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Biosynthesis and turnover of anandamide and other N-acylethanolamines in peritoneal macrophages

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Polyunsaturated N-acylethanolamines (NAEs), including anandamide (20:4n-6 NAE), elicit a variety of biological effects through cannabinoid receptors, whereas saturated and monounsaturated NAEs are inactive. Arachidonic acid mobilization induced by treatment of intact mouse peritoneal macrophages with  $\text{Ca}^{2+}$  ionophore A23187 had no effect on the production of NAE or its precursor N-acylphosphatidylethanolamine (N-acyl PE). Addition of exogenous ethanolamine resulted in enhanced NAE synthesis by its N-acylation with endogenous fatty acids, but this pathway was not selective for arachidonic acid. Incorporation of  $^{18}\text{O}$  from  $\text{H}_2^{18}\text{O}$ -containing media into the amide carbonyls of both NAE and N-acyl PE demonstrated a rapid, constitutive turnover of both lipids.