

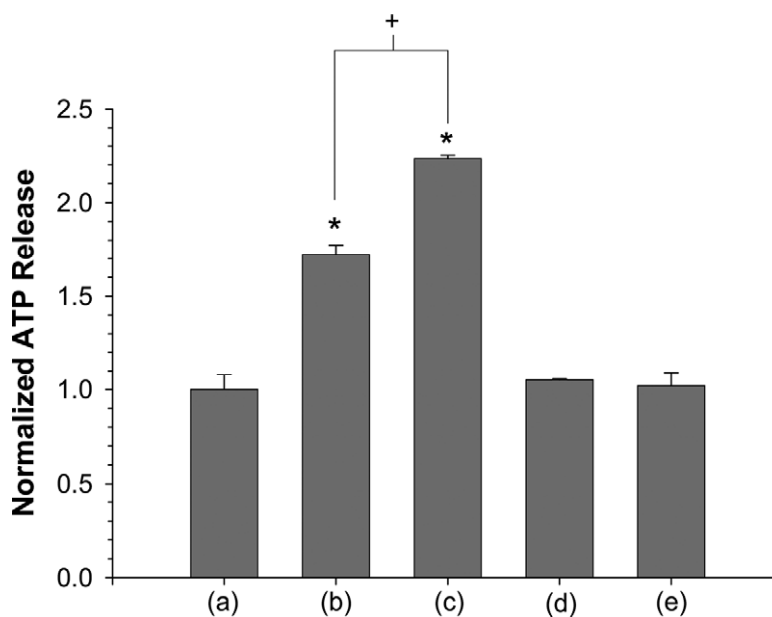


Fig. S1. Normalized ATP release of rabbit ERYs incubated (a) alone, (b) with 20 nmol l⁻¹ Zn²⁺ and C-peptide, (c) with 20 nmol l⁻¹ Zn²⁺, C-peptide and 30μmol l⁻¹ metformin, (d) 30μmol l⁻¹ metformin and 20 nmol l⁻¹ Zn²⁺, and (e) 20 nmol l⁻¹ Zn²⁺. Error bars are ± SE (*n*=3). * represents values statistically different from ERYs alone, + represents values statistically different from values indicated by connecting lines. *P*-values < 0.001.

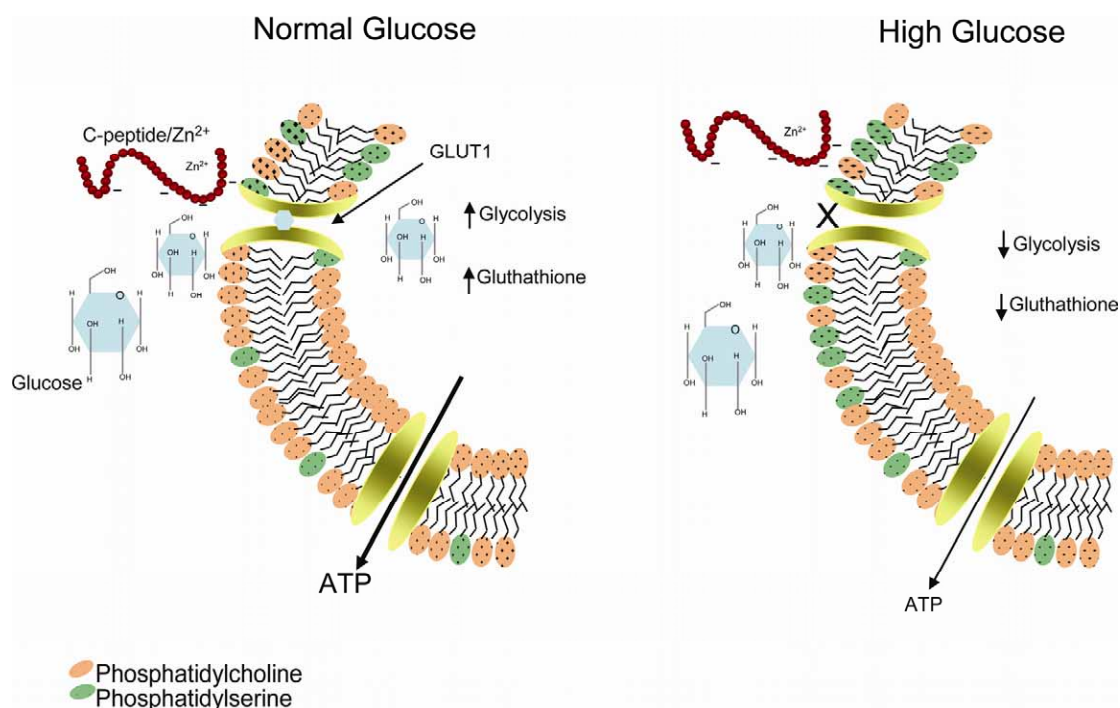


Fig. S2. Under normoglycemic conditions the Zn^{2+} -activated C-peptide is able to interact with the cell membrane and stimulate an increase in glucose transport into the erythrocyte, which increases glutathione levels and glycolysis in the cell, ultimately increasing the amount of ATP released by the erythrocyte. However, under hyperglycemic conditions, the increased glucose concentration may result in an overall decrease in glutathione levels due to an increased rate of the sorbitol pathway. An increase in the sorbitol pathway would decrease glutathione, resulting in the externalization of PS, resulting in less Zn^{2+} -activated C-peptide interaction with the membrane.

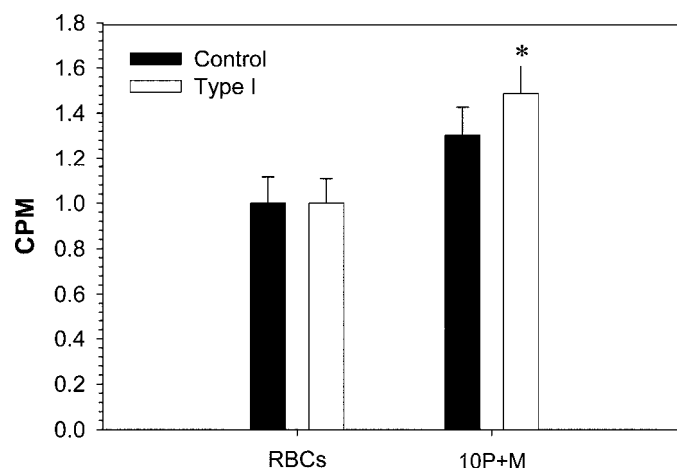


Fig. S3. The ability of metal-activated C-peptide (10P+M) to increase the intracellular glucose concentration of the erythrocyte obtained from type 1 diabetic rat models and controls. The counts per min (CPM) of erythrocytes incubated with metal-activated C-peptide (type I, white) showed a 49% increase ($p<0.01$) over diabetic ERYs alone and control ERY incubated with metal-activated C-peptide (black) rat resulted in an increase of 33% ($p<0.05$) over ERYs alone ($n=4$). * represent values statistically different from erythrocytes alone. Error bars are $\pm$ SE.