well as 43 corresponding metastatic lymph nodes and 45 distant metastases (29 hepatic and 16 omental). Twenty biopsies from the right and left colon of ten patients affected by irritable bowel syndrome and 45 additional specimens of transitional mucosa were also studied.

Independent of tumour stage, a variable staining intensity was encountered in 61.2% of carcinomatous samples. In particular, a strong MT expression was noted in neoplastic areas with comedo-like appearance or rich in inflammatory cells. All adenomatous samples exhibited a distinct MT staining, mostly limited to the basal glandular portions (Fig. 1). Lymph node samples showed a variable MT immunoreactive pattern in 55.8% of cases (Fig. 2), independent of the immunoreactivity or the staining intensity of the corresponding carcinomas. Reactivity of hepatic metastases was seen in five cases (17.2%), while MT expression was noted in 43.8% of omental secondaries. Enterocytes present at the luminal surface and crypts of normal colonic mucosa were generally reactive, with a more pronounced staining of the transitional mucosa.

Since our observations have shown MT immunoreactivity in normal colonic mucosa and adenomas as well as in a conspicuous percentage of primary and metastatic sites of carcinoma, the suggestion made by Ofner et al. that MT expression may represent an early event in colonic carcinogenesis associated with tumour progression should be considered with caution. However, the role for MT as a free radical scavenger as well as the capability of some cytokines to induce MT synthesis in vitro and in vivo [2] remains to be fully elucidated in normal and neoplastic colonic cells.

References

1. Öfner D, Maier H, Riedmann B, Bammer T, Rumer A, Winde G, Böcker W, Jasani B, Schmid KW (1994) Immunohistochemical metallothionein expression in colorectal adenocarcinoma - correlation with tumour stage and patients survival. Virchows Arch 425:491–497
2. Sato M, Bremner I (1993) Oxygen free radicals and metallothionein. Free Radic Biol Med 14:325–337
3. Schmid KW, Ellis IO, Gee JMW, Darke BM, Lees WE, Kay J, Cryer A, Stark JM, Hittmair A, Öfner D, Dünser M, Margreiter R, Daxenbichler G, Nicholson RI, Bier B, Böcker W, Jasani B (1993) Presence and possible significance of immunocytochemically demonstrable metallothionein over-expression in primary invasive ductal carcinoma of the breast. Virchows Arch [A] 422:153–159
4. Zelger B, Hittmair A, Schir M, Öfner C, Öfner D, Fritsch PO, Böcker W, Jasani B, Schmid KW (1993) Immunohistochemically demonstrated metallothionein expression in malignant melanoma. Histopathology 23:257–264

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Reply

Sirs: We thank Drs. Tuccari, Giuffrè and Barresi for their interest in our paper [3] dealing with immunohistochemically detectable metallothionein (MT) expression in colorectal carcinoma. We acknowledge the close resemblance of their data to ours with respect to the incidence of focal or diffuse MT expression in adenomatous remnants, carcinomas and normal and transitional mucosa. Our study was focused specifically on expression in colorectal carcinomas. Pure adenomas or lymph node metastases were not included though we did examine liver metastases in two cases; nor did we examine MT expression in relation to inflammatory cell infiltrates. Tuccari's work therefore provides additional useful information. In this respect, the differing rates of MT expression in lymph nodes, omental deposits and liver metastases are worthy of note, as is their observation of strong MT expression in neoplastic areas rich in inflammatory cells. As for the adenomas, we have recently completed an analysis of MT expression in a series of 205 pure adenomas and our findings in general correlate with their observations. We would however, like to clarify that we did not mean to imply that MT expression is an *early* event in colorectal tumour development, but rather that it appears to be an *earlier* event in tumour progression when compared with what we have observed in breast cancer and melanoma [1, 2, 4].

References

1. Bier B, Douglas-Jones A, Tötsch M, Dockhorn-Dworniczak B, Böcker W, Jasani B, Schmid KW (1994) Immunohistochemical demonstration of metallothionein in normal human breast tissue and benign and malignant breast lesions. Breast Cancer Res Treat 30:213–221
2. Douglas-Jones AG, Schmid KW, Bier B, Horgan K, Lyons K, Dallimore ND, Moneypenny I, Jasani B (1995) Metallothionein (MT) expression in duct carcinoma in situ (DCIS) of the breast. Hum Pathol 26:217–222
3. Öfner D, Maier H, Riedmann B, Bammer T, Rumer A, Winde G, Böcker W, Jasani B, Schmid KW (1994) Immunohistochemical metallothionein expression in colorectal adenocarcinoma - correlation with tumour stage and patients survival. Virchows Arch 425:491–497
4. Zelger B, Hittmair A, Schir M, Öfner C, Öfner D, Fritsch PO, Böcker W, Jasani B, Schmid KW (1993) Immunohistochemically demonstrated metallothionein expression in malignant melanoma. Histopathology 23:257–264

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