

What neurodegeneration, brain malformation and cancer might have in common?

An abnormal gene expression!

Fernando Kok

In this issue of **Arquivos de Neuro-Psiquiatria**, three interesting publications over totally different subjects, but having Genetics as a common ground might be appreciated.

In the more classical manuscript, Valadares and cols.¹ presented their clinical and molecular findings regarding a large family with 10 affected individuals with juvenile neuronal ceroid-lipofuscinosis (CLN3), in which the common 1.03 kb deletion of *CLN3* gene was found. In this severe neurodegenerative disorder, in which almost all patients shared the same mutation, it is noteworthy, but not surprising, that phenotype and clinical presentation were moderately variable: variability in Mendelian disorder are more common than initially believed and represent an additional challenge to clinicians. Additionally, investigation of large families like this one is a good way to look for new disorders, or to collect more clinical information on already identified genetic conditions. And time is rushing, as large consanguineous families are becoming rarer!

In the second publication, Machado and cols.² studied genomic imbalances in fetuses with holoprosencephaly (HPE), a devastating brain malformation in which both genetic and environmental factors might be involved. Using a technique known as comparative genomic hybridization (CGH), which is be-

coming a standard of care for investigation of several conditions, including autism, developmental delay/mental retardation and a wide range of brain or systemic congenital malformations, they detected submicroscopic chromosomal abnormalities in four fetuses with HPE. Intensive use of CGH-array might help to identify chromosomal regions in which a critical gene for a determined phenotype is located. Nevertheless, interpretation of CGH-array results should be always made with caution: it is recommended to verify if detected abnormalities were inherited from one of the parents or occurred as a *de novo* event. Clinical significance of inherited submicroscopic abnormalities is uncertain, since variants are frequently found. It is also useful to confirm the detected abnormal imbalance with a complementary technique, such as fluorescent *in situ* hybridization (FISH), to validate the result of CGH. Finally, in order to give an appropriate counseling, we should be aware that an apparently *de novo* genomic rearrangement might be caused by a balanced translocation in one of the parents, which might bring for his descendants an elevated risk for chromosomal abnormalities.

The third publication, from Vulcani-Freitas and cols.³ is a study about expression of the gene *PRAME* in medulloblastoma (MB), a malignant cerebellar tumor more commonly seen in childhood. Using

Correspondence

Fernando Kok
Av. Dr. Enéas de Carvalho
Aguiar 255 / sala 5011
05403-000 São Paulo SP - Brasil
E-mail: fernando.kok@fleury.com.br

O QUE NEURODEGENERAÇÃO, MALFORMAÇÃO CEREBRAL E CÂNCER PODEM TER EM COMUM? UMA EXPRESSÃO GENÉTICA ANORMAL!

MD, PhD, Associate Professor, Child Neurology Service, Hospital das Clínicas of University of São Paulo School of Medicine, São Paulo SP, Brazil.

real-time PCR to quantify the messenger RNA coded by *PRAME*, they were able to demonstrate in samples of 37 patients with MB an overexpression of this message in 31 of them. It has been previously reported that upregulation of *PRAME* is associated with poor clinical outcome in some solid tumors, a fact that was not confirmed in this sample of NB. It is universally accepted that cancer biogenesis is related to change in the pattern of gene expression, and to find good biological markers for tumors, that also can be used as therapeutic targets, is a long coveted holy grail.

Patterns of gene expression do not explain everything,

but everything in living organisms might somehow be controlled by regulation of gene expression. It is in fact more appropriate to say *Control your genes!* instead of *Control your nerves!*

REFERENCES

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