HSP60–HSP10 complex is involved in activation of the caspase cascade (apoptotic machinery) in mitochondria during hypoxic–ischemic damage, we are studying the intracytoplasmic molecular pathways of these proteins in hope of finding some analogies during carcinogenesis. We maintain that modulation of their expression, by gene therapy, may modify the natural history of these cancers. At the same time, we consider it to be great interest for clinicians to use the levels of HSPs in the sera of patients with preneoplastic or neoplastic lesions as a prognostic tool during follow-up.

Dr. Francesco Cappello\*

*Human Anatomy Section*

*Department of Experimental Medicine*

*University of Palermo*

*via del Vespro 129, 90127 Palermo, Italy*

doi:10.1016/j.ygyno.2003.08.009

### **References**

- [1] Park CS, Joo IS, Song SY, Kim DS, Bae DS, Lee JH. An immunohistochemical analysis of heat shock protein 70, p53, and estrogen receptor status in carcinoma of the uterine cervix. *Gynecol Oncol* 1999;74:53–60.
- [2] Cappello F, Bellafiore M, Palma A, Marcianò V, Martorana G, Belfiore P, et al. 60kDa heat shock protein (HSP60) expression increases during carcinogenesis of uterine exocervix. *Pathobiology* 2002;70:83–8.
- [3] Cappello F, Bellafiore M, David S, Anzalone R, Zummo G. 10 kDa heat shock protein (HSP10) is overexpressed during carcinogenesis of large bowel and uterine exocervix. *Cancer Lett* 2003;196:35–41.
- [4] Cappello F, Bellafiore M, Palma A, David S, Marcianò V, Bartolotta T, et al. 60kda chaperonin (hsp60) is over-expressed during colorectal carcinogenesis. *Eur J Histochem* 2003;47:105–10.
- [5] Cappello F, Rappa F, David S, Anzalone R, Zummo G. Immunohistochemical evaluation of PCNA, p53, HSP60, HSP10 and MUC-2 presence and expression in prostate carcinogenesis. *Anticancer Res* 2003;23:1325–31.

---

\* Fax: +39-091-6553518.