

P014 Parabutopirin competes with p47^{phox} as a PKC-substrate and inhibits the assembly and activation of NADPH-oxidase in human neutrophils

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Here, parabutopirin (PP), a 45-mer amphipathic α -helical antimicrobial peptide isolated from scorpion venom, was investigated in order to understand its strong inhibitory effect on superoxide production by NADPH-oxidase in human polymorphonuclear neutrophils (PMN). We describe that PP is a good substrate for all PKC-isotypes, known to be implicated in phosphorylations leading to the assembly and activation of NADPH-oxidase. We also demonstrate that PP is a potent competitive inhibitor of *in vitro* p47^{phox}-phosphorylation by PKC- α , - β 1, - β 2, and - δ , but not PKC- ζ . Furthermore, we demonstrate that PP inhibits the translocation of p47^{phox} to the membrane. To assess the PKC-dependency of PP's inhibitory effect on superoxide production, we then investigated the effect of PP on NADPH-oxidase activation under PKC-independent conditions, and also made use of a PP-mutant, lacking the 2 serine PKC-targets. All these observations indicate that PP inhibits the assembly and activity of NADPH-oxidase in a manner that is strongly PKC-dependent.