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Contributions of translational medicine to the development of novel drugs for epilepsy

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Abstract

The decade of the brain in the 1990s contributed much basic neuroscience knowledge to epilepsy mechanisms, leading to novel drugs targetting the GABA-A-receptor and the associated benzodiazepine site. New antiepilepsy drugs (AEDs) approved in the last decade include Clobazam, Vigabatrin, Gabapentin and Pregabalin. Other AEDs with novel mechanisms on action include levetiracetam, retigabine, lacosamide, rufinamide and perampanel (acting at the AMPA-R site).

Pharmacogenetic factors include the discovery that the presence of genotype HLA-B*1502 increases the risk of severe hypersensitivity reactions to aromatic AEDs markedly, but only in Han Chinese subjects, whereas other genotypes may contribute to risk among Caucasians. An in vitro test (Lymphocyte Toxicity Assay) with peripheral lymphocytes may be predictive of subjects at risk without harm to study subjects.

With the discovery of an increasing number of epilepsy genes due to single mutations the era of personal medicine in epilepsy therapy is here. The challenge for the 21st century is to determine the aberrant gene products and their perturbation of the neuronal circuitry leading to the epilepsy phenomenon and to find appropriate targets for intervention to improve the quality of life in persons with epilepsy.