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Journal Article

Expression of inducible nitric oxide synthase in smooth muscle cells from rat penile corpora cavernosa

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Nitric oxide (NO), the main mediator of penile erection, is assumed to be synthesized in the penis by the neuronal constitutive nitric oxide synthase (nNOS). However, nNOS has not been identified in the penile smooth muscle, the target of NO action. The other NOS isozymes, the inducible NOS (iNOS) and the endothelial NOS (eNOS) have not been reported in any penile tissue. The smooth muscle vascular and trabecular tissue from rat corpora cavernosa is represented in vitro by cell cultures designated RPSMC. To determine whether iNOS can be expressed in penile smooth muscle, RPSMC were treated with different lymphokines and/or bacterial lipopolysaccharide (LPS). The selected inducer, LPS/interferon, elicited at 48 hours up to a 50-fold increase in nitrites in the medium; the nitroarginine methyl ester (L-NAME), aminoguanidine, actinomycin D, cycloheximide, transforming growth factor-beta1 (TGF-beta1), and dexamethasone, but was resistant to nifedipine and platelet-derived growth factor AB (PDGF-AB). iNOS induction increased with cell passage. The [3H] L-arginine/citrulline measurement of NO synthesis with intact cells confirmed these results. Incubations of soluble and particulate fractions showed that the cytosol contained most of the activity ($K_m = 43 \mu\text{M}$), which was partially inhibited by ethyleneglycol-bis-tetraacetic acid (EGTA). The 4.4-kb iNOS mRNA peaked at a late period (24-30 hours) and remained high for up to 72 hours. iNOS mRNA induction was strongly inhibited by actinomycin D and dexamethasone, partially inhibited by TGF-beta1, inhibited slightly by PDGF-AB, and unaffected by nifedipine. These results show that iNOS can be expressed in RPSMC in a cell passage-dependent fashion that has so far not been reported for other cell lines, and that the induction reaches much higher levels than in rat or human vascular smooth muscle cells. The expression pattern is also distinctive for the penile cells in time course of induction, Ca^{2+} dependence, response to certain agents, and mRNA stability.

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