

Identifying Epilepsy Genes and Tracing their Cellular Expression

1. "Why, if I could only study one disease to understand the brain, it would be epilepsy."
2. Definitions of a seizure, an epilepsy syndrome, and an 'epilepsy gene'.
3. Epilepsy Therapies
4. Genes for human epilepsy syndromes
5. Other genomes as sources of candidate epilepsy genes
6. Utility of single locus mutations in mice
 - Gene discovery – candidate loci for human susceptibility
 - Target discovery – developmental and activity-dependent plasticity
 - Drug Discovery – biological test systems for therapy to prevent, reverse phenotype
7. Genes for epilepsy in mice
 - Knockouts and other transgenics
 - Classical mutations
8. Major Cell Biological Mechanisms of epileptogenic lesions
 - Proliferation – The neuroD mouse
 - Migration – UPAR and DLX1 genes
 - Excitability – Sodium and Potassium Channels
 - Cell Death – cystatin b protease inhibitor
9. Analysis of neuronal plasticity and downstream gene dysregulation in epileptic brain
 - Connectivity - locus coeruleus, mossy fiber sprouting, and growth factors (tg, stg)
 - Synaptic strength and "neotransmitters" - induced NPY (stg), and tyrosine hydroxylase (tg)
 - Ion channel density - changes in axonal Na and K distribution (shiverer)
 - Ion channel stoichiometry - potassium channel dysregulation (HypK)
10. Genetic strategies for analysis of complex disease: ion channelopathies.