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NEUROSCIENCE
2010

SOCIETY FOR NEUROSCIENCE
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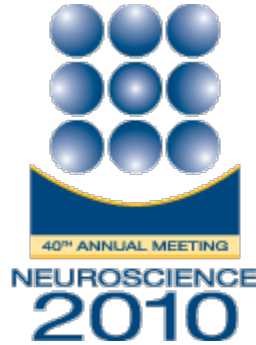
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SOCIETY FOR NEUROSCIENCE

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Presentation Abstract

Program _____ : 387.12/EEE4

Title: Evolution of cis-regulatory variation at the *avpr1a* locus and its pseudogene

Location: Halls B-H

Presentation Time: Monday, Nov 15, 2010, 11:00 AM -12:00 PM

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Abstract: Individual and species differences in gene expression underlie a tremendous diversity of behavior. Expression of the vasopressin 1a receptor (V1aR), for example, governs behavioral differences between the monogamous prairie vole (*Microtus ochrogaster*) and the promiscuous montane vole (*M. montanus*). Field data demonstrate that natural selection favors pair-bonding by male prairie voles; such selection may promote uniformly high levels of V1aR in the ventral pallidum (VPal), a region central to male pairing. In contrast, field data suggest selection actively maintains variation in the retrosplenial cortex (RSctx), a region implicated in spatial memory, territorial intrusions and sexual infidelity. Differences in gene expression are often due to variation in cis-regulatory sequences; alternatively, duplicated loci can also function as regulators of the original locus. We examined the evolution of cis-regulatory sequences of the prairie and montane vole *avpr1a* loci, as well as an *avpr1a*-pseudogene thought to be unique to prairie voles. We first tested for evidence of selection acting on the prairie vole *avpr1a*. To do so, we sequenced 20 *avpr1a* alleles from wild-caught prairie voles for ~2.5kb upstream of the translation start site, and homologous sequence from the montane vole. We compared the ratio

of between- and within-species nucleotide polymorphisms at the *avpr1a* locus (36:18) with that at neutral loci (21:20). We found a trend toward reduced polymorphism at the prairie vole *avpr1a* ($p < 0.10$), suggesting overall purifying selection at the locus. A single 50bp region seems to have been under stronger purifying selection than the locus as a whole ($p < 0.05$), and much stronger selection than is evident for neutral loci ($p < 0.01$). This is consistent with the fitness value of V1aR-mediated pair-bonding, and suggests a novel enhancer for high pallidal V1aR. A 300bp segment exhibited a trend toward higher levels of standing variation ($p = 0.11$), a signature of balancing selection. Remarkably, this same segment contained SNPs associated with individual differences in RSctx V1aR. Lastly, we sequenced 20 alleles of the pseudogene to determine whether its cis-regulatory sequences have been under selection since divergence from the *avpr1a* locus. We found much lower standing variation (between:within, 19:1) than predicted based on neutral loci (21:20), indicating strong purifying selection on the pseudogene cis-regulatory region ($p < 0.001$). Together, our data suggest novel regulators of *avpr1a* expression, including the possible involvement of a pseudogene previously assumed to be non-functional.

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