Embryo-like construction of cancer and the potential implication of connective tissue and fractones in cancer progression

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According to the literature, the presence of punctate extracellular matrix (ECM) in cancer has been interpreted as a destructive process resulting in basement membrane (BM) fragmentation. Using immunohistochemistry and confocal microscopy on 90 surgical tissues of human cancer, we show here that these ECM puncta are fractones, the ECM structures characterizing stem cell niches. We previously demonstrated that fractones bind and activate growth factors, which in turn transduce regulatory signals for cell proliferation, differentiation and migration. In the present study, fractones were omnipresent in the tumor masses of colon, stomach, brain, liver, lung, kidney, ovary, breast and pancreas, regardless of cancer stage. Fractones abounded in cell masses devoid of BM, and along thin branches of connective tissue without overlying BM. Focusing on colon carcinoma, we nevertheless characterized BM in a highly-organized meshwork of large connective tissue, instead of their typical location under a typical mono-layered glandular epithelium. We anatomically demonstrate that the process of carcinoma construction resembles that of the developing embryo, particularly that of early stages of brain morphogenesis. Similarly to the brain neuroepithelium, scaffolding meninges and ventricles, colon carcinoma developed multi-cell layers sandwiched between fluid cavities and connective tissue. Our results demonstrate that cancer is characterized by the presence of fractones and a modified connective tissue architecture. We anticipate that both dictate the characteristics of tumor formation and evolution. Understanding the function of fractones in cancer will provide new insights into the basic mechanisms of cancer and will suggest us how to stop the progression of the pathology.