

**Figure 4**

**HA staining in poorly differentiated stromal areas:** Top row, (A, B, C) represents breast, stomach and gallbladder. Middle row, (D, E, F) represents colon, caecum and prostate. Bottom row, (G, H) represents urinary bladder and renal cell carcinoma. The stromal and intratumoral areas are highly positive for HA in all tumors, where as the loss of HA expression observed in the tumor cells. Arrow shows the tumor cells and the asterisk shows stroma. Scale bars, 50  $\mu$ m.

medulloblastoma, osteosarcoma, endocervix and non-Hodgkin's lymphoma expressed increased amount of HA in both tumor epithelia and the intratumoral areas.

Considerable evidence has been documented the significance of hyaluronan expression during human tumor progression where it was frequently observed in elevated levels around tumor cells facilitating tumor migration and proliferation [20]. High levels of HA expression correlates with poor tumor differentiation and poor survival rates [11,12]. Tumor cells differentiation during malignant transformation in bronchial and squamous cell carcinoma demonstrated the changes in HA distribution [15].

Albeit many tumor cells are enriched in HA [26], they nonetheless showed considerable variations in HA expression depending on their origin as well as on the histological type of the tumors [17]. Elevated levels of HA are found in most carcinomas of squamous-cell origin, colorectal epithelial [11], ovarian [21] and breast [22]. On the other hand loss of HA in progressive carcinomas from laryngeal, esophageal, colorectal and cutaneous melanomas [27] was observed. This generalization, and many years of investigations with conflicting reports on the spatial distribution of hyaluronan in early and late malignancy have increased the depth of the dilemma about the role of HA during tumor progression.