Anti-Leukemia Effect by Stimulated-Macrophages in Co-Culture

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CD47 is over-expressed in Acute Myeloid Leukemia (AML) and functions as inhibitory signal, suppressing phagocytosis by binding to signal regulatory protein α (SIRPα) on the surface of macrophages. Inhibition of CD47 restores the immune surveillance of AML cells. However, the inhibition of CD47 in AML by activated macrophages and the subsequent effects on different immune response parameters are not fully understood. Here, we demonstrate the use of a distinct co-culture method to inhibit CD47 and therefore eliminate AML cells by macrophages in vitro, shown in Figure 1. Human chemical induced THP-1 macrophages were activated by using different concentrations of lipopolysaccharide (LPS) and co-culturing with three AML cancer cell lines (HL-60, NB4, and THP-1), respectively, as well as normal cells. CD47 inhibition was successful and selective in AML but not normal cells. Additionally, calreticulin (CRT) levels were elevated in the same cell lines simultaneously, after co-culturing with activated human macrophages, but not in normal cells. We also show that activated macrophages secreted high levels of cytokines including, IL-12p70, IL-6 and TNF-α, consistent with the elimination of AML by macrophages. [1] Our study reveals the potential of this model for screening new drugs against AML and the possibility to use human macrophages in AML treatment in the future.