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Research Interests

Monoamines are uniquely distributed in the brain to modulate neural networks governing complex behaviors. Serotonin, in particular, is implicated in a wide array of limbic functions. Many psychotropic medications modulate global serotonin levels, serotonin precursor depletion induces relapse in patients suffering major depression, and measures of serotonergic content/turnover have been associated with a number of behavioral parameters. A novel paralog of the rate-limiting enzyme for serotonin biosynthesis (tryptophan hydroxylase; TPH) was recently identified. We showed that in brain, this new gene, TPH2, is expressed exclusively in raphe neurons. Our lab focuses on 1) engineering conditional transgenic mouse models to study the role of TPH2 expression in the developing animal, particularly as regards vulnerability to stress and the emergence of complex behavioral phenotypes including learning, memory, anxiety, despair, aggression, etc., and 2) understanding how TPH2 is regulated at the transcriptional level throughout development and in the mature animal in response to stress, physiologic, and pharmacologic challenge.

Using a novel RNAi-based targeting strategy, we are designing mice to down-regulate TPH2 while simultaneously expressing a marker protein, e.g., enhanced green fluorescent protein (EGFP). Figure 1 shows a newborn litter containing transgenic pups along with non-transgenic littermates, demonstrating widespread EGFP fluorescence. Preliminary evidence suggests we successfully down-regulated the target gene. These mice are currently being bred for behavior studies.

Serotonergic neurotransmission is thought to be linked to TPH2 activity. In an effort

to establish the transcription factors responsible for developmental and dynamic regulation of TPH2, we are analyzing TPH2 promoter deletions and mutations in cultured mammalian cells. We have identified an unusual and potent silencing element that bears resemblance to a known target for a developmental regulatory gene. Current studies are aimed at elucidating the specific proteins and mechanisms involved.

Stress corticosteroids and serotonergic neurotransmission intersect at multiple points along the psychobiology spectrum. An ongoing interest of this laboratory is understanding the regulation of brain receptors for glucocorticoid (GR) and mineralocorticoid (MR) receptors in models of developmental stress. In collaboration with a primate lab at Stanford University, we are looking at the effects of early maternal separation on the expression of GR, MR, and components of the serotonergic pathway in the brains of the New World primate, Saimiri sciureus (figure 2). This model will helping to clarify the long term effects of early life experiences and ways in which the stress system adapts.

Selected References

Her, S., Patel, P. D., Schatzberg, A. F., and Lyons, D. M. (2005). Mutations in squirrel monkey glucocorticoid receptor impair nuclear translocation. J Steroid Biochem Mol Biol In press.

Patel, P. D., Pontrello, C., and Burke, S. (2004). Robust and tissue-specific expression of TPH2 versus TPH1 in rat raphe and pineal gland. Biol Psychiatry 55, 428-433.

Chen, Z. Y., Patel, P. D., Sant, G., Meng, C. X., Teng, K. K., Hempstead, B. L., and Lee, F. S. (2004). Variant brain-derived neurotrophic factor (BDNF) (Met66) alters the intracellular trafficking and activity-dependent secretion of wild-type BDNF in neurosecretory cells and cortical neurons. J Neurosci 24, 4401-4411.

Patel, P. D., Lopez, J. F., Lyons, D. M., Burke, S., Wallace, M., and Schatzberg, A. F. (2000). Glucocorticoid and mineralocorticoid receptor mRNA expression in squirrel monkey brain. J Psychiatr Res 34, 383-392.

Patel, P. D., Lyons, D. M., Zhang, Z., Ngo, H., and Schatzberg, A. F. (2000). Impaired transactivation of the glucocorticoid receptor cloned from the Guyanese squirrel monkey. J Steroid Biochem Mol Biol 72, 115-123.

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