ABSTRACT
Recent developments in psychiatric research have led to the hypothesis that inflammatory processes may be involved in the pathogenesis of depression. Furthermore, several lines of evidence indicate that decreased neurogenesis may also be implicated in psychiatric disorders. As the complete role of cytokines in physiological and pathological conditions of neurogenesis is not known, we investigated the effect of the pro-inflammatory cytokines interleukin-6 (IL-6) and interleukin-1β (IL-1β) on human hippocampal stem cells. We used a conditionally immortalized stem cell line (HPC1A07, ReNeuron, UK) as a model. Our PCR studies demonstrate that these cells constitutively express IL-1 receptor, IL-6 receptor and its signal transducing membrane protein gp130.

RESULTS
IL-1β and IL-6 increase neural stem cell proliferation

The IL-6 synthesis induced by IL-1β is dependent on p38 activity

The IL-6 synthesis induced by IL-1β is decreased by glucocorticoids

CONCLUSIONS
These data indicate that human hippocampal stem cells constitutively express receptors for IL-1β and IL-6. Upon treatment with both proinflammatory cytokines cells showed increased proliferation. IL-1β acts on neural precursors to induce the synthesis of IL-6, and the signaling mechanisms are dependent on p38 MAPK activity.

The IL-1β induced IL-6 synthesis is decreased by dexamethasone, which suggests the involvement of the glucocorticoid pathway.

Our findings show immune properties of neural precursors and provide further evidence of molecular pathways by which inflammation could be related to glucocorticoid resistance in the human brain.

ACKNOWLEDGMENTS
This research is funded by the Medical Research Council (UK) and the European Union Framework 7. JP acted as a consultant and received payment from ReNeuron group within the last 2 years.