

Interaction between Bradykinin and Urodilatin – a possible mechanism of clinical relevance

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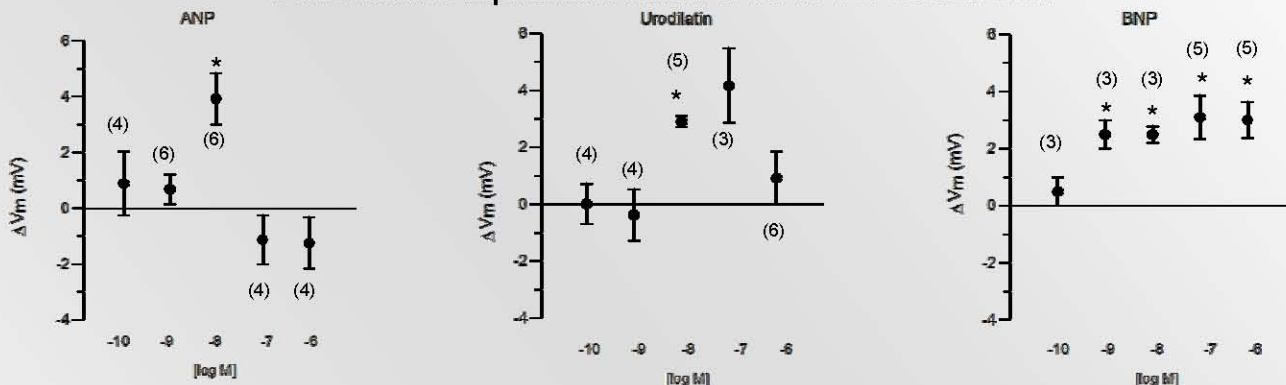
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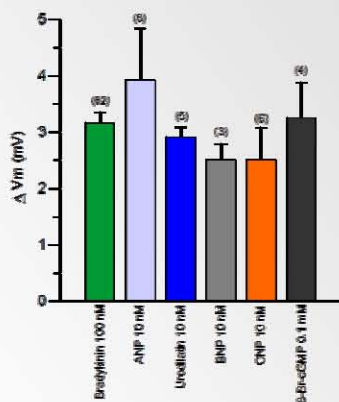
Bradykinin (BK) plays a significant role in pathophysiology of different diseases from angioedema to brain stroke and heart attack by inducing vasodilatation and increasing capillary permeability. We investigate the potential effects of natriuretic peptides (NP) on BK signaling by measuring membrane potential (V_m) of HEK293 cells using the whole cell patch clamp technique. HEK293-cells are an excellent model since they display the natriuretic peptide receptor type A as well as both BK receptors (BR1 and BR2).

RESULTS

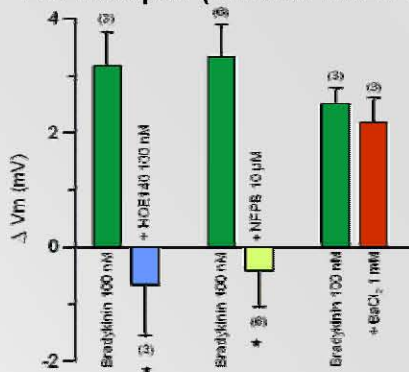
Concentration-dependence curves of the NPs in HEK293 cells



Depolarizations of HEK293 cells caused by NPs and BK



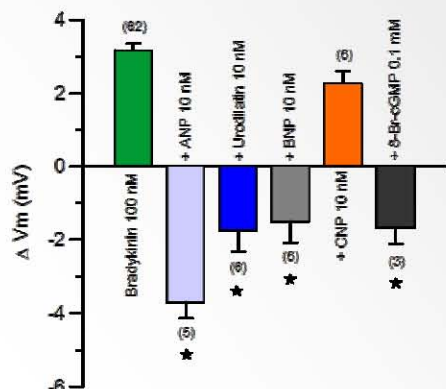
BK changes activity of Cl⁻ but not K⁺ channels (inhibitors NPPB and BaCl₂) via BR2 receptor (inhibitor HOE140)



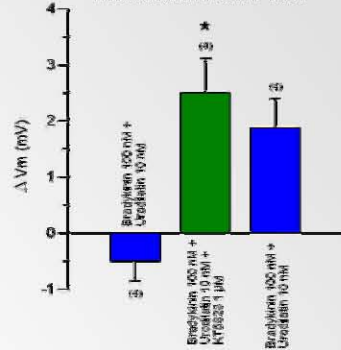
CONCLUSIONS

- BK depolarized HEK293 cells due to the activation of Ca²⁺-dependent Cl⁻ channels while NPs inhibited K⁺ channels
- BK effect can be blocked by various NPs via activation of protein kinase G except CNP (acting through GC-B)
- This pathway might be similar to that in human vasculature suggesting a potential use of NPs in the treatment of bradykinin-mediated angioedema

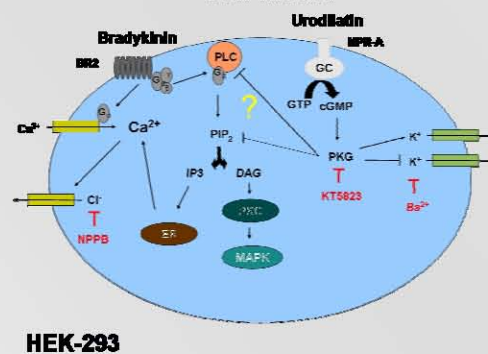
Effect of NPs on BK



Effect of NPs is blocked by inhibition of PKG



Cell Model



HEK-293