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Rolling in the Deep:

Employing blood cells as drug carriers to target disseminating tumor cells

Abstract: Metastasis contributes to over 90% of cancer-related deaths. Many types of cancer metastasize via the bloodstream, where circulating tumor cells (CTCs) originating from the primary tumor can undergo selectin-mediated adhesion with the blood vessel wall and subsequently transmigrate to anatomically distant organs. In an effort to neutralize CTCs with the potential to form metastases, a new therapeutic approach has been developed in which circulating leukocytes are functionalized with TRAIL protein to target and kill cancer cells in the bloodstream. The resulting ‘unnatural killer cells’, proven effective *ex vivo* with human blood samples and also in the living mouse, holds promise in neutralizing CTCs to interrupt the metastasis process. One can exploit the unique responses of cancer cells to physiological levels of fluid shear stress to identify optimal therapeutics for targeting CTCs in blood. A related approach functionalizes natural killer cells with therapeutic liposomes, which reside in the draining lymph nodes and block the formation of new metastases there. This platform technology of cellular drug delivery will be discussed, along with future directions in the effort to translate liposome-based TRAIL therapy to benefit human patients.