

Supplement material

# The Natural Cyclic AMP Antagonist Prostaglandylinositol Cyclic Phosphate (Cyclic PIP) Triggers, Depending on Time, Two Opposing Alpha-Adrenoceptor Effects on Glucose Release from Rat Liver

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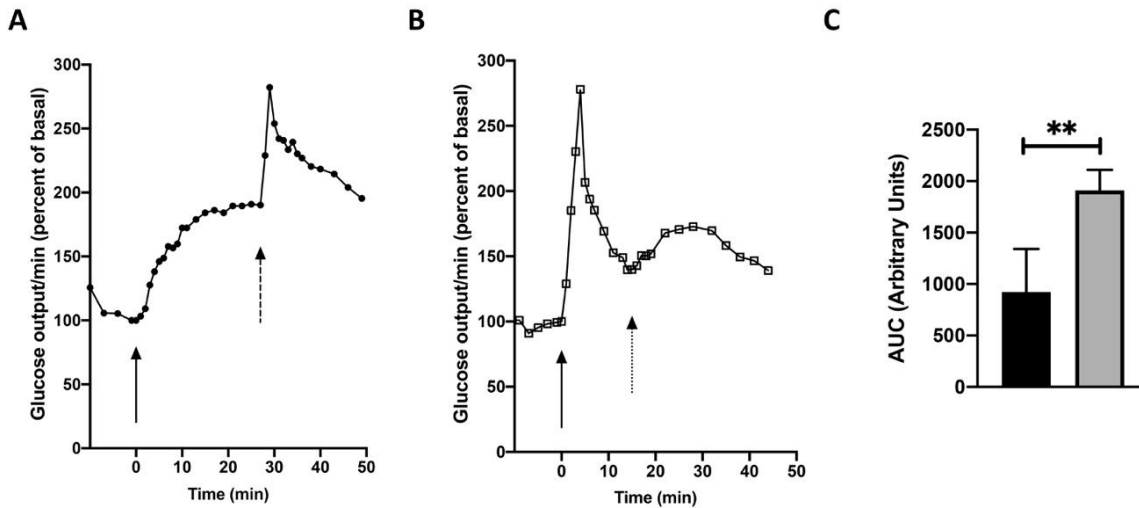
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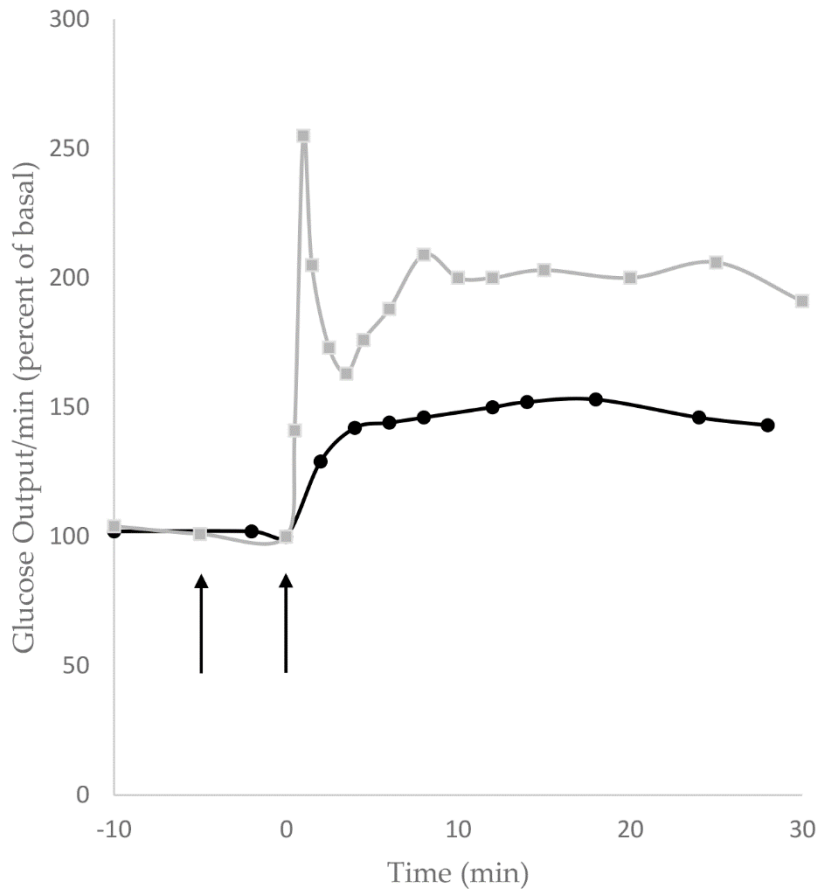
<sup>a</sup> See acknowledgement.

<sup>b</sup> Retired.



**Figure S1.** Time course of glucose release from male rat liver on successive stimulation with glucagon and adrenaline. **(A)** Stimulation with glucagon ( $10^{-9}$  M) at 0 min and with adrenaline ( $10^{-7}$  M) at 27 min; **(B)** Stimulation with adrenaline ( $10^{-6}$  M) at 0 min and with glucagon ( $10^{-9}$  M) at 15 min. (The arrows indicate the times of hormone addition.) **(C)** The glucagon-stimulated glucose release after adrenaline stimulation (Figure S1B) is significantly smaller (Figure S1 C, black bar) than the glucose release on a first stimulation with glucagon (Figure S1 C, grey bar). The baseline used was the glucose release on adrenaline stimulation (Figure 5, male rat). \*\*  $p < 0.005$  with versus without preceding adrenaline stimulation.

Figure S1A shows that the stimulation of glucose release with glucagon and adrenaline is additive, since  $10^{-9}$  M glucagon stimulated glucose release maximally [52, pp. 236–238]. This result indicates that two different reaction pathways are involved. On stimulation the other way around the second stimulation with glucagon is significantly decreased because on the first stimulation with adrenaline the synthesis of cyclic PIP was increased, which inhibits adenylate cyclase and therefore on the second stimulation with glucagon a decreased glucose release was determined.



**Figure S2.** Adrenaline ( $10^{-6}$  M) stimulated glucose release in the absence (gray curve) and presence (black curve) of  $10^{-6}$  M phentolamine (alpha-adrenoceptor antagonist) from female rat livers. Phentolamine prevented the  $\alpha$ -adrenoceptor triggered, spike-shaped glucose release, but not the  $\beta$ -adrenoceptor triggered component. However, because of a small affinity of phentolamine to the  $\beta$ -adrenoceptor, the cyclic AMP triggered glucose release is lower in the presence than in the absence of phentolamine.