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Role of Endothelin-1 in the Migration of Human Olfactory Gonadotropin-Releasing Hormone-Secreting Neuroblasts

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FNC-B4 neuroblasts that express both neuronal and olfactory markers have been established and cloned. These cells express GnRH and both the endothelin-1 (ET-1) gene and protein and respond in a migratory manner to GnRH in a dose-dependent manner. Previous research has shown that FNC-B4 cells produce and respond to ET-1 by regulating the secretion of GnRH through endothelin type A receptors and by stimulating their proliferation through endothelin type B (ETB) receptors. In this study, we found that FNC-B4 cells are able to migrate in response to ET-1 through the involvement of ETB receptors. Combined immunohistochemical and biochemical analyses showed that ET-1 triggered actin cytoskeletal remodeling and a dose-dependent increase in migration (up to 6-fold). Whereas the ETB receptor antagonist (B-BQ788) blunted the ET-1-induced effects, the ETA receptor antagonist (A-BQ123) did not. Moreover, we observed that FNC-B4 cells were independently and selectively stimulated by ET-1 and GnRH. We suggest that ET-1, through ETB receptor activation, may be required to maintain an adequate proliferative stem cell pool in the developing olfactory epithelium and the subsequent commitment to GnRH neuronal migratory pattern. The coordinate interaction between ET receptors and GnRH receptor participates in the fully expressed GnRH-secreting neuron phenotype. (*Endocrinology* 146: 4321–4330, 2005)