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Chondroitin sulfate structure is modified in human milk produced by breast affected by invasive carcinoma

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A 35-year-old premenopausal woman presented during the second month of lactation a hypoecogen nodule with disomogeneus patterns in the superior lateral quadrant of the left breast area. The core biopsy showed multiple fragments of a tumor completely formed by papillae with a fibrovascular core and lined by multiple layer of neoplastic cells. The tumor was diagnosed as papillary infiltrating carcinoma, grade 3 according to Elston-Ellis. Right breast was unaffected.

Glycosaminoglycans from milk samples produced from left and right breasts were extracted and quantified by analytical procedures reported in details in Coppa et al.[1] HPLC separation of chondroitin sulfate (CS) disaccharides from milk produced by normal breast showed ~70% ΔDi-0s, ~7% ΔDi-4s and ~23% ΔDi-6s (Fig. 1A). As a consequence, the CS showed a very low charge density value of 0.30 and a nonsulfated/monosulfated ratio of ~2.3, according to previous study.[1] On the contrary, disaccharides obtained from human milk CS extracted from cancer left breast (Fig. 1B) mainly produced ΔDi-6s (61%) with a strong decrease of ΔDi-0s (30%, −57% vs normal breast) and a low percentage of ΔDi-4s (9% quite similar to normal breast) accounting for a higher charge density value of 0.70 and a nonsulfated/monosulfated ratio of ~0.4.

For the first time we demonstrated that the structure and properties of CS present in human milk produced by a breast affected by invasive carcinoma are different from healthy tissues. In particular, an increase in the disaccharide sulfated in position 6 of *N*-acetylgalactosamine unit with a strong increase in CS sulfation of milk from cancer-affected breast was observed. Finally, modifications in the structure of CS and CS-proteoglycans of tumor stroma and extracellular matrix[2–4] are reflected in the composition of the main product of the breast during lactation, i.e. human milk, having implications in tumor development and treatment also possibly related to its diagnosis.

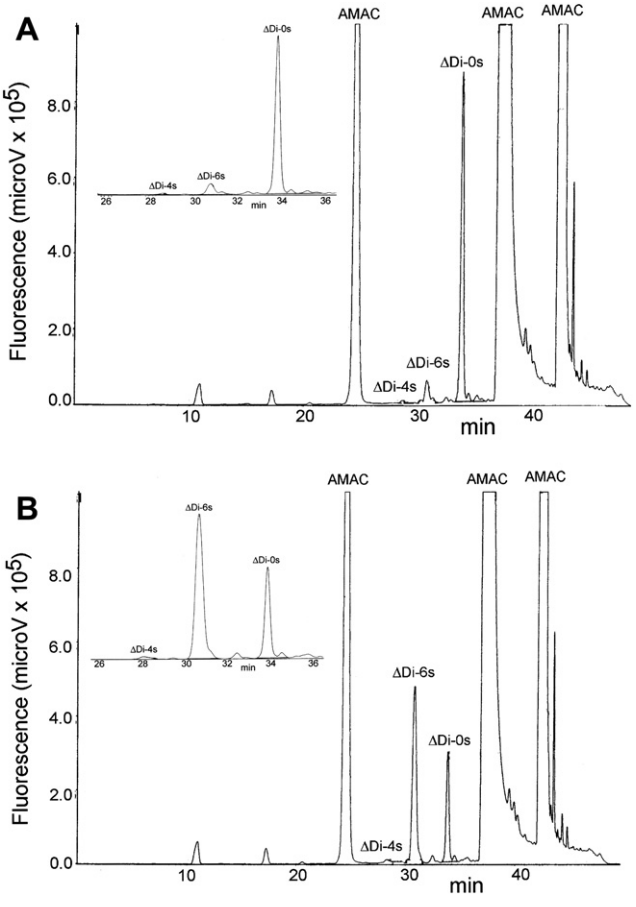

Fig. 1. HPLC chromatograms of unsaturated disaccharides from milk CS produced by right (A) and left (B) breast treated with chondroitinase ABC and fluorotagged with AMAC. Expanded chromatograms from 26 to 36 min are illustrated inside the panels A and B. AMAC, 2-Aminoacridinone. ΔDi-0s, ΔUA-GalNAc. ΔDi-4s, ΔUA-GalNAc(4s). ΔDi-6s, ΔUA-GalNAc(6s).

Contributors

N.V. developed the applied methodologies. F. Mac. performed the experimental procedures and analyses. F. Man. contributed in

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milk sample collection. N.V. designed and developed the experimental design, performed data analysis and wrote the manuscript. A.S. performed histologic and immune-histochemical analyses. All authors reviewed and approved the study.

Conflicts of interest statement

We declare that we have no conflicts of interest.

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