EXPERIMENTAL EVIDENCE SUPPORTING THE USE OF GABAPENTIN FOR THE MANAGEMENT OF CHRONIC PELVIC PAIN ASSOCIATED TO ENDOMETRIOSIS.

Authors

Levi, Giovanni, Author

Abstract Body

Endometriosis, associated or not to other conditions, is observed in the majority of women presenting chronic pelvic pain (CPP). Treatment of endometriosis-associated CPP is difficult due to its poorly-understood ethiology, its complex clinical presentation and natural history. Differential gene expression analyses comparing endometriotic lesions to eutopic endometrium from the same patient have shown that the two transcription factors *DLX5* and *DLX6* are drastically down-regulated in the pathological tissue. We have shown that mice in which *Dlx5/6* are selectively inactivated in the uterus present an endometrial phenotype reminiscent of human endometriotic lesions. We have now compared genes differentially expressed in normal and *Dlx5/6*-null mouse uteri with those differentially expressed in eutopic and ectopic (endometriotic) human endometrium. We have identified 22 genes similarly deregulated in three independent human studies and in the mutant mouse uterus confirming that targeted inactivation of *Dlx5/6* results in a molecular signature similar to that of endometriotic lesions. Genes overexpressed in endometriotic lesions could be used to design targeted treatment of endometriosis. We find that *CACNA2D3*, a component of the voltage-dependent calcium channel complex, is strongly up-regulated, together with its close homologue CACNA2D1, in mouse mutant uteri and in endometriotic lesions. CACNA2D3 has been associated to pain sensitization and heat nociception in animal models. In humans, CACNA2D3 variants associate with reduced sensitivity to acute noxious stimuli and to chronic back pain. The presence of CACNA2D3 in endometriotic lesions indicates a possible origin of CPP and suggests a likely therapeutic target.CACNA-alpha-2-deltas bind to gabapentin a drug used to treat various forms of chronic pain. Our findings provide experimental evidence suggesting that gabapentin could be used for the management of peripheral CPP in endometriosis. Indeed recent small-scale clinical studies have shown that gabapentin might be effective in women CPP. Our findings reinforce the need for a large definitive trial.