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## Maternal leukemia inhibitory factor (LIF) promotes fetal neurogenesis via a LIF-ACTH-LIF signaling relay pathway.

Simamura E, Shimada H, Higashi N, Uchishiba M, Otani H, Hatta T
*Endocrinology* 2010 Apr **151**(4):1853-62 [abstract on PubMed]
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**Selected by** | Lizzy Cottrell and Jonathan Seckl NEW
Evaluated 26 Apr 2010
Relevant Sections

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**Faculty Member**

Lizzy Cottrell and
**Jonathan Seckl**
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Neuroscience

Confirmation
New Finding

**Comments**

**This study elegantly demonstrates the presence of a new maternal-placental-fetal signalling pathway important for the development of the fetal brain. This is the first demonstration of a delineated pathway of this nature and begs the question of what other signals are transmitted from mother to fetus (or vice versa) to regulate fetal development.**

Leukemia inhibitory factor (LIF) is a pleiotropic cytokine that plays a role in the development of hematopoiesis and the central nervous system. Previous studies in the mouse have linked a peak in LIF in fetal cerebrospinal fluid with cerebral neurogenesis {1}, but until now the source and regulation of this peak in LIF was unknown. The authors hypothesized that maternal LIF induces a rise in fetal LIF by indirect mechanisms, as LIF is unable to pass the placenta. They measured the ontogenic profile of LIF in maternal and fetal compartments and demonstrated that a peak in maternal LIF at gestational day (GD) 14.5 is associated with a rise in fetal adrenocorticotropic hormone (ACTH) and is followed by a peak in fetal LIF at GD15.5. Injection of LIF into dams at GD15.5 increased fetal ACTH and LIF, an effect prevented by intra-fetal injection of anti-ACTH antibodies. In vitro experiments confirmed that placental trophoblast cells are the most likely source of ACTH, responding to LIF with the upregulation of expression of its encoding gene (pro-opiomelanocortin [POMC]) and increased ACTH secretion. Indeed, bromodeoxyuridine (BrdU) labelling increased in the untreated fetal cortex at GD15.5, coincident with the endogenous peak in fetal LIF, and was further enhanced by maternal LIF treatment. Altogether, these results demonstrate a maternal-placental-fetal pathway of importance to fetal brain development. This model is also of interest in maternal infection or stress, as the proinflammatory cytokine interleukin-6 (IL-6) or maternal glucocorticoids stimulate placental ACTH secretion. Both maternal challenges affect normal brain development.

References: {1} Hatta et al. Neuroreport 2006, 17:1863-6 [PMID:17179859].

**Competing interests:** None declared
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How to cite this evaluation

## Faculty Comments & Author Responses

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Jonathan Seckl: Faculty of 1000 Biology, 26 Apr 2010 http://f1000biology.com/article/id/3024963/evaluation