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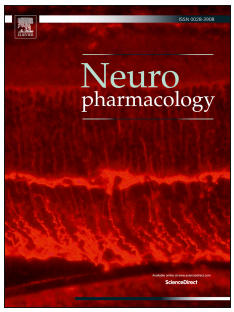

Kynurenic acid and zaprinast induce analgesia by modulating HCN channels through GPR35 activation

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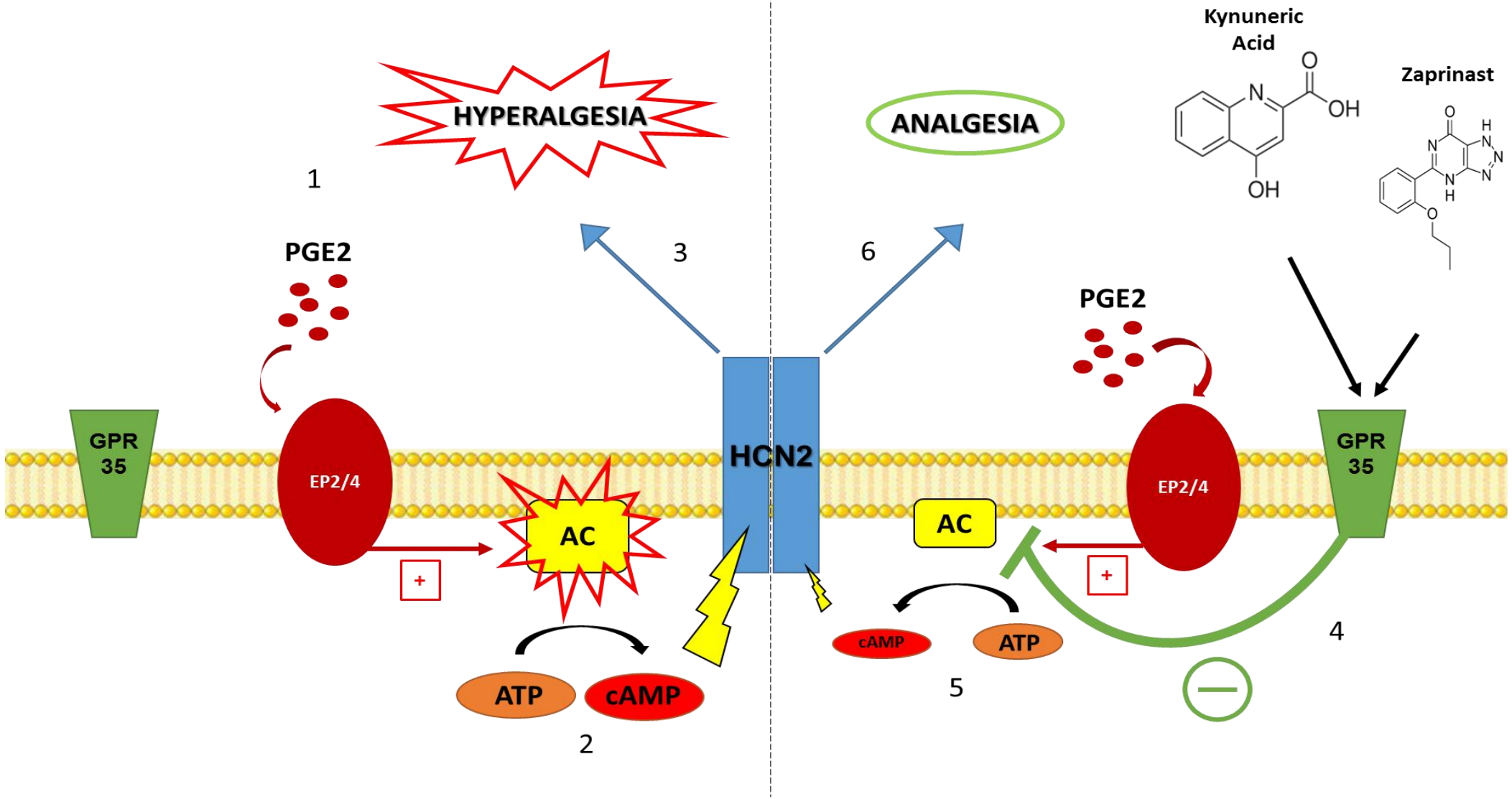

Hyperalgesia could be induced through PGE2 receptor activation (1) leading to increased intracellular cAMP formation (2) thus activating HCN2 channels inducing DRG neurons increased excitability (3). GPR35 activation by inhibiting Adenylate Cyclase (AC) activity (4), reduced cAMP intracellular concentration (5) thus restoring HCN2 channel function leading to analgesia (6).