Targeting of natural killer cells to mammary carcinoma via naturally occurring tumor cell-bound iC3b and beta-glucan-primed CR3 (CD11b/CD18).

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Source
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Abstract
Previous reports have suggested that malignant cells frequently generate a humoral immune response that is ineffective in tumor destruction. Despite coating tumors with IgM and IgG that activate the C system via the classical pathway, normal membrane regulators of C (e.g., membrane cofactor protein and CD59) prevent cytotoxicity. Moreover, C3 deposition on tumors does not result in cytotoxic recognition by phagocytes or NK cells bearing C3 receptors capable of mediating destruction of C3-opsonized bacteria or yeast. The current investigation showed that freshly excised mammary tumors bore IgM, IgG, and C3 detectable by flow cytometry. Normal sera contained natural IgM and IgG Abs reactive with breast tumor cell lines, and IgG Ab titers were increased in patients with breast cancer. Breast tumor cell lines incubated in normal serum from AB+ individuals activated the classical, but not the alternative, pathway of C and became coated with C3. Despite exhibiting membrane-bound C3, serum-opsonized breast tumor cell lines were not killed by CR3 (CD11b/CD18)-bearing NK cells. Priming of NK cell CR3 with small soluble yeast beta-glucan polysaccharides enabled CR3-dependent killing of these same C3-bearing tumor cell lines. Tests of mammary carcinoma cells from freshly excised tumors demonstrated that they also bore sufficient amounts of opsonic C3 for cytotoxic recognition by NK cells bearing polysaccharide-primed CR3, whereas they were largely resistant to NK cells bearing unprimed CR3. This study demonstrates the potential utility of using naturally occurring opsonic C3 on tumor cells for specific immunotherapeutic targeting by NK cells and phagocytes bearing polysaccharide-primed CR3.

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