

Poster presentation

NO-cGMP signaling in the guinea pig bladder

Jan de Vente*¹, Marjanne Markerink-van Ittersum¹ and James I Gillespie²

Address: ¹European Graduate School of Neuroscience (EURON), Maastricht University, Dept. of Psychiatry and Neuropsychology, Maastricht, The Netherlands and ²The Urophysiology Research Group, The Medical School, The University, Newcastle upon Tyne, UK

Email: Jan de Vente* - j.devente@np.unimaas.nl

* Corresponding author

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The bladder urothelium is a complex heterogeneous structure consisting of surface urothelial cells, intermediate cells and basal cells. It acts as a barrier but also, in conjunction with accessory cells may play a sensory role responding to bladder deformation. NO may be involved in the sensory element affecting nerves in the suburothelial space. However, there may be other mechanisms. Little is known about the urothelial cells producing NO and possible other cellular targets. In order to probe the physiology of the urothelium and the underlying suburothelial structures, interstitial cells, we have studied possible sources and targets of NO in the guinea pig bladder.

The bladder was removed from 12 guinea pigs. The areas of the dome, lateral wall and base were isolated and incubated separately in Krebs buffer, pH 7.4, containing 1 mM IBMX to block phosphodiesterase activity. Tissue pieces were exposed to the NO donor DEANO (10 min, 10 μ M). NO-independent stimulation of soluble guanylyl cyclase (sGC) activity was studied using BAY 41-2272. In some experiments the NOS inhibitor L-NAME (100 μ M) was present for the duration of the experiment. All samples were fixed with 4% formaldehyde and processed for immunocytochemistry.

In the lateral wall of the bladder nNOS was detected in the three layers of the urothelium but was particularly abundant in the basal cells. The basal urothelial cells did not show an elevation in cGMP in response to NO and did not express cGMP-PK-I or -PK-II, or the β -1 subunit of sGC. Thus, these cells are specialised in the production of NO but do not respond to it.

Interstitial cells lying immediately below the urothelium showed a rise in cGMP in response to NO. However, there

was a sub-population of cells which appeared as a distinct network, necklace cells, which did not respond to NO. Both sub-urothelial interstitial cells and necklace cells expressed cGMP-PK-I. DEANO also stimulated cGMP production in intramural ganglia, cholinergic fibres and interstitial cells associated with the outer muscle layers

BAY 41-2272 for 20 min stimulated cGMP synthesis in the suburothelial interstitial cells and in some interstitial cells in the outer muscle layer. The effect of BAY 41-2272 was inhibited partly by L-NAME, indicating ongoing NO synthesis.

It is concluded that the structures of the bladder wall shows complexities in response towards exogenous and endogenous produced NO. It is likely that these different structures reflect distinct, as yet unidentified, integrated physiological functions.

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