

ET-1 modulates tubular and reticular structures in the nucleus

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The present study aimed at investigating the presence of nuclear structures which could contribute to the regulation of nuclear Ca^{2+} homeostasis by ET-1. Using real 3D confocal microscopy, coupled to utilization of appropriate organelle probes and specific antibodies, we identified two entities in the nuclei of intact human vascular smooth muscle cells (hVSMCs) as well as in isolated hVSMCs' and hepatocytes' nuclei. Our results demonstrate the presence of an ER-like nuclear reticular structure in nuclei of intact hVSMCs and in isolated nuclei. Similar to the ER/SR, this structure possesses thapsigargin binding sites, IP_3 Rs and RyRs, thus it was named nucleoplasmic reticulum (NR). Furthermore, nuclear tubular structures were also detected. The latter, similar to the nuclear envelope membranes, possess nuclear pores, thapsigargin binding sites, Angiotensin II receptor AT_2 , ET-1 receptors and are associated with Lamin A/C. These tubular structures were found to be modulated by ET-1. The nuclear tubular structures were called Nuclear T-Tubules (NTTs). Our calcium studies in isolated nuclei utilizing IP_3 and Ryanodine suggest that the NR may participate in ET-1 nuclear Ca^{2+} signalling. In conclusion, two distinct structures are present in the nucleus of hVSMCs and might play an important role in ET-1 modulation of nuclear Ca^{2+} homeostasis.