

Exploring the Responsible Gene for a Familial ALS by Next-generation Sequencer

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The genes underlying mendelian disorders have been identified through positional cloning, a process of meiotic mapping, physical mapping, and candidate-gene sequencing. Before the process of candidate-gene sequencing during positional cloning, it is important to narrow and well characterize the candidate region for the disease, which needs to investigate the genome in large number of families or patients. Due to the performance of the conventional sequencer, it is difficult to identify causative mutations for uncharacterized mendelian disorders, such as a disease consists of small number of familial cases.

Next-Generation Sequencing technologies have brought new approaches of genetic analyses for personal genome or human diseases. The technologies can accurate giga-base order of sequence within a single run, allowing for complete re-

sequencing of whole candidate region of a genetic disease in patients, whose responsible gene is not identified.

Amyotrophic lateral sclerosis is a neurodegenerative disorder characterized by the death of motor neurons in the brain, brainstem, and spinal cord, resulting in fatal paralysis. It is well known that the ALS has genetic heterogeneity. Approximately 10% of ALS cases are familial. Many types of ALS, which have not been identified causative mutations, are still remaining.

We introduce one of the useful approaches, 'resequencing of whole candidate region for a genetic disease' based on massively parallel sequencing using next-generation sequencer. We pick such strategy applying for a familial ALS to identify a causative mutation and discuss its utility in medical genetics.

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