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**Attenuation of Platelet Activating Factor (PAF)-induced
Stimulation of Rabbit Platelet GTPase by Phorbol
Ester, Dibutyryl cAMP and Desensitization :
Concomitant Effects on PAF Receptor
Binding Characteristics***

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The GTPase activities of rabbit platelet membrane were stimulated by platelet activating factor (PAF) in a receptor-mediated manner. The activities of the GTPase were investigated in the platelets which had been pretreated with tetradecanoyl phorbol acetate (TPA), dibutyryl cAMP, and PAF. The specific binding of PAF to intact platelet cells was also determined in these treated cells. In platelets which had been pretreated with PAF and then specifically desensitized to PAF, higher concentrations were required for stimulation of the receptor-coupled GTPase. In addition the extent of stimulation of the GTPase by PAF was also decreased. By contrast thrombin stimulation of GTPase activity was unaffected by this process. In platelets pretreated with high levels of dibutyryl cAMP (4 mM), the specific binding of PAF was reduced to nearly 50% of the control. Although this specific binding apparently was not inhibited by lower concentrations of dibutyryl cAMP (2 mM), PAF could stimulate the receptor-coupled GTPase only to a much lower extent in these treated cells. TPA had virtually no effect on PAF specific binding. However, higher concentrations were needed for stimulation of the GTPase. On the other hand, the extent of PAF stimulation of the GTPase was not altered. Interestingly in the TPA-treated platelet membrane, thrombin stimulated GTPase activity to a higher level than that in untreated platelet membrane. Thus, TPA, dibutyryl cAMP, and desensitization affected the PAF receptor binding and the receptor-coupled GTPase activities in a characteristic fashion. The molecular mechanisms of these effects are discussed.

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