Profilin-1 downregulation in CTL of pancreatic cancer patients results in increased migration and killing efficiency

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CTL roam the body to find and fight cancerous or pathogen infected cells. Until today little is known how CTL in humans adapt their migration or killing behavior in the cancer context. In this work we found that actin-binding protein profilin-1 (PFN1) levels are significantly downregulated in pancreatic cancer patients compared to healthy individuals. PFN1 overexpression correlated with decreased CTL cytotoxicity, whereas PFN1 down-regulation resulted in increased CTL cytotoxicity, which was paralleled by enhanced CTL migration and invasion. Using the Y59A mutant of PFN1, which cannot bind actin, we show that PFN1 tunes the preference of CTL to form similar-sized (balanced), differently-sized (unbalanced) or single dominant protrusions. Higher probability of dominant protrusion formation correlated with enhanced migration velocity and persistence in a collagen matrix. We conclude that in pancreatic cancer patients PFN1 down-regulation is correlated with increased CTL functionality. Thus, PFN1 down-regulation might well be a compensatory mechanism employed by CTL to fight cancer.