

# Monitoring of treatment response in patients with temporal lobe epilepsy by gene expression analyses

Kirsten Annette Nielsen, Marina Nikanorova, Valeri Nikaronov, Ejvind Lyders Hansen, Christian Pilebæk Hansen  
Danish Epilepsy Centre, Kolonivej 11, DK-4293 Dianalund, DENMARK

## Purpose:

The purpose is to study possibilities of obtaining valid and reproducible expression values of drug regulated mRNAs in peripheral blood cells of epilepsy patients. This is based on previous publications of pilot projects (1,2). The hypothesis is that mRNA expression reflects the genetic background in epilepsy patients. Thus studies of expression profiles may elucidate the patient's disposition for epilepsy and the risk of developing drug resistance (3-5). Inclusion criteria, identification of included patients and the experimental design are described.

## Methods:

Included patients were selected among children treated at the Danish Epilepsy Centre. Children that met inclusion criteria were identified using the Danish National **Epibase** database. Included patients are children with a well-characterized temporal lobe epilepsy (TLE) diagnosis undergoing only one out of five established medical treatments (Table 1). The patients are grouped into a total of 20 subgroups based on the presence or absence of seizure control and the accumulation of side effects due to medical treatment. This subdivision is performed to identify correlation between mRNA expression profiles and therapeutic response and to be able to distinguish mRNA expression patterns of response resulting in seizure control from mRNA expression patterns reflecting drug resistance and accumulation of side effects (Figure 1).

**Table 1: Features of included TLE patients**

Medication	Valproic acid	Valproic acid Lamotrigin	Valproic acid Topiramate	Valproic acid Levetiracetam	Valproic acid Oxcarbazepin
Seizure-control	- +	- +	- +	- +	- +
Side effects	- + - +	- + - +	- + - +	- + - +	- + - +

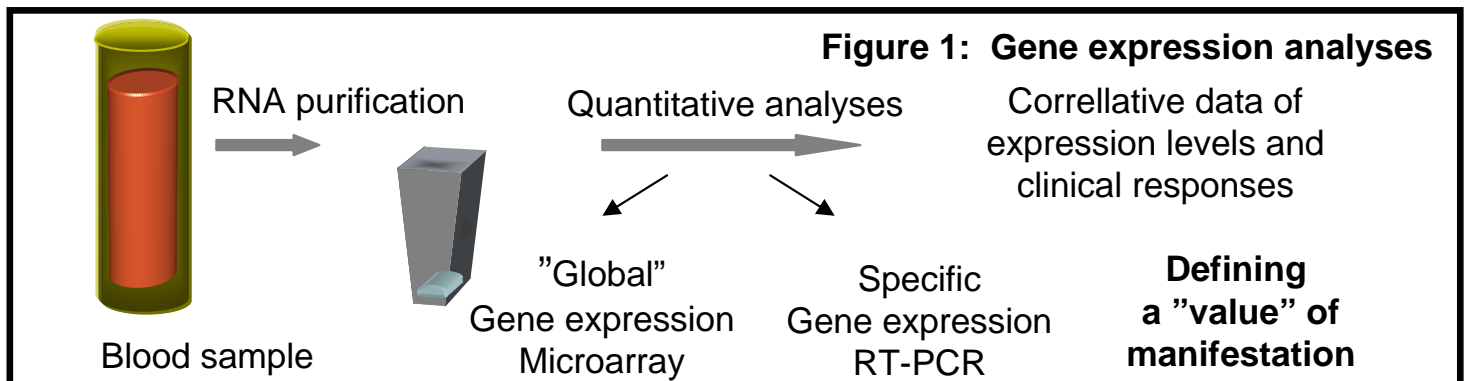
## Results:

Children have been characterized in terms of seizure control, adverse reactions, manifestation of the epileptic syndrome, family predisposition to epilepsy, epilepsy etiology and behavioural deficits. Based on these data 78 children were identified. Among these a cohort with complete seizure control (n=15) and a cohort without seizure control (n=49) were defined. The experimental design of five medical treatment schedules defines five groups within each cohort.

**Conclusion:**  
Patients fitting the inclusion criteria were identified.

## Future prospects:

In order to limit the expected high variation in gene expression profiles among patients mRNA analysis is restricted to patients with temporal lobe epilepsy (TLE) according to (1,2). Focus is made on identification of mRNA expression levels that are related to the efficacy of certain anti-epileptic drugs. For each patient blood samples are collected for mRNA extraction and subsequent expression analysis (Figure 1). An additional blood sample is collected for storage in a bio bank with the prospect of future elucidation of the genetic background



## Acknowledgements:

The project is approved by the local Independent Ethics Committee (IEC), Datatilsynet and the project is carried out in compliance with the ICH-GCP guidelines.

## References:

- 1: Lindberg RLP, et al *J Neuroimm.* (2004)152: 154-167
- 2: Tang Y, et al *Acta Neurol Scand* (2004) 109: 159-168
- 3: Tan NCK, et al *Epilepsia* (2004) 45:1429-42
- 4: Hansen CP & Wolf P *Ugeskr Laeger.* (2004) 166: 3186-9
- 5: George Jr. A *Arch. Neurol.* (2004) 61: 473-478