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P2X1 RECEPTORS AS NEW REGULATORS OF NEUTROPHIL LIFE SPAN

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**Abstract**

**Introduction:** Extracellular ATP locally released at the inception of inflammation acts as a danger signal notably through activation of leucocyte P2X7 receptors.

**Methods:** We used RT-PCR, Western blotting and immunofluorescence experiments to demonstrate that P2X1 receptors are present on both human and mouse peripheral blood neutrophils. We then sought to determine whether P2X1 influenced in vitro spontaneous neutrophil apoptosis. Human neutrophils were incubated with the selective P2X1 agonist, ,-meATP and stained with annexin V and propidium iodide (PI).

**Results:** After 3 hours, ,-meATP increased the percentage of annexin V-stained cells from about 10 to 20% while it increased the percentage of PI-stained cells after 20 hours from 20 to 30%. Treatment of neutrophils with the P2X1 antagonist, NF449, reduced PI incorporation after 20 hours by about 25%. The , -meATP effects could not be correlated with increased caspase-3 activation or with a reduction of FcRIII expression unless protein synthesis was inhibited, suggesting that ,-meATP triggers both survival and death signals. A microarray analysis revealed that a 3-hour incubation with ,-meATP changes the expression of genes encoding both pro-apoptotic (e.g., PTEN, Foxo3A, caspase-8) and anti-apoptotic (e.g., NF-B2) proteins. Peripheral blood neutrophils from P2X1-deficient mice displayed delayed late apoptosis, as revealed by a 2-fold reduction of annexin V- and PI-stained cell percentage after 20 hours as compared to wild-type mice. In contrast, the percentage of annexin V-stained cells after 3, 6 and 9 hours were identical.

**Conclusions:** Hence, activation of P2X1 receptors by extracellular ATP may represent novel mechanisms that control neutrophil life span.